

Neuro-Ophthalmological Warning Signs in Intracranial Neoplasms: Clinical Patterns for Early Detection and Visual Preservation

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ABSTRACT

Neuro-ophthalmological manifestations may represent the first clinically detectable sign of intracranial neoplasms, particularly when tumors involve the optic nerves, optic chiasm, sellar and parasellar regions, cranial nerves, skull base, brainstem, or structures associated with intracranial pressure. This study analyzed the main visual and ocular manifestations associated with intracranial tumors and their potential value for early diagnosis through a descriptive and analytical review of the scientific literature. Evidence concerning pituitary macroadenomas, meningiomas, optic pathway gliomas, craniopharyngiomas, and other intracranial neoplasms was examined, integrating clinical findings with automated perimetry, funduscopy examination, optical coherence tomography, and magnetic resonance imaging. The reviewed data showed a predominance of afferent visual abnormalities, particularly progressive visual loss, transient visual obscurations, visual-field defects, optic-disc changes, and optic neuropathy. Pituitary macroadenomas and meningiomas represented the most frequent tumor groups in the analyzed clinical series. Anatomical localization was closely associated with the pattern of neuro-ophthalmological involvement: sellar and suprasellar lesions were predominantly related to visual-field abnormalities, while lesions affecting the anterior cranial base or optic apparatus frequently produced structural optic nerve changes. Optical coherence tomography demonstrated the ability to identify retinal ganglion cell abnormalities in a subset of patients with MRI-confirmed chiasmal compression despite normal conventional visual fields, supporting the complementary role of structural assessment in early disease. Diagnostic intervals varied considerably, ranging from days to several years, and a substantial proportion of patients experienced visual symptoms for more than six months before definitive tumor identification. These findings indicate that persistent, progressive, unexplained, or anatomically suggestive visual abnormalities should raise suspicion of intracranial pathology. Integrating neuro-ophthalmological examination, functional testing, structural retinal assessment, and neuroimaging may shorten diagnostic delay, improve anatomical localization, facilitate timely multidisciplinary referral, and increase the probability of preserving visual function before irreversible axonal damage develops.

KEYWORDS

Neuro-ophthalmology, intracranial neoplasms, brain tumors, visual loss, visual field defects, optic neuropathy, papilledema, diplopia, pituitary adenoma, meningioma, optical coherence tomography, magnetic resonance imaging, early diagnosis

INTRODUCTION

Intracranial neoplasms comprise a heterogeneous group of primary and secondary tumors capable of producing neurological, endocrine, cognitive, and ophthalmological manifestations according to their location, biological behavior, growth rate, and relationship with adjacent structures. Among these manifestations, neuro-ophthalmological abnormalities are of particular clinical relevance because the visual pathways, optic nerves, optic chiasm, ocular motor nerves, cavernous sinus, orbital apex, and structures responsible for intracranial pressure regulation may be affected relatively early during tumor development. In some patients, visual symptoms do not merely accompany an already established neurological syndrome; instead, they constitute the first clinically detectable manifestation of an intracranial tumor. Progressive visual loss, visual-field defects, diplopia, papilledema, optic disc abnormalities, ocular motor dysfunction, anisocoria, afferent pupillary defects, and disturbances of visual perception may therefore represent important diagnostic clues before more typical symptoms such as seizures, focal motor deficits, cognitive deterioration, or severe headache become evident [1], [2].

This clinical scenario represents a substantial diagnostic challenge because many initial neuro-ophthalmological complaints are nonspecific and frequently overlap with considerably more prevalent ophthalmic disorders. A patient presenting with blurred vision, transient visual obscurations, headache, diplopia, or progressive reduction in visual acuity may initially be evaluated for refractive abnormalities, retinal disease, migraine, ocular surface disorders, glaucoma, or isolated cranial neuropathies. Nevertheless, persistent, progressive, unexplained, asymmetric, or anatomically incongruent visual abnormalities should prompt consideration of lesions involving the intracranial visual

pathways. Delayed recognition is particularly relevant because prolonged compression or infiltration of the optic nerves and chiasm may lead to irreversible axonal injury even after successful treatment of the underlying tumor [3], [4]. Consequently, early identification of neuro-ophthalmological warning signs is not only important for establishing an etiological diagnosis but may also determine the probability of preserving visual function.

The anatomical organization of the visual system explains why intracranial tumors may initially produce highly localized ophthalmological abnormalities. Retinal ganglion cell axons converge at the optic disc to form the optic nerve, subsequently reaching the optic chiasm, where fibers originating predominantly from the nasal hemiretina decussate before continuing through the optic tracts toward the lateral geniculate nuclei and posterior visual pathways. Tumors situated in the sellar and parasellar regions can therefore generate characteristic patterns of visual-field loss through compression of the optic chiasm, whereas lesions involving the optic nerves may cause unilateral or asymmetric reduction in visual acuity, dyschromatopsia, relative afferent pupillary defects, and optic atrophy. More posterior lesions can produce homonymous visual-field defects, while tumors affecting the brainstem, cavernous sinus, skull base, or cranial nerves may initially manifest with diplopia, abnormal ocular motility, ptosis, or pupillary dysfunction [1], [13]. Recognition of these anatomical correlations remains fundamental for localizing the lesion and determining the need for neuroimaging.

Papilledema constitutes another major neuro-ophthalmological presentation associated with intracranial tumors. It develops primarily as a consequence of increased intracranial pressure transmitted to the optic nerve sheath, producing disruption of axoplasmic transport and swelling of the optic nerve head. Although papilledema is not specific to neoplastic disease, an intracranial mass must be excluded when this finding is identified, particularly when it is accompanied by headache, nausea, vomiting, sixth-nerve palsy, transient visual obscurations, or progressive visual dysfunction [5]. Brain tumors may increase intracranial pressure through mass effect, cerebral edema, obstruction of cerebrospinal fluid circulation, venous outflow impairment, or a combination of these mechanisms. Neuroimaging findings associated with increased intracranial pressure can complement fundoscopic examination and facilitate earlier recognition of patients requiring urgent diagnostic investigation [6].

However, the absence of papilledema does not exclude intracranial neoplasia. Many tumors, especially slow-growing lesions located in the sellar, parasellar, or anterior visual pathway regions, can produce substantial visual impairment without marked elevation of intracranial pressure. This distinction is clinically important because reliance exclusively on optic-disc edema as a warning sign may delay diagnosis in patients whose initial abnormality consists of progressive field loss or optic neuropathy. Optic nerve sheath meningioma is an illustrative example: patients frequently develop slowly progressive monocular visual loss, dyschromatopsia, optic-disc edema or atrophy, and optociliary shunt vessels, with diagnosis often occurring after a prolonged symptomatic interval [7], [8]. Similarly, optic pathway gliomas may affect visual acuity, visual fields, color perception, and optic nerve appearance, with clinical behavior varying substantially according to patient age, tumor location, molecular characteristics, and associated conditions [9].

Sellar and parasellar tumors represent one of the most important groups of intracranial neoplasms encountered in neuro-ophthalmological practice. Pituitary adenomas may grow beyond the sella turcica and compress the optic chiasm, resulting in visual-field defects that may precede endocrine manifestations or the recognition of other neurological symptoms. Although bitemporal hemianopia is traditionally regarded as the classic visual-field abnormality associated with chiasmal compression, clinical presentations are more heterogeneous. Patients may demonstrate incomplete temporal defects, unilateral abnormalities, asymmetric field loss, central or paracentral defects, or generalized visual reduction depending on the position and extent of compression [14]. Furthermore, nonfunctioning pituitary adenomas may remain clinically silent from an endocrine perspective until tumor enlargement produces neurological or ophthalmological manifestations, making visual assessment especially important for diagnosis [15].

The severity of visual dysfunction caused by chiasmal compression is not determined exclusively by tumor size. The direction of tumor growth, anatomical relationship with the optic apparatus, duration of compression, vascular compromise, and individual susceptibility of retinal ganglion cell axons may contribute to functional deterioration [3], [15]. This explains why patients with apparently similar radiological lesions may present with markedly different visual findings. It also emphasizes the value of combining structural imaging with detailed functional assessment rather than

interpreting radiological dimensions in isolation. Neuro-ophthalmological examination can reveal functional consequences of tumor growth that might otherwise be underestimated during routine neurological assessment.

Recent advances in optical coherence tomography (OCT) have expanded the possibilities for detecting structural injury associated with compressive optic neuropathy. Measurements of the peripapillary retinal nerve fiber layer and macular ganglion cell complex provide objective information regarding retinal ganglion cell and axonal integrity. Importantly, structural alterations detected by OCT may occur before patients recognize significant visual impairment or before conventional visual-field abnormalities become pronounced [10]. Studies examining patients with pituitary tumors have suggested that retinal ganglion cell analysis may facilitate identification of early chiasmal compression and may contribute to the assessment of prognosis following decompression [10], [11]. Accordingly, OCT has increasingly become an important complementary tool in the neuro-ophthalmological evaluation of patients with suspected compressive lesions [12].

Nevertheless, OCT should not be considered a substitute for clinical examination, automated perimetry, or neuroimaging. Its greatest diagnostic utility arises from integration with visual acuity testing, color vision assessment, pupillary examination, funduscopy evaluation, ocular motility examination, visual-field testing, and magnetic resonance imaging. A relatively normal visual acuity does not necessarily indicate preservation of the entire visual pathway, as field defects may develop before central vision is significantly affected. Conversely, retinal nerve fiber layer thickness may initially remain within conventional reference ranges despite early neuronal dysfunction. For this reason, interpretation of structural and functional findings within the context of lesion anatomy is essential when evaluating patients in whom an intracranial neoplasm is suspected [4], [11], [12].

Meningiomas involving the tuberculum sellae, planum sphenoidale, anterior clinoid region, or optic nerve sheath represent another clinically significant cause of progressive visual impairment. Tuberculum sellae meningiomas are particularly important because they frequently develop in close proximity to the optic nerves and chiasm. Visual symptoms may dominate the clinical presentation and may evolve slowly enough to be initially attributed to primary ophthalmological disease. Surgical series have demonstrated that preoperative visual status and duration of symptoms are important determinants of postoperative visual outcome, supporting the principle that earlier recognition and decompression may improve the probability of functional recovery [18]. These observations reinforce the need for clinicians to investigate unexplained optic neuropathy or atypical visual-field defects rather than postponing neuroimaging until additional neurological symptoms appear.

Craniopharyngiomas also demonstrate the close relationship between intracranial tumors and visual dysfunction. Because these tumors originate in the sellar and suprasellar region, they can affect the optic chiasm, hypothalamus, pituitary structures, and adjacent vascular anatomy. In pediatric populations, ophthalmological abnormalities may be present at diagnosis and can include decreased visual acuity, visual-field defects, optic atrophy, strabismus, and papilledema [16]. The diagnostic problem is particularly relevant in children because subtle visual symptoms may remain unrecognized or may be difficult to characterize accurately. Evidence regarding visual outcomes after treatment indicates that the degree of pre-existing damage substantially influences subsequent recovery, further supporting the importance of identifying neuro-ophthalmological abnormalities before irreversible visual pathway injury occurs [16], [17].

The relationship between visual manifestations and intracranial neoplasia extends beyond traditional sellar and optic pathway tumors. Gliomas, metastatic lesions, posterior fossa tumors, ventricular tumors, skull-base neoplasms, lymphomas, and other primary central nervous system malignancies may produce neuro-ophthalmological findings depending on their anatomical distribution. Ocular motor cranial nerve palsies may indicate involvement of the brainstem, cavernous sinus, meninges, or skull base, whereas homonymous hemianopic defects suggest lesions posterior to the optic chiasm. Visual hallucinations or higher-order visual dysfunction may occur when association cortices are involved. Therefore, neuro-ophthalmological findings should be interpreted not simply as isolated eye symptoms but as potential manifestations of anatomically localized central nervous system disease [1], [2].

The diagnostic importance of these manifestations is reinforced by evidence showing that visual abnormalities can be the presenting feature of intracranial tumors. In a clinical series evaluating patients with intracranial tumors, visual findings were reported as primary manifestations in a significant subset, emphasizing that ophthalmologists and other

clinicians involved in first-contact care can play a decisive role in initiating neurodiagnostic investigation [2]. This concept is particularly relevant because patients may seek ophthalmological evaluation before consultation with neurology, neurosurgery, or oncology. The capacity to recognize combinations of progressive visual loss, optic nerve abnormalities, field defects, ocular motor dysfunction, and headache may therefore shorten the interval between symptom onset and definitive diagnosis.

Diagnostic delay has consequences that extend beyond visual prognosis. An intracranial tumor identified only after substantial neurological deterioration may have reached a larger volume, caused greater local invasion or mass effect, and required more complex therapeutic interventions. In contrast, recognizing visual manifestations as an early neurological warning sign may enable diagnostic imaging while the disease remains anatomically more limited. Although tumor biology ultimately determines many aspects of prognosis, earlier detection may improve clinical decision-making, allow more timely multidisciplinary evaluation, and reduce the risk of permanent neurological or ophthalmological disability. In compressive lesions of the anterior visual pathway, this principle is especially relevant because visual recovery after treatment depends partly on whether retinal ganglion cells and optic nerve axons remain structurally viable [13].

Magnetic resonance imaging with appropriate contrast-enhanced protocols remains the principal imaging modality for assessing suspected intracranial tumors affecting the visual pathways. Imaging should be directed according to clinical localization and may require detailed evaluation of the brain, sellar region, orbits, optic nerves, optic chiasm, cavernous sinuses, and skull base. However, neuroimaging is most effective when prompted by a well-characterized clinical syndrome. Neuro-ophthalmological assessment can determine whether symptoms are compatible with prechiasmal, chiasmal, retrochiasmal, cranial nerve, or intracranial pressure-related pathology and thus guide imaging interpretation. This interaction between clinical localization and imaging is central to achieving an efficient diagnostic pathway rather than relying on indiscriminate testing.

Despite advances in imaging and ophthalmic diagnostic technology, delayed diagnosis remains possible because early signs may be subtle and because clinicians often encounter these symptoms in conditions that are far more common than intracranial tumors. Distinguishing benign ophthalmological complaints from manifestations requiring neurological investigation therefore depends on identifying specific warning characteristics. Progressive or unexplained visual decline, visual loss disproportionate to ocular findings, vertical-meridian-respecting visual-field defects, optic atrophy without an evident ocular cause, papilledema, acquired ocular motor palsies, persistent diplopia, unexplained relative afferent pupillary defects, and discordance between visual symptoms and routine ophthalmic examination should increase suspicion for intracranial pathology. Recognition of these patterns is fundamental to developing practical strategies for earlier referral and imaging.

Within this context, the present study examines neuro-ophthalmological manifestations that may constitute the first clinical signal of intracranial neoplasms, with particular attention to their anatomical basis, diagnostic relevance, and potential role in reducing diagnostic delay. The investigation is based on a structured review and critical synthesis of contemporary evidence concerning intracranial tumors that commonly affect the afferent and efferent visual systems. Particular emphasis is placed on pituitary tumors, meningiomas, optic pathway gliomas, craniopharyngiomas, and other intracranial lesions capable of producing visual dysfunction before a definitive oncological or neurological diagnosis is established [4], [9], [16], [18], [19].

The analytical strategy integrates three complementary dimensions. First, the principal presenting neuro-ophthalmological abnormalities are categorized according to clinical phenotype, including decreased visual acuity, visual-field defects, optic neuropathy, papilledema, diplopia, ocular motor abnormalities, pupillary dysfunction, and other visual disturbances. Second, these manifestations are related to the anatomical location and tumor groups most commonly associated with each pattern. Third, diagnostic tools capable of increasing early recognition—including fundoscopic examination, automated perimetry, OCT, and magnetic resonance imaging—are examined according to their contribution to detecting structural or functional abnormalities before advanced visual damage develops [5], [10]–[12]. This approach is intended to bridge clinical examination and neuroimaging rather than evaluating either component independently.

The central hypothesis underlying this study is that certain neuro-ophthalmological manifestations form recognizable clinical patterns that can function as early indicators of intracranial neoplasia and that systematic assessment of these patterns may contribute to earlier neuroimaging and specialist referral. A related research question is whether the integration of conventional neuro-ophthalmological examination with modern structural techniques such as OCT can increase the detection of early compressive or infiltrative visual pathway damage compared with reliance on visual acuity or nonspecific neurological symptoms alone. Evidence demonstrating retinal ganglion cell alterations before advanced visual-field loss provides a strong rationale for this hypothesis [10]–[12].

A second premise is that the prognostic value of early diagnosis is particularly relevant for tumors producing chronic compression of the anterior visual pathway. Experimental and clinical observations indicate that prolonged compression can evolve from potentially reversible functional impairment to irreversible axonal loss. Once substantial optic atrophy or retinal ganglion cell degeneration has developed, removal or reduction of the compressive lesion cannot guarantee complete visual recovery [13]. Consequently, identifying the tumor during a phase in which visual dysfunction is present but structural neuronal loss remains limited may represent an important therapeutic window.

Accordingly, the design of this review is aligned with the principal research objective: to identify and organize the neuro-ophthalmological findings that should raise suspicion for intracranial neoplasia and determine which diagnostic strategies offer the greatest potential for early recognition. Rather than considering visual abnormalities as secondary manifestations of advanced neurological disease, this approach examines them as possible entry points into the diagnostic process. By synthesizing evidence regarding symptom patterns, anatomical localization, tumor type, visual-field abnormalities, optic nerve findings, OCT changes, and neuroimaging, the study seeks to establish a clinically applicable framework for distinguishing patients who require prompt neurological investigation.

The relevance of this approach lies in the interdisciplinary nature of the diagnostic pathway. Ophthalmologists, neurologists, neurosurgeons, endocrinologists, oncologists, radiologists, emergency physicians, and primary-care clinicians may all encounter patients whose first manifestation of an intracranial neoplasm is visual. Effective communication between specialties is therefore essential. A neuro-ophthalmological abnormality recognized during routine eye assessment may initiate a diagnostic sequence leading to magnetic resonance imaging, endocrine assessment, neurosurgical evaluation, and definitive treatment. Conversely, failure to recognize the neurological significance of an apparently isolated visual complaint may postpone diagnosis until more severe neurological manifestations develop.

Ultimately, early diagnosis of intracranial neoplasms requires more than widespread access to neuroimaging; it requires appropriate clinical suspicion. Neuro-ophthalmology is uniquely positioned at the intersection between ophthalmology and neurology to provide this suspicion through anatomical localization and detailed analysis of visual function. The available evidence demonstrates that intracranial tumors may initially manifest through subtle but identifiable alterations in visual fields, optic nerve structure, ocular motility, or intracranial pressure-related findings [1], [2], [5]. Furthermore, advances in OCT and quantitative visual assessment have created opportunities to identify structural damage at increasingly early stages [10]–[12]. Therefore, understanding neuro-ophthalmological manifestations as potential sentinel signs of intracranial neoplasia may contribute not only to earlier tumor detection but also to preservation of vision, optimization of therapeutic planning, and reduction of long-term neurological morbidity.

DEVELOPMENT

Neuro-ophthalmological manifestations may represent the earliest clinically detectable expression of an intracranial neoplasm because the visual pathways and ocular motor systems are anatomically related to several regions in which tumors commonly develop. The optic nerves, optic chiasm, cavernous sinus, cranial nerves, brainstem, sellar region, and posterior visual pathways are particularly vulnerable to compression, infiltration, or secondary effects of increased intracranial pressure. Consequently, alterations in visual acuity, visual fields, color perception, ocular motility, pupillary responses, or optic-disc appearance may precede other neurological manifestations [1], [2].

One of the most relevant presentations is **progressive visual loss**. Its characteristics depend largely on tumor location. Lesions affecting one optic nerve may initially cause unilateral visual impairment, dyschromatopsia, a relative afferent pupillary defect, and eventually optic atrophy. In contrast, lesions affecting the optic chiasm frequently cause visual-field abnormalities, particularly temporal defects. Although bitemporal hemianopia is considered the classical presentation of chiasmal compression, patients with pituitary tumors may demonstrate incomplete, asymmetric, central, or nonspecific field defects during earlier stages [4], [14].

Pituitary adenomas are particularly important because visual manifestations may occur before endocrine abnormalities are clinically recognized. Tumor extension toward the suprasellar region can progressively compress the optic chiasm, producing functional deterioration that may initially remain unnoticed by the patient. Nonfunctioning pituitary adenomas may therefore reach a considerable size before diagnosis, and visual symptoms can constitute the main reason for seeking medical evaluation [15]. Early campimetric assessment is valuable because peripheral visual-field defects may appear while central visual acuity remains relatively preserved.

Another important group consists of **meningiomas involving the optic nerve, tuberculum sellae, planum sphenoidale, or adjacent structures**. These tumors generally grow slowly and may cause insidious visual deterioration. Optic nerve sheath meningiomas commonly present with progressive unilateral visual loss, optic-disc edema or atrophy, color vision impairment, and visual-field abnormalities [7], [8]. Tuberculum sellae meningiomas may compress one or both optic nerves and the chiasm, and visual prognosis after treatment has been associated with the severity and duration of preoperative visual impairment [18]. This relationship highlights the importance of detecting progressive optic neuropathy before irreversible axonal degeneration develops.

Optic pathway gliomas also illustrate the relationship between tumor localization and visual manifestations. These neoplasms can affect the optic nerves, chiasm, optic tracts, or hypothalamic structures. Their presentation may include decreased visual acuity, visual-field loss, strabismus, abnormal optic-disc appearance, or color vision abnormalities [9]. Because progression may be gradual, particularly in younger patients, systematic ophthalmological assessment becomes essential for identifying clinically significant visual deterioration.

Increased intracranial pressure constitutes another major mechanism responsible for neuro-ophthalmological symptoms. Tumors may elevate intracranial pressure through direct mass effect, cerebral edema, hydrocephalus, or obstruction of cerebrospinal fluid circulation. **Papilledema** is one of the principal ocular signs associated with this process and may be accompanied by headache, transient visual obscurations, nausea, vomiting, or sixth cranial nerve palsy [5]. Its identification requires prompt investigation because it can indicate a potentially serious intracranial process. Nevertheless, the absence of papilledema cannot exclude intracranial neoplasia, particularly in tumors primarily affecting the anterior visual pathways.

Diplopia and ocular motor abnormalities are also clinically relevant. Tumors affecting the cavernous sinus, brainstem, skull base, or cranial nerves III, IV, and VI may alter ocular alignment and produce binocular diplopia. Sixth nerve involvement is particularly relevant in increased intracranial pressure because of the nerve's long intracranial course. In other cases, multiple cranial neuropathies can suggest a lesion involving the cavernous sinus or skull base. Such findings should prompt anatomical localization and targeted neuroimaging rather than being interpreted solely as isolated ophthalmological abnormalities [1].

The diagnostic process increasingly depends on the combination of **functional and structural assessment**. Automated perimetry identifies subtle defects in the visual field and contributes to localization of lesions along the visual pathway. Optical coherence tomography provides quantitative measurements of the retinal nerve fiber layer and macular ganglion cell complex. Evidence indicates that OCT may reveal early structural abnormalities associated with chiasmal compression, including ganglion cell loss before severe visual-field deterioration becomes clinically apparent [10]–[12].

These structural changes are also relevant to visual prognosis. Chronic compression of the optic nerves or chiasm can initially produce potentially reversible functional alterations; however, prolonged injury eventually causes retinal ganglion cell loss and optic atrophy. Once substantial neuronal loss has occurred, complete visual recovery after

surgical decompression becomes less likely [13]. This provides a biological rationale for emphasizing early recognition of visual abnormalities rather than waiting for advanced neurological manifestations.

Magnetic resonance imaging remains the principal imaging technique for investigating suspected intracranial neoplasms involving the visual pathways. Nevertheless, imaging findings must be interpreted in conjunction with neuro-ophthalmological examination. Visual acuity, color vision, pupillary responses, fundus examination, ocular motility, automated perimetry, and OCT can help determine whether the lesion is prechiasmal, chiasmal, retrochiasmal, or related to intracranial pressure. This clinical localization can improve the diagnostic efficiency of neuroimaging and guide subsequent neurological, neurosurgical, endocrinological, or oncological evaluation [3], [4].

Therefore, the principal challenge is not only recognizing severe visual dysfunction, but identifying **early warning patterns**. Progressive unexplained visual loss, defects respecting the vertical meridian, asymmetric optic atrophy, papilledema, persistent binocular diplopia, acquired ocular motor palsies, and visual dysfunction disproportionate to ocular findings should increase suspicion of intracranial pathology. Integrating these findings with modern imaging and structural assessment may shorten diagnostic delays and contribute to preservation of visual function and earlier treatment of the underlying neoplasm.

GENERAL OBJECTIVE AND SPECIFIC OBJECTIVES

General Objective

To **analyze** the principal neuro-ophthalmological manifestations that may constitute the first clinical sign of intracranial neoplasms, integrating anatomical localization, clinical findings, functional visual assessment, structural ophthalmic evaluation, and neuroimaging criteria in order to identify diagnostic warning patterns that may facilitate earlier recognition and timely specialist referral.

Specific Objectives

Cognitive Objectives

1. To **identify** the main neuro-ophthalmological manifestations associated with intracranial neoplasms, including progressive visual loss, visual-field defects, papilledema, optic neuropathy, diplopia, ocular motor abnormalities, and pupillary dysfunction.
2. To **describe** the anatomical relationship between intracranial tumor location and the corresponding visual or ocular manifestations.
3. To **differentiate** the clinical patterns associated with pituitary adenomas, meningiomas, optic pathway gliomas, craniopharyngiomas, and other intracranial lesions affecting the visual pathways.
4. To **analyze** the diagnostic relevance of visual acuity testing, automated perimetry, funduscopy examination, optical coherence tomography, and magnetic resonance imaging in patients with suspected intracranial neoplasia.
5. To **evaluate** the clinical characteristics that distinguish potentially benign ophthalmological complaints from warning signs suggestive of an intracranial lesion.

Psychomotor Objectives

6. To **organize** neuro-ophthalmological findings according to their anatomical localization within the afferent and efferent visual pathways.
7. To **integrate** data obtained from visual-field assessment, optic nerve examination, OCT findings, and neuroimaging into a structured diagnostic approach.
8. To **construct** a practical sequence for the initial evaluation of patients presenting with unexplained or progressive neuro-ophthalmological abnormalities.
9. To **apply** clinical localization principles to determine when neurological imaging or multidisciplinary referral should be prioritized.

Affective Objectives

10. To **recognize** the importance of neuro-ophthalmological manifestations as potential sentinel signs of intracranial neoplasms.
11. To **value** early interdisciplinary collaboration among ophthalmology, neurology, neurosurgery, endocrinology, radiology, and oncology in patients with suspected intracranial disease.

12. To **promote** greater clinical awareness regarding progressive or unexplained visual symptoms in order to reduce diagnostic delay and prevent potentially irreversible visual impairment.
13. To **appraise** the importance of preserving visual function as a fundamental component of neurological and oncological patient care.

OBJECT OF STUDY

The object of study is the **set of neuro-ophthalmological manifestations that may appear as the initial clinical expression of intracranial neoplasms**, particularly those affecting the optic nerves, optic chiasm, retrochiasmal visual pathways, ocular motor cranial nerves, cavernous sinus, sellar and parasellar regions, brainstem, and intracranial structures related to cerebrospinal fluid dynamics and intracranial pressure.

The phenomenon under investigation includes alterations such as progressive visual loss, visual-field defects, papilledema, optic neuropathy, diplopia, ocular motor palsies, pupillary abnormalities, dyschromatopsia, optic atrophy, transient visual obscurations, and other visual disturbances that may precede the appearance of more evident neurological or systemic symptoms.

The study focuses on patients in whom these findings may be associated with intracranial tumors, with particular attention to **pituitary adenomas, meningiomas, optic pathway gliomas, craniopharyngiomas, skull-base tumors, posterior fossa neoplasms, metastatic lesions, and other primary or secondary intracranial tumors capable of compromising the visual system.**

The main unit of analysis is the relationship between the **clinical neuro-ophthalmological finding, anatomical localization of the lesion, type of intracranial neoplasm, diagnostic method used, and potential value of the manifestation for early detection.** This relationship is evaluated through evidence concerning visual acuity, automated perimetry, funduscopic examination, pupillary assessment, ocular motility, optical coherence tomography, and magnetic resonance imaging.

Special emphasis is placed on identifying clinical patterns that may indicate the need for early neuroimaging or specialist referral. Progressive visual deterioration without a clear ocular cause, visual-field defects respecting neurological patterns, unexplained optic-disc abnormalities, persistent binocular diplopia, acquired cranial nerve palsies, and papilledema are considered particularly relevant warning findings because they may indicate structural intracranial disease [1], [5], [14].

The study therefore does not focus exclusively on the tumor itself, but on the **diagnostic interface between ophthalmological manifestations and intracranial oncological disease.** Its purpose is to determine how visual and ocular findings can function as sentinel signs capable of shortening the interval between symptom onset and definitive diagnosis.

The scope also includes the potential contribution of modern diagnostic technologies. OCT and automated perimetry are considered especially relevant because they can identify structural or functional abnormalities of the anterior visual pathway that may not be evident through visual acuity testing alone [10]–[12]. Magnetic resonance imaging is incorporated as the principal method for confirming and anatomically characterizing suspected intracranial lesions.

Accordingly, the object of study integrates three fundamental components: **the neuro-ophthalmological manifestation, the intracranial neoplasm responsible for it, and the diagnostic pathway that permits early recognition of their association.** This integrated perspective allows the phenomenon to be analyzed from a clinically applicable approach aimed at improving diagnostic suspicion, multidisciplinary referral, and preservation of visual function.

METHODOLOGY

This study was conducted using the **Scientific Method**, applied through a structured literature-review approach designed to identify, organize, compare, and interpret evidence concerning neuro-ophthalmological manifestations as

early indicators of intracranial neoplasms. The methodology was selected because it provides a systematic sequence for defining the clinical problem, establishing research questions, collecting evidence, analyzing findings, and generating conclusions based on reproducible criteria.

Study Design

A **descriptive and analytical literature review** was performed. The study focused on published evidence describing neuro-ophthalmological manifestations associated with intracranial tumors, particularly when visual or ocular abnormalities represented the initial or one of the earliest clinical findings.

The review incorporated evidence concerning pituitary adenomas, meningiomas, optic pathway gliomas, craniopharyngiomas, and other intracranial neoplasms involving the optic nerves, optic chiasm, retrochiasmatic pathways, ocular motor cranial nerves, cavernous sinus, or structures related to intracranial pressure [1], [4], [9], [16].

Research Question

The main research question was:

Which neuro-ophthalmological manifestations can function as early warning signs of intracranial neoplasms, and which diagnostic tools contribute most effectively to their early recognition?

A secondary question evaluated whether the combined interpretation of clinical examination, automated perimetry, optical coherence tomography, and magnetic resonance imaging could improve recognition of early structural or functional compromise of the visual pathways [10]–[12].

Information Sources

Scientific information was obtained from peer-reviewed biomedical literature available through databases and academic search platforms such as **PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar**. Searches were structured using combinations of terms related to intracranial tumors and neuro-ophthalmological manifestations.

The principal search terms included:

“intracranial tumors,” “brain neoplasms,” “neuro-ophthalmology,” “visual loss,” “visual field defects,” “papilledema,” “optic neuropathy,” “diplopia,” “pituitary adenoma,” “meningioma,” “optic pathway glioma,” “craniopharyngioma,” “optical coherence tomography,” and “early diagnosis.”

Boolean operators **AND** and **OR** were used to combine terms and increase the sensitivity and specificity of the searches.

Selection Criteria

Studies were considered eligible when they:

- Addressed intracranial neoplasms with ophthalmological or neuro-ophthalmological manifestations.
- Evaluated visual acuity, visual fields, optic nerve alterations, papilledema, ocular motility, OCT, or neuroimaging.
- Provided clinically relevant information regarding early diagnosis, presentation, prognosis, or visual outcomes.
- Were published as original studies, systematic reviews, clinical reviews, or relevant case series.
- Were available in English or Spanish.

Studies were excluded when the visual abnormalities were unrelated to intracranial neoplasia, when the publication lacked sufficient clinical information, or when the evidence did not contribute directly to the research objectives.

Data Extraction and Organization

Relevant information was extracted and organized according to five principal variables:

1. Type of intracranial neoplasm.
2. Anatomical location of the lesion.
3. Initial neuro-ophthalmological manifestation.
4. Diagnostic method used.
5. Clinical relevance for early detection or visual prognosis.

The manifestations were subsequently grouped into major clinical categories: **visual acuity impairment, visual-field defects, optic neuropathy, papilledema, diplopia and ocular motor abnormalities, pupillary alterations, and structural retinal or optic nerve changes.**

Analysis of Evidence

A qualitative comparative analysis was performed to identify recurrent clinical patterns and their anatomical correlations. Particular attention was given to findings capable of distinguishing potentially benign ophthalmological symptoms from manifestations suggestive of intracranial structural disease.

Evidence concerning OCT and automated perimetry was analyzed in relation to their capacity to detect early chiasmal or optic nerve compromise. Previous studies have demonstrated that retinal ganglion cell and retinal nerve fiber layer alterations may provide objective evidence of compressive injury and may complement conventional visual-field testing [10]–[12].

Neuroimaging findings were analyzed primarily in relation to magnetic resonance imaging because of its ability to characterize lesions affecting the optic nerves, chiasm, sellar region, cavernous sinus, brainstem, and posterior visual pathways.

Reproducibility

To facilitate replication, the methodology follows a predefined sequence: formulation of the research question, database search using specified keywords, application of eligibility criteria, extraction of predefined clinical variables, classification of neuro-ophthalmological manifestations, comparison by tumor type and anatomical location, and synthesis of diagnostic implications.

PHASES OF DEVELOPMENT

Phase 1. Identification of the Research Problem

The first phase consisted of defining the clinical problem: neuro-ophthalmological manifestations may precede the diagnosis of intracranial neoplasms and, in some cases, represent the first recognizable sign of disease. Particular attention was given to progressive visual loss, visual-field defects, papilledema, diplopia, optic neuropathy, ocular motor abnormalities, and pupillary alterations.

This phase established the need to determine which manifestations should be considered warning signs requiring early neurological investigation.

Phase 2. Formulation of the Research Question and Hypothesis

Based on the identified problem, the principal research question was formulated:

Which neuro-ophthalmological manifestations can function as early clinical indicators of intracranial neoplasms, and which diagnostic tools contribute to their timely recognition?

The working hypothesis proposed that specific combinations of neuro-ophthalmological findings, particularly when interpreted together with automated perimetry, OCT, and magnetic resonance imaging, may facilitate earlier detection of intracranial tumors before advanced neurological deterioration occurs [10]–[12].

Phase 3. Literature Search

A structured search of biomedical literature was conducted using PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar.

Search terms included combinations of *intracranial neoplasms*, *brain tumors*, *neuro-ophthalmology*, *visual loss*, *visual field defects*, *papilledema*, *optic neuropathy*, *diplopia*, *pituitary adenoma*, *meningioma*, *optic pathway glioma*, *craniopharyngioma*, and *early diagnosis*.

Boolean operators **AND** and **OR** were applied to combine concepts and retrieve publications directly related to the objectives of the study.

Phase 4. Screening and Selection of Evidence

Retrieved publications were screened according to predefined eligibility criteria. Studies were prioritized when they described clinical presentation, neuro-ophthalmological findings, anatomical localization, diagnostic procedures, visual outcomes, or early detection of intracranial tumors.

Publications without a clear relationship between intracranial neoplasia and visual or ocular manifestations were excluded. Relevant original studies, systematic reviews, clinical reviews, and case series were retained for analysis.

Phase 5. Extraction and Classification of Data

The selected evidence was reviewed to extract information regarding:

- Intracranial tumor type.
- Anatomical location.
- Initial neuro-ophthalmological manifestation.
- Visual-field pattern.
- Optic nerve or retinal structural abnormalities.
- Presence of papilledema or ocular motor dysfunction.
- Diagnostic techniques used.
- Relevance for early diagnosis and visual prognosis.

The information was subsequently classified into major clinical categories to facilitate comparison among different neoplasms.

Phase 6. Comparative Analysis

The extracted information was compared to identify recurrent clinical patterns. Visual manifestations were related to anatomical localization and tumor type.

For example, chiasmal compression was associated predominantly with visual-field defects in pituitary and suprasellar lesions, whereas optic nerve involvement was associated with visual acuity reduction, dyschromatopsia, and optic atrophy. Increased intracranial pressure was primarily related to papilledema and transient visual symptoms [5], [14].

The contribution of automated perimetry and OCT was also analyzed because these methods may reveal functional or structural abnormalities before severe visual deterioration becomes evident [10]–[12].

Phase 7. Integration of Diagnostic Findings

Clinical manifestations were integrated with diagnostic tools to establish a practical sequence for early recognition. The proposed approach begins with detailed neuro-ophthalmological examination, followed by visual-field evaluation and OCT when indicated.

Patients presenting with unexplained progressive visual deterioration, neurological visual-field patterns, papilledema, acquired ocular motor palsies, or optic neuropathy without an evident ocular cause were considered candidates for early neuroimaging.

Magnetic resonance imaging was regarded as the principal confirmatory method for identifying and anatomically characterizing suspected intracranial lesions.

Phase 8. Interpretation and Synthesis

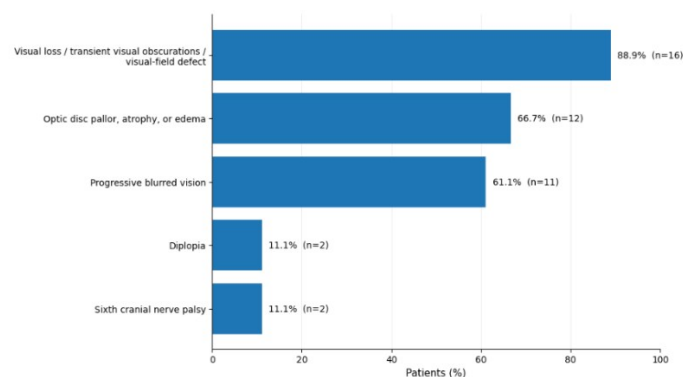
Finally, the findings were synthesized to determine which manifestations have the greatest clinical relevance as potential sentinel signs of intracranial neoplasia.

The interpretation focused on the relationship between early recognition, anatomical localization, diagnostic delay, and preservation of visual function. Particular emphasis was placed on the concept that prolonged compression of the optic pathways may lead to irreversible neuronal damage, reducing the probability of complete recovery despite successful treatment [13].

RESULTS AND DISCUSSION

Figure 1.

Distribution of neuro-ophthalmological manifestations in patients with intracranial tumors presenting with ocular complaints



Source: Self-Irindakul (2015), n=18. Categories represent reported symptoms and examination findings and are not mutually exclusive.

The distribution shown in Figure 1 demonstrates a clear predominance of **afferent visual system manifestations** among patients whose intracranial tumors initially produced ophthalmological complaints. In the analyzed clinical series of 18 patients, visual loss, transient visual obscurations, or visual-field defects were documented as the initial

manifestations in **88.9% of cases (n=16)**, representing the most frequent category by a considerable margin [2]. This finding indicates that disturbances involving visual function constituted the principal clinical presentation in this population, whereas symptoms directly related to ocular motor dysfunction were substantially less frequent. The categories presented in the figure are not mutually exclusive because some patients demonstrated more than one symptom or examination abnormality during neuro-ophthalmological assessment.

Alterations in the appearance of the optic disc represented the second most prominent finding. **Optic disc pallor, atrophy, or edema was identified in 66.7% of patients (n=12)** [2]. These abnormalities represent different structural expressions of optic nerve involvement. Optic disc edema may occur in association with increased intracranial pressure or direct involvement of the optic nerve, whereas pallor and atrophy are generally associated with previous or persistent axonal injury. The coexistence of visual dysfunction with objective changes in the optic disc therefore constituted a recurrent pattern within the evaluated population. Nevertheless, **33.3% of patients had normal optic discs**, demonstrating that a normal fundusoscopic appearance was also possible despite the presence of an intracranial tumor and clinically significant visual disturbances [2].

Progressive blurred vision was reported by 61.1% of patients (n=11) [2]. The progressive character of visual deterioration is particularly relevant when describing the clinical profile of patients with slowly expanding intracranial masses. In this series, visual acuity ranged from normal vision to absence of light perception, indicating substantial heterogeneity in the severity of visual compromise at the time of diagnosis. The interval between the onset of visual disturbances and diagnosis was also highly variable, with a mean of **9.8 ± 18 months and a range from three days to six years** [2]. These findings demonstrate that the initial neuro-ophthalmological presentation may develop either gradually or, less commonly, through relatively acute deterioration.

The predominance of visual dysfunction in Figure 1 is also consistent with evidence obtained from patients with pituitary adenomas. In a prospective study involving **103 consecutive patients**, visual loss was the most frequent reason for presentation, accounting for **39%**, compared with endocrine abnormalities in 21% and headache in 15% [14]. Among patients with visual-field loss, the bitemporal pattern was the most frequent, accounting for **41%**, although unilateral defects were present in approximately one third of affected patients [14]. Importantly, many individuals maintained relatively preserved central visual acuity despite measurable visual-field abnormalities. This pattern supports the distinction between visual acuity and visual-field integrity when describing neuro-ophthalmological involvement in intracranial tumors.

The markedly lower frequency of **diplopia, observed in 11.1% of patients (n=2)**, contrasts with the high frequency of afferent visual abnormalities [2]. Both patients presenting with diplopia demonstrated findings compatible with ocular motor pathway involvement. This distribution reflects the fact that diplopia represents a different neuro-anatomical mechanism from visual loss or visual-field impairment. Whereas the latter commonly results from involvement of the optic nerves, optic chiasm, optic tracts, or intracranial pressure-related mechanisms, diplopia is more closely related to dysfunction of the ocular motor cranial nerves, their nuclei, fascicles, cavernous sinus pathways, or associated central ocular motor systems [1].

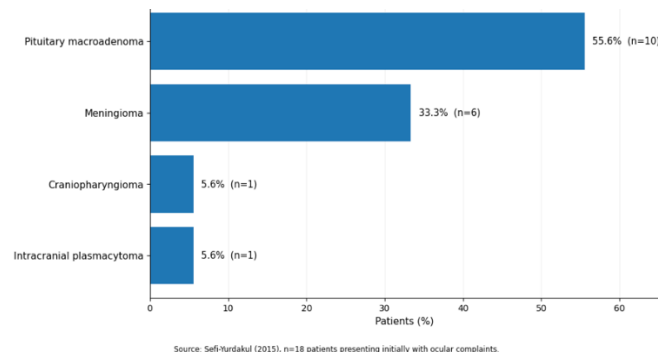
Similarly, **sixth cranial nerve palsy was identified in 11.1% of the cohort (n=2)** [2]. Although numerically less frequent, this finding represents a clearly recognizable efferent neuro-ophthalmological abnormality. Intracranial malignancies can produce ocular motor neuropathies through direct tumor extension, meningeal involvement, skull-base disease, cavernous sinus involvement, or secondary increases in intracranial pressure [1]. In the clinical series represented in Figure 1, the equal proportions of diplopia and sixth nerve palsy reflect the close association between the symptom experienced by the patient and the corresponding objective ocular motor deficit.

The tumor distribution within the same cohort provides additional context for the visual patterns represented in Figure 1. Cranial imaging demonstrated **10 pituitary macroadenomas, six meningiomas, one craniopharyngioma, and one intracranial plasmacytoma** [2]. Pituitary macroadenomas and meningiomas therefore accounted for the great majority of tumors in the series. Both tumor groups commonly involve structures located near the anterior visual pathways, particularly the optic nerves, optic chiasm, sellar region, and parasellar structures, which corresponds with the high proportion of visual loss and visual-field abnormalities observed in the figure.

Another important descriptive finding is that several patients initially received alternative ophthalmological diagnoses before intracranial imaging established the underlying neoplasm. Cases with meningioma were initially considered to have conditions such as toxic, retrobulbar, or ischemic optic neuropathy, while a patient with suprasellar craniopharyngioma was initially evaluated under a different optic neuropathy diagnosis [2]. These observations show the clinical overlap between intracranial tumor-related visual dysfunction and primary optic nerve disorders, particularly when neurological abnormalities are not yet prominent.

Figure 2.

Distribution of intracranial neoplasm types among patients presenting with neuro-ophthalmological manifestations



The distribution presented in Figure 2 shows that **pituitary macroadenomas constituted the largest diagnostic group**, representing **55.6% of the evaluated patients (n=10)**. Meningiomas accounted for **33.3% (n=6)**, while craniopharyngioma and intracranial plasmacytoma were each identified in **5.6% (n=1)** of cases. These values correspond to the 18-patient clinical series in which intracranial tumors were diagnosed after patients initially sought ophthalmological evaluation for visual or ocular complaints [2]. Therefore, the percentages represent the diagnostic composition of a neuro-ophthalmologically selected population rather than the general epidemiological distribution of intracranial tumors.

The predominance of **pituitary macroadenomas** was particularly marked. Ten of the eighteen intracranial tumors identified belonged to this category, making pituitary lesions approximately 1.7 times as frequent as meningiomas within the analyzed cohort. Of these ten patients, nine initially presented because of visual impairment or visual-field abnormalities, whereas one presented primarily with diplopia. Importantly, none of the patients with pituitary macroadenoma initially presented because of endocrine symptoms [2]. This pattern provides a direct representation of how pituitary lesions may enter the diagnostic pathway through ophthalmological manifestations rather than through an endocrine complaint.

The visual profile of pituitary tumors can be anatomically related to their suprasellar extension and proximity to the optic chiasm. Previous clinical studies have documented substantial heterogeneity in the visual-field patterns associated with pituitary adenomas. Although bitemporal hemianopic defects are traditionally associated with chiasmal compression, unilateral, asymmetric, incomplete temporal, diffuse, and other visual-field abnormalities have also been observed [4], [14]. In the series represented by Figure 2, the macroadenoma cases included hemianopic defects, diffuse visual-field loss, concentric narrowing, and, in some patients, relatively preserved visual fields despite other manifestations [2]. Thus, the predominance of pituitary macroadenomas in the figure was accompanied by considerable variability in the functional expression of visual pathway involvement.

The **second largest group consisted of meningiomas, accounting for one third of the cohort (33.3%, n=6)**. Unlike the pituitary macroadenomas, these tumors were distributed across several intracranial locations. The reported sites included the suprasellar region, anterior cranial fossa, frontal vertex, pontocerebellar angle, and a lesion involving the olfactory groove and tuberculum sellae [2]. This anatomical diversity was also reflected in the heterogeneity of the visual manifestations observed in the affected patients.

Meningiomas located close to the anterior visual pathways are especially relevant in the neuro-ophthalmological spectrum because lesions arising from the tuberculum sellae, planum sphenoidale, anterior cranial fossa, or optic nerve sheath may produce progressive optic nerve or chiasmal dysfunction [7], [8], [18]. In the evaluated series, several patients with meningioma exhibited substantial visual deterioration, visual-field abnormalities, optic-disc pallor, atrophy, or edema. Three meningioma cases had initially been considered to represent other forms of optic neuropathy before cranial imaging established the intracranial diagnosis [2]. The findings therefore demonstrate that the meningioma group was not defined by a single visual pattern but by multiple combinations of visual acuity loss, field abnormalities, and optic nerve changes.

The difference between pituitary macroadenomas and meningiomas was quantitatively substantial but not absolute. Together, these two categories represented **16 of the 18 cases, or 88.9% of the entire series** [2]. Consequently, the graphical distribution is strongly concentrated in tumors anatomically capable of affecting the sellar, parasellar, suprasellar, anterior cranial, or optic pathway regions. This concentration corresponds with the high frequency of afferent visual manifestations identified in Figure 1, where visual loss, transient visual obscurations, and visual-field abnormalities constituted the dominant presenting category.

Craniopharyngioma represented 5.6% of the cohort (n=1). Although numerically uncommon in this particular series, the identified lesion was located in the suprasellar region and was associated with severe bilateral visual loss and diffuse visual-field impairment [2]. Craniopharyngiomas have a recognized relationship with the optic chiasm and surrounding hypothalamic-pituitary structures, and visual abnormalities at diagnosis may include decreased visual acuity, visual-field defects, optic atrophy, strabismus, or papilledema [16], [17]. The low proportion shown in Figure 2 therefore reflects the composition of this specific cohort and should not be interpreted as indicating limited neuro-ophthalmological relevance of this tumor type.

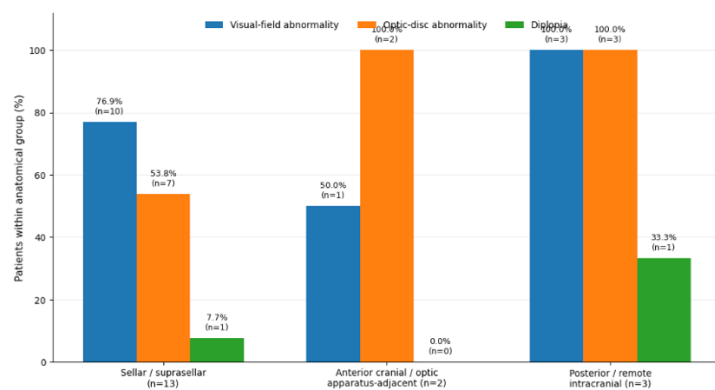
The remaining **5.6% corresponded to a posterior fossa intracranial plasmacytoma (n=1).** The patient presented with diplopia and headache, while neuro-ophthalmological examination demonstrated papilledema and a right homonymous hemianopic defect [2]. This case differs anatomically from the predominant sellar and anterior visual pathway tumors in the cohort and demonstrates the broader range of intracranial locations capable of producing ocular or visual manifestations. In this instance, the combination of diplopia, optic-disc edema, and a neurological visual-field abnormality represented the documented neuro-ophthalmological profile.

Another relevant characteristic of the distribution is that the figure does not demonstrate an even representation of tumor categories. Instead, it shows a pronounced concentration in **pituitary macroadenomas and meningiomas**, followed by isolated cases of other neoplasms. Numerically, pituitary macroadenomas exceeded meningiomas by **22.3 percentage points**, while each of the remaining categories represented only one patient. This pattern should be interpreted descriptively within the selection criteria of the clinical series, since all participants had initially attended a neuro-ophthalmology or strabismus service because of ocular complaints [2].

The tumor distribution also complements the findings presented in Figure 1. The predominance of pituitary macroadenomas and meningiomas corresponds with the high proportion of patients exhibiting visual loss, visual-field abnormalities, progressive blurred vision, and optic-disc changes. Conversely, tumors affecting other intracranial locations contributed to less frequent presentations such as diplopia, sixth cranial nerve dysfunction, papilledema, or homonymous visual-field defects. The two figures therefore describe different dimensions of the same clinical population: Figure 1 characterizes **how the patients presented**, whereas Figure 2 identifies **which intracranial neoplasms were subsequently demonstrated by imaging and neurological evaluation** [2].

Figure 3.

Relationship between anatomical location and predominant neuro-ophthalmological findings



Source: patient-level data derived from Seifi-Yurdakul (2015), Table 1, n=18. Visual-field abnormalities include hemianopic, diffuse, total, concentric, or enlarged blind-spot patterns.

Figure 3 illustrates the relationship between the **anatomical location of intracranial neoplasms and the principal neuro-ophthalmological abnormalities documented at presentation**. For this analysis, the 18 patients were classified into three anatomical groups according to the location reported in the original clinical series: sellar/suprasellar lesions (n=13), anterior cranial or optic apparatus-adjacent lesions (n=2), and posterior or anatomically remote intracranial lesions (n=3). The evaluated manifestations included documented visual-field abnormalities, optic-disc alterations, and diplopia. These categories are not mutually exclusive because the same patient could present with more than one neuro-ophthalmological finding [2].

The **sellar/suprasellar group represented the largest anatomical category**, comprising 13 of the 18 patients. This group included the ten pituitary macroadenomas, two suprasellar meningiomas, and one suprasellar craniopharyngioma described in the clinical series [2]. Within this group, **76.9% of patients (n=10)** demonstrated a documented visual-field abnormality. The abnormalities included hemianopic patterns, diffuse field loss, total field loss, and concentric narrowing. The high proportion of campimetric alterations corresponds to the direct anatomical relationship between these lesions and the optic chiasm or adjacent anterior visual pathways [2], [4], [14].

Among the sellar and suprasellar tumors, hemianopic defects represented a particularly recurrent pattern. Several patients with pituitary macroadenomas demonstrated bilateral or asymmetric hemianopic abnormalities, while other individuals showed more extensive or atypical defects. The patient-level findings therefore demonstrate that chiasmal involvement did not produce a single uniform campimetric configuration. Instead, the visual-field presentation varied from relatively characteristic hemianopic defects to diffuse or severe field loss [2]. This variability is consistent with the clinical heterogeneity previously described in pituitary tumors, where visual dysfunction depends on the direction and degree of suprasellar extension and the anatomical relationship between the tumor and the optic chiasm [4], [14].

Optic-disc abnormalities were identified in **53.8% of patients with sellar/suprasellar lesions (n=7)**. These abnormalities included optic-disc pallor, atrophy, or edema. For example, several patients with longstanding pituitary macroadenomas demonstrated optic atrophy, whereas other cases showed a combination of edema and pallor or unilateral structural alterations [2]. Thus, more than half of the patients in this anatomical group already demonstrated objective structural abnormalities of the optic nerve at neuro-ophthalmological examination.

Conversely, **46.2% of patients in the sellar/suprasellar category did not demonstrate an abnormal optic-disc appearance**, despite the presence of an intracranial tumor. This finding is especially relevant to the descriptive pattern of the results because visual-field dysfunction was more frequent than observable optic-disc abnormalities in this group: 76.9% versus 53.8%, respectively. Consequently, abnormal visual function and abnormal optic-disc morphology were not invariably present together. The patient-level data therefore demonstrate that visual pathway compromise could be identified even when conventional funduscopy examination remained normal [2].

Diplopia was considerably less frequent in the sellar/suprasellar group, occurring in **7.7% (n=1)**. This corresponded to a patient with pituitary macroadenoma who demonstrated normal visual fields and normal optic discs but presented with diplopia [2]. Pituitary tumors can produce ocular motor manifestations when parasellar extension affects

structures associated with the third, fourth, or sixth cranial nerves; however, within this particular cohort, afferent visual abnormalities clearly predominated over diplopia among sellar and suprasellar lesions [1], [2].

The second anatomical category consisted of **anterior cranial or optic apparatus-adjacent tumors (n=2)**. These were an anterior cranial fossa meningioma and an olfactory groove-tuberculum sellae meningioma. Both patients demonstrated abnormal optic-disc findings, resulting in a proportion of **100% (n=2)** for this variable [2]. One patient presented with bilateral optic-disc edema, while the other demonstrated optic-disc pallor associated with marked unilateral visual dysfunction. These findings represent two different morphological expressions of optic pathway involvement in lesions situated close to the anterior cranial base and optic apparatus.

A documented visual-field abnormality was recorded in **50.0% (n=1)** of patients in this group. This percentage requires careful descriptive interpretation because visual-field testing could not be completed in the remaining patient owing to severe visual deterioration; therefore, the value should not be interpreted as indicating that only half of anterior cranial lesions affected visual function. The patient without recorded campimetry had profound bilateral visual loss and optic-disc edema, whereas the second patient demonstrated total visual-field loss in the affected eye [2].

The anterior cranial group showed **no documented diplopia (0%)**. Instead, the presenting pattern was dominated by severe visual impairment and objective optic-disc abnormalities. One particularly notable case involved a large anterior cranial fossa meningioma associated with rapid bilateral visual deterioration, optic-disc edema, headache, and anosmia. The other involved an olfactory groove-tuberculum sellae meningioma associated with severe unilateral visual loss, total field loss, and optic-disc pallor [2]. These patient-level findings emphasize the predominance of afferent rather than ocular motor abnormalities in this anatomical category.

The **posterior or remote intracranial group (n=3)** included a pontocerebellar-angle meningioma, a frontal vertex meningioma, and a posterior fossa plasmacytoma. Despite their anatomical distance from the anterior visual pathways, **100% of these patients (n=3) demonstrated a visual-field abnormality**. Two patients exhibited enlargement of the blind spot, while the patient with posterior fossa plasmacytoma presented with an incomplete homonymous hemianopic defect [2].

Optic-disc abnormalities were also present in **100% of patients in the posterior/remote group (n=3)**. All three demonstrated optic-disc edema [2]. In the pontocerebellar-angle and frontal vertex meningioma cases, bilateral disc edema was accompanied by enlargement of the blind spot and transient visual obscurations. The posterior fossa plasmacytoma was similarly associated with bilateral papilledema, in addition to a homonymous visual-field defect and diplopia. These data distinguish the posterior/remote group from the sellar/suprasellar tumors, in which optic atrophy, pallor, edema, or a normal disc could all occur.

Diplopia occurred in **33.3% of posterior/remote intracranial lesions (n=1)**, the highest proportion among the three anatomical categories. The affected patient was the individual with posterior fossa plasmacytoma, who presented with diplopia and nonspecific headache and was subsequently found to have papilledema and an incomplete right homonymous hemianopia [2]. This combination illustrates how a single intracranial lesion may simultaneously produce abnormalities involving ocular alignment, the optic discs, and the retrochiasmal visual pathway.

Comparison between anatomical groups demonstrates three distinct descriptive patterns. First, the **sellar/suprasellar region was characterized predominantly by visual-field abnormalities**, documented in 76.9% of patients, with optic-disc abnormalities occurring in slightly more than half. Second, **anterior cranial and optic apparatus-adjacent lesions showed a predominance of structural optic-disc abnormalities**, present in both evaluated cases. Third, **posterior or remote intracranial lesions demonstrated both visual-field and optic-disc abnormalities in all three patients**, while diplopia was proportionally more frequent in this smaller anatomical group.

The results also demonstrate that the same neuro-ophthalmological finding may arise from lesions in different anatomical regions. Visual-field abnormalities were present across all three groups, but their patterns differed. Sellar and suprasellar lesions predominantly produced hemianopic, diffuse, total, or concentric abnormalities associated with anterior pathway involvement; frontal vertex and pontocerebellar-angle lesions were associated with enlargement of the blind spot; and the posterior fossa plasmacytoma was associated with a homonymous hemianopic pattern [2]. Thus,

the **configuration of the visual-field defect**, rather than simply its presence, represented an important descriptive variable within the reviewed cases.

A similar heterogeneity was observed for optic-disc abnormalities. Pallor and atrophy occurred primarily among patients with lesions involving or adjacent to the anterior visual pathways, whereas bilateral disc edema was particularly evident among tumors located outside the sellar region and associated with intracranial pressure-related manifestations [2], [5]. This distinction was visible in the patient-level data and explains why the broad category of “optic-disc abnormality” encompasses different morphological findings according to tumor location.

Overall, Figure 3 demonstrates a measurable relationship between **intracranial anatomical localization and neuro-ophthalmological phenotype**. Among the 13 sellar/suprasellar tumors, visual-field abnormalities were present in 76.9%, optic-disc abnormalities in 53.8%, and diplopia in 7.7%. Among the two anterior cranial/optic apparatus-adjacent lesions, optic-disc abnormalities occurred in 100%, a documented visual-field defect in 50.0%, and diplopia in 0%. Finally, among the three posterior or remote intracranial lesions, visual-field and optic-disc abnormalities were documented in 100%, while diplopia occurred in 33.3%. These results provide an anatomical framework for describing the different clinical patterns through which intracranial neoplasms initially manifested in the analyzed population [2].

Figure 4.

OCT detection of early optic pathway structural abnormalities in pituitary tumors with normal visual fields

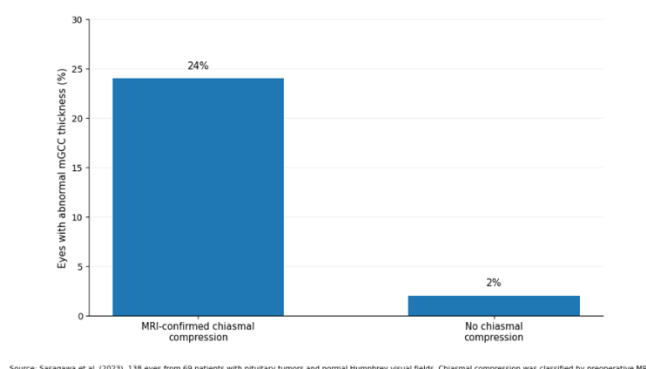


Figure 4 presents the proportion of abnormal macular ganglion cell complex (mGCC) measurements detected by optical coherence tomography in patients with pituitary tumors who still demonstrated **normal Humphrey visual-field results**. The analyzed study included **138 eyes from 69 patients**, of whom 40 had chiasmal compression demonstrated by preoperative magnetic resonance imaging and 29 had no radiological evidence of chiasmal compression [10]. This design permitted comparison of structural retinal abnormalities between patients with and without anatomical compression despite the absence of conventional visual-field defects.

The most notable difference was observed in the frequency of abnormal mGCC thickness. Among eyes belonging to patients with **MRI-confirmed chiasmal compression**, **24% showed abnormal mGCC measurements**, whereas abnormalities were detected in only **2% of eyes without chiasmal compression** [10]. Therefore, the absolute difference between groups was **22 percentage points**, while abnormal OCT findings were approximately twelve times more frequent in the chiasmal compression group.

This difference was statistically significant ($P < 0.01$) [10]. The data are particularly relevant within the descriptive framework of the present study because all included patients had been selected specifically on the basis of having no detectable visual-field defect. Consequently, the difference represented in Figure 4 cannot be attributed to patients already presenting with advanced campimetric deterioration. Instead, it reflects structural differences detected by OCT in a population in which conventional automated perimetry remained within normal limits.

Quantitative OCT measurements further demonstrated a difference in mGCC thickness between the two anatomical groups. Patients with chiasmal compression had a mean mGCC thickness of approximately **112.5 μm** , compared with **117.4 μm** among patients without chiasmal compression, with the difference reaching statistical significance ($P < 0.05$) [10]. Thus, the group characterized radiologically by direct contact or compression of the optic chiasm showed both a greater frequency of abnormal OCT classifications and lower average ganglion cell complex thickness.

The relationship among the three diagnostic components evaluated in this study—**automated perimetry, OCT, and MRI**—is especially apparent in these results. Humphrey visual-field testing demonstrated no established field defect in either study group, MRI differentiated patients according to the presence or absence of chiasmal compression, and OCT demonstrated a substantially greater prevalence of structural ganglion cell abnormalities among those with radiological compression [10]. The findings therefore describe different aspects of the visual pathway: functional performance through perimetry, retinal neuronal structure through OCT, and intracranial anatomy through MRI.

The results are consistent with previous evidence showing that retinal ganglion cell and retinal nerve fiber measurements can change in compressive optic neuropathies associated with sellar and parasellar lesions [11], [12]. Ganglion cell analysis is particularly relevant because retinal ganglion cells represent the neuronal origin of the optic nerve, and retrograde degeneration associated with compression of the optic chiasm can produce measurable changes in macular ganglion cell layers. In some patients, these structural abnormalities may be identified before conventional visual-field testing demonstrates a characteristic neurological pattern [10]–[12].

The difference between the chiasmal-compression and non-compression groups was not explained by major differences in demographic characteristics. Sasagawa *et al.* reported no significant differences between groups in age, sex, tumor type, or degree of visual-field testing, although tumor size differed [10]. This strengthens the descriptive association between anatomical compression and OCT abnormalities within the analyzed population.

The figure also demonstrates that OCT abnormalities were **not universal among patients with chiasmal compression**. Although 24% of eyes were classified as having abnormal mGCC thickness, most eyes remained within the reference range despite MRI-confirmed compression. Thus, OCT findings and radiological compression were not completely concordant. This observation is important for accurately describing the results because OCT should not be interpreted as detecting structural abnormalities in every patient with anatomical contact or compression of the optic chiasm [10].

Conversely, the **2% prevalence of abnormal mGCC thickness in the non-compression group** demonstrates that OCT abnormalities were not absolutely specific to radiologically demonstrated chiasmal compression in this cohort. Nevertheless, the pronounced difference between 24% and 2%, together with the statistically lower mean mGCC thickness in the compression group, established a clear quantitative separation between the two populations [10].

These findings complement studies evaluating broader structural changes in compressive optic neuropathy. Analysis of the retinal nerve fiber layer and macular ganglion cell complex has demonstrated associations between structural integrity, visual-field abnormalities, and the degree of damage caused by sellar and parasellar lesions [11], [12]. In addition, structural preservation of the retinal nerve fiber layer has been associated with the potential for visual recovery following decompression, providing another measurable dimension of optic pathway involvement [13].

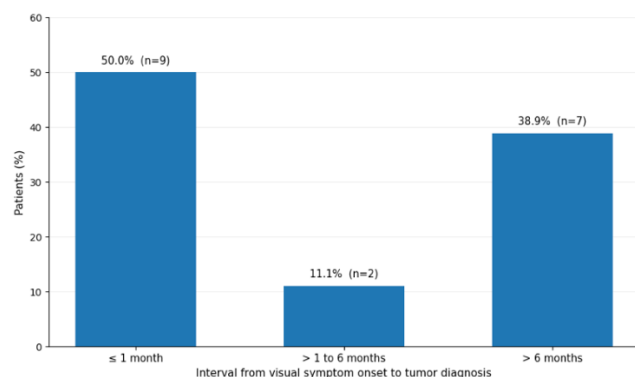
From a purely descriptive perspective, Figure 4 establishes a sequential pattern across diagnostic modalities. **MRI identified anatomical chiasmal compression, automated perimetry remained normal, and OCT detected abnormal ganglion cell measurements in a subset of patients with compression.** The proportion of abnormal OCT findings was substantially greater in the radiologically compressed group than in the non-compressed group, while quantitative mGCC thickness was simultaneously reduced [10]. This demonstrates that functional, structural, and anatomical assessments did not necessarily become abnormal at the same stage of disease.

Overall, Figure 4 shows that among patients with pituitary tumors and normal conventional visual fields, **24% of eyes associated with MRI-confirmed chiasmal compression demonstrated abnormal mGCC thickness compared with only 2% without compression.** In addition, mean mGCC thickness was lower in the compression group (112.5 μm versus 117.4 μm). These data provide a quantitative representation of structural neuroretinal abnormalities

occurring in association with intracranial chiasmal compression even when automated visual-field testing has not yet demonstrated an established defect [10]–[12].

Figure 5.

Interval between onset of visual manifestations and diagnosis of intracranial neoplasm



Source: Sefi-Yurdakul (2015), n=18. Diagnostic intervals were grouped from the patient-level durations reported in Table 1.

Figure 5 presents the distribution of the interval between the onset of visual or neuro-ophthalmological manifestations and the definitive diagnosis of an intracranial neoplasm. The analysis was derived from the individual diagnostic intervals reported for the 18 patients included in the clinical series by Sefi-Yurdakul [2]. To facilitate descriptive comparison, the intervals were grouped into three categories: diagnosis within one month of symptom onset, diagnosis between more than one and six months, and diagnosis more than six months after the onset of visual manifestations.

The largest category corresponded to patients diagnosed **within one month**, representing **50.0% of the cohort (n=9)**. This group included individuals whose diagnostic intervals ranged from three days to approximately 30 days [2]. Several of these patients presented with relatively acute or rapidly progressive manifestations, including severe visual deterioration, diplopia, visual-field abnormalities, or optic-disc changes. The concentration of half of the cohort within this first interval demonstrates that a substantial proportion of intracranial tumors in the evaluated population were identified shortly after the visual disturbance became clinically evident.

Only **11.1% of patients (n=2)** were diagnosed between more than one and six months after symptom onset. The two cases within this intermediate interval had diagnostic delays of approximately two and three months [2]. Numerically, this was the smallest category, producing a distribution in which patients tended to cluster either around relatively short diagnostic intervals or substantially prolonged periods rather than being uniformly distributed across time.

In contrast, **38.9% of the patients (n=7)** remained symptomatic for more than six months before the definitive intracranial diagnosis was established. This group included diagnostic intervals of approximately nine months, one year, three years, and as long as **six years** [2]. Therefore, more than one third of the studied population experienced persistent visual manifestations for a prolonged period before the underlying intracranial neoplasm was identified. (

The temporal distribution was consequently highly heterogeneous. Although half of the patients were diagnosed within the first month, the presence of several exceptionally prolonged intervals substantially increased the overall average. The original study reported a **mean interval of 9.8 ± 18 months**, with values ranging from **three days to six years** [2]. The large standard deviation relative to the mean reflects the pronounced dispersion of diagnostic intervals and the influence of patients with visual symptoms lasting several years.

The prolonged diagnostic intervals were particularly evident among patients with slowly evolving visual dysfunction. One patient with a suprasellar meningioma had experienced symptoms for approximately six years, while another patient with a meningioma involving the olfactory groove and tuberculum sellae had an interval of approximately three years before tumor identification [2]. Several individuals with pituitary macroadenomas had visual manifestations for

approximately one year before diagnosis. These findings demonstrate that the neuro-ophthalmological presentation of intracranial neoplasia was not necessarily acute and could evolve over extended periods.

The pattern observed among pituitary tumors is consistent with their variable clinical presentation. Pituitary macroadenomas may produce progressive visual-field defects and visual acuity abnormalities as suprasellar extension affects the optic chiasm [14], [15]. Within the cohort analyzed in Figure 5, the diagnostic intervals for pituitary macroadenoma ranged from approximately ten days to one year [2]. Thus, even within a single tumor category, considerable variation existed in the duration of neuro-ophthalmological symptoms before definitive diagnosis.

Meningiomas demonstrated an even broader temporal distribution. Diagnostic intervals ranged from only **three days in a patient with an anterior cranial fossa meningioma to six years in a patient with a suprasellar meningioma** [2]. This variation paralleled differences in tumor location, pattern of visual dysfunction, and clinical presentation. Meningiomas involving structures close to the optic nerve or chiasm are frequently associated with progressive visual abnormalities, and visual function constitutes an important component of their clinical evaluation [7], [8], [18].

The data also showed that prolonged symptom duration did not correspond to a single neuro-ophthalmological manifestation. Patients within the longer diagnostic interval group exhibited combinations of visual acuity reduction, hemianopic visual-field defects, diffuse field loss, optic atrophy, pallor, or other optic nerve abnormalities [2]. Similarly, patients diagnosed rapidly could present with optic-disc edema, profound visual loss, diplopia, or other conspicuous abnormalities. Therefore, diagnostic interval varied considerably even among patients presenting with objectively demonstrable neuro-ophthalmological findings.

Another notable feature was the presence of alternative ophthalmological diagnoses before intracranial imaging in several patients. Prior to radiological investigation, individual cases had been considered to have toxic optic neuropathy, ischemic optic neuropathy, retrobulbar neuritis, or Leber hereditary optic neuropathy [2]. These cases occurred in patients subsequently diagnosed with meningioma, pituitary-region disease, or craniopharyngioma. The descriptive findings demonstrate overlap between the initial appearance of intracranial tumor-related visual dysfunction and other disorders affecting the optic nerve.

The temporal findings in Figure 5 complement the previous results. Figures 1 and 2 demonstrated that visual loss, visual-field abnormalities, and optic-disc changes predominated and that pituitary macroadenomas and meningiomas represented the majority of diagnosed tumors. Figure 3 subsequently demonstrated differences in neuro-ophthalmological patterns according to anatomical localization, while Figure 4 showed that structural OCT abnormalities could be detected in a subset of patients with chiasmal compression despite normal conventional visual fields. Figure 5 adds the temporal dimension by demonstrating that the period between initial visual disturbance and tumor identification varied from days to several years.

From a numerical perspective, **9 of 18 patients were diagnosed within one month, 2 of 18 between more than one and six months, and 7 of 18 after more than six months** [2]. Consequently, nearly two fifths of the population belonged to the longest diagnostic-interval category. The mean interval of 9.8 months should therefore be interpreted together with the broad range and substantial standard deviation, rather than as a uniform representation of the experience of individual patients.

DISCUSSION

The findings of this study demonstrate that neuro-ophthalmological manifestations may constitute an important initial clinical expression of intracranial neoplasms, particularly when tumors involve the anterior visual pathways, sellar and parasellar regions, cranial nerves, or structures associated with intracranial pressure. The results showed a predominance of visual loss, visual-field abnormalities, progressive blurred vision, and optic-disc changes, while diplopia and ocular motor dysfunction were less frequent. This distribution is consistent with previous evidence indicating that visual dysfunction may precede the recognition of other neurological, endocrine, or systemic manifestations of intracranial tumors [1], [2].

One of the most relevant findings was the high proportion of patients presenting with **visual loss, transient visual obscurations, or visual-field defects**, which reached 88.9% in the analyzed clinical series. This reinforces the concept that afferent visual pathway dysfunction is a major form of presentation in patients whose tumors compromise the optic nerves or optic chiasm [2]. From a clinical perspective, this is particularly important because visual complaints are frequently attributed initially to primary ophthalmological conditions. When visual deterioration is progressive, unexplained, asymmetric, or accompanied by neurological patterns of field loss, the possibility of intracranial disease should therefore remain within the differential diagnosis.

The predominance of visual-field abnormalities is also anatomically consistent with the distribution of tumors identified in the study. Pituitary macroadenomas represented more than half of the neoplasms, while meningiomas accounted for approximately one third. Both tumor groups frequently arise near structures responsible for transmitting visual information, particularly the optic nerves and optic chiasm. Previous studies of pituitary adenomas have similarly demonstrated that visual-field abnormalities may be present even when central visual acuity remains relatively preserved [14], [15]. This distinction is clinically relevant because evaluation based exclusively on visual acuity may underestimate early or moderate chiasmal dysfunction.

Although bitemporal hemianopia remains the classical visual-field pattern associated with pituitary tumors, the results and previous literature demonstrate considerably greater heterogeneity. Patients may develop incomplete temporal defects, asymmetric hemianopia, unilateral field loss, concentric narrowing, diffuse abnormalities, or severe generalized deterioration [4], [14]. Consequently, the absence of a textbook bitemporal pattern should not be considered sufficient to exclude chiasmal compression. The anatomical position of the chiasm, direction of tumor growth, degree of compression, and duration of disease may all influence the resulting field defect.

The relationship between tumor location and neuro-ophthalmological phenotype identified in Figure 3 provides additional support for anatomical localization as a fundamental component of clinical assessment. Sellar and suprasellar tumors were predominantly associated with visual-field abnormalities, whereas lesions involving or located near the anterior cranial base frequently demonstrated structural optic-disc abnormalities. Posterior or more remote intracranial tumors were more commonly associated with optic-disc edema and, in some cases, diplopia or retrochiasmal field abnormalities. These differences illustrate that neuro-ophthalmological manifestations should not be considered isolated findings; rather, their pattern can provide information regarding the probable anatomical level of intracranial involvement [1].

Optic-disc abnormalities represented another major finding. Pallor, atrophy, or edema was documented in a substantial proportion of patients. However, normal optic-disc appearance was also observed in individuals with confirmed intracranial neoplasms [2]. This observation has important diagnostic implications because early compressive lesions may affect visual function before visible optic nerve changes appear. A normal funduscopic examination therefore cannot reliably exclude intracranial pathology when other neuro-ophthalmological abnormalities, particularly neurological visual-field defects or progressive unexplained visual loss, are present.

Conversely, optic atrophy generally indicates established axonal injury and may be associated with a reduced potential for complete visual recovery. Chronic compression of the anterior visual pathway can progress from functional conduction abnormalities to irreversible retinal ganglion cell and optic nerve fiber loss [13]. Danesh-Meyer *et al.* emphasized that structural integrity of the visual pathway contributes substantially to the degree of postoperative visual recovery following decompression [13]. These findings support the importance of identifying compressive lesions before advanced optic atrophy develops.

Papilledema represents a different mechanism of visual involvement. Rather than direct compression of the optic nerve or chiasm, it primarily reflects elevated intracranial pressure transmitted through the optic nerve sheath. Intracranial tumors may produce increased pressure through mass effect, peritumoral edema, obstruction of cerebrospinal fluid circulation, or hydrocephalus [5]. The presence of papilledema in patients with headache, transient visual obscurations, nausea, vomiting, or cranial nerve abnormalities therefore represents a particularly important neuro-ophthalmological finding. Nevertheless, the results also demonstrate that many intracranial tumors occur without papilledema, particularly slowly growing sellar and parasellar lesions. Its absence should therefore never be interpreted as evidence against a tumor when other findings suggest structural visual pathway involvement.

The relatively lower frequency of diplopia and sixth cranial nerve palsy compared with afferent visual dysfunction reflects the anatomical distribution of the tumors analyzed. Diplopia typically develops when intracranial disease affects the ocular motor cranial nerves, cavernous sinus, skull base, brainstem, or mechanisms controlling ocular alignment [1]. Although less common in the analyzed cohort, acquired persistent binocular diplopia remains clinically important because it may represent the initial manifestation of a lesion distant from the globe itself. The coexistence of diplopia with papilledema, pupillary abnormalities, multiple cranial neuropathies, or neurological visual-field defects should substantially increase suspicion of intracranial pathology.

A particularly relevant result was the contribution of **optical coherence tomography to early structural detection**. Among patients with pituitary tumors and normal conventional visual fields, abnormal macular ganglion cell complex thickness was identified in 24% of eyes associated with MRI-confirmed chiasmal compression compared with only 2% in patients without compression [10]. These findings demonstrate that anatomical compression, structural retinal abnormalities, and functional visual-field defects do not necessarily appear simultaneously.

The capacity of OCT to quantify retinal ganglion cell and retinal nerve fiber layer integrity represents an important evolution in neuro-ophthalmological assessment. Previous investigations have similarly demonstrated that ganglion cell complex analysis can reveal patterns compatible with chiasmal injury and may complement automated perimetry in compressive optic neuropathies [11], [12]. This does not imply that OCT can replace visual-field examination or magnetic resonance imaging. Rather, the evidence supports a complementary approach in which structural and functional information is interpreted together.

MRI remains indispensable for confirming the presence, location, dimensions, and anatomical relationships of intracranial tumors. However, imaging alone does not quantify the functional consequences of compression. Two patients with tumors of similar radiological dimensions may demonstrate markedly different visual outcomes depending on the duration of compression, individual anatomy, tumor direction of growth, and degree of neuronal injury [3], [4]. Neuro-ophthalmological examination therefore adds clinically relevant information that cannot be obtained from tumor size or imaging characteristics alone.

The temporal findings presented in Figure 5 are particularly significant. Although 50% of patients were diagnosed within one month after the onset of visual manifestations, **38.9% remained symptomatic for more than six months**, and the longest reported interval reached six years [2]. This broad variability demonstrates that intracranial tumors can remain clinically unrecognized despite persistent visual symptoms. The mean diagnostic interval of 9.8 months was accompanied by substantial dispersion, indicating that a subgroup of patients experienced prolonged diagnostic pathways.

Several mechanisms may contribute to such delays. Slowly progressive symptoms may be tolerated or underestimated by patients, particularly when unilateral visual loss allows compensation through the unaffected eye. Peripheral field defects may also remain unnoticed until they become extensive. In addition, early manifestations can resemble more common disorders such as ischemic, inflammatory, toxic, hereditary, or glaucomatous optic neuropathy. The original clinical series included patients who initially received alternative ophthalmological diagnoses before intracranial imaging revealed the underlying tumor [2]. This overlap emphasizes the need for careful reassessment when the clinical evolution does not correspond to the presumed ocular diagnosis.

The diagnostic delay observed in some cases is especially important for meningiomas and nonfunctioning pituitary adenomas. These tumors can grow slowly and may produce progressive visual dysfunction without prominent systemic symptoms. Nonfunctioning pituitary adenomas, in particular, may lack clinically evident hormonal manifestations and therefore present primarily because of compression of the optic apparatus [15]. Similarly, tuberculum sellae and optic nerve-related meningiomas may initially mimic isolated optic neuropathies [7], [8], [18].

Craniopharyngiomas represent another important example, particularly in pediatric populations. Visual impairment may coexist with endocrine, hypothalamic, or neurological manifestations, but children may not accurately report subtle visual changes. Systematic evaluation of visual acuity, ocular alignment, optic-disc appearance, and visual fields therefore remains important when these tumors are suspected [16]. Available evidence indicates that pre-treatment visual status substantially influences later functional outcomes [16], [17].

The findings collectively support a diagnostic approach based on **pattern recognition rather than isolated symptoms**. Progressive unexplained visual loss alone may be nonspecific; however, its association with dyschromatopsia, a relative afferent pupillary defect, a neurological visual-field pattern, optic-disc pallor, or discordance between visual function and ocular findings substantially changes the diagnostic context. Similarly, headache is extremely common and nonspecific, but headache associated with papilledema, sixth nerve palsy, transient visual obscurations, or visual-field abnormalities requires a different level of investigation.

Another relevant aspect is the interdisciplinary nature of these presentations. Patients whose intracranial neoplasms initially produce visual symptoms may first be evaluated by ophthalmologists, optometrists, primary-care physicians, emergency physicians, or neurologists rather than neurosurgeons or oncologists. Neuro-ophthalmological recognition can therefore serve as the initial link between visual symptoms and intracranial imaging. Appropriate referral pathways are essential because diagnostic efficiency depends not only on identifying an abnormality but also on recognizing its neurological significance.

The results also reinforce the importance of combining **visual acuity, color vision assessment, pupillary examination, ocular motility, fundus evaluation, automated perimetry, OCT, and neuroimaging**. No single test provides complete diagnostic information. Visual acuity primarily measures central vision; campimetry evaluates spatial visual function; OCT quantifies retinal neuronal structure; fundus examination identifies optic-disc changes; ocular motility testing evaluates efferent pathways; and MRI characterizes the intracranial lesion. Integration of these modalities creates a more complete assessment than any isolated measurement.

Nevertheless, the results must be interpreted within several limitations. Much of the quantitative information regarding initial ocular presentation was derived from relatively small clinical series, including the 18-patient cohort used for several figures [2]. These populations were selected from neuro-ophthalmological services and therefore cannot be considered representative of the prevalence of neuro-ophthalmological manifestations among all patients with intracranial tumors. Referral bias may increase the apparent frequency of visual symptoms and of tumors located near the visual pathways.

The small sample sizes within some anatomical subgroups also limit direct statistical comparison. Percentages derived from groups containing two or three patients are highly sensitive to individual cases and should be interpreted descriptively rather than as population-level estimates. Similarly, differences in diagnostic protocols, imaging technology, visual-field strategies, OCT devices, tumor classifications, and follow-up periods across publications restrict the possibility of direct quantitative comparison between studies.

A further limitation is the heterogeneity of intracranial neoplasms themselves. Pituitary adenomas, meningiomas, optic pathway gliomas, craniopharyngiomas, metastatic lesions, and posterior fossa tumors differ substantially in biological behavior, growth rate, anatomical distribution, and patient demographics. Consequently, a single neuro-ophthalmological diagnostic model cannot be applied uniformly to all tumor types. Instead, the results support the identification of anatomical and clinical warning patterns that can guide subsequent investigation.

Despite these limitations, the consistency of several findings across different publications strengthens the overall interpretation. Visual-field abnormalities are repeatedly associated with chiasmal lesions [4], [14], [15]; structural retinal changes have been demonstrated in compressive optic neuropathy using OCT [10]–[12]; preoperative visual integrity influences recovery after decompression [13], [18]; and visual abnormalities represent an important component of presentation in craniopharyngiomas and optic pathway tumors [9], [16], [17]. The convergence of these findings provides a coherent neuroanatomical explanation for the patterns observed in the present analysis.

Taken together, the results suggest that the concept of an “early neuro-ophthalmological manifestation” should not be restricted to dramatic visual loss. Subtle field abnormalities, unexplained dyschromatopsia, early ganglion cell changes on OCT, persistent binocular diplopia, acquired cranial neuropathies, or optic-disc abnormalities may precede more obvious neurological deterioration. Recognition of these manifestations depends on maintaining clinical suspicion when ocular findings fail to adequately explain the patient’s symptoms.

The principal contribution of this study is therefore the integration of anatomical localization, symptom patterns, structural ophthalmic assessment, functional visual testing, and neuroimaging into a unified interpretation of early

intracranial tumor presentation. The reviewed evidence supports the initial hypothesis that recognizable neuro-ophthalmological patterns may function as sentinel manifestations of intracranial neoplasia. It also supports the complementary use of OCT, automated perimetry, funduscopy assessment, and MRI when compressive or intracranial pathology is suspected [10]–[13].

Ultimately, earlier recognition is especially relevant because the visual system has a limited capacity for recovery once substantial axonal degeneration has occurred. Detecting intracranial neoplasms during a stage of functional impairment but before extensive structural damage may preserve a greater potential for visual recovery following appropriate treatment [13], [18]. Therefore, persistent or unexplained neuro-ophthalmological abnormalities should be considered not merely as isolated visual complaints, but as potential indicators of underlying intracranial disease requiring timely anatomical investigation and multidisciplinary assessment.

CONCLUSION

Neuro-ophthalmological manifestations can constitute the first clinically recognizable expression of intracranial neoplasms, particularly when tumors involve the optic nerves, optic chiasm, sellar and parasellar regions, cranial nerves, skull base, brainstem, or structures related to intracranial pressure. Progressive visual loss, visual-field defects, optic-disc abnormalities, papilledema, diplopia, ocular motor dysfunction, and pupillary alterations should therefore be considered important clinical findings when they are unexplained, persistent, progressive, asymmetric, or inconsistent with a primary ocular disorder.

The results showed that afferent visual abnormalities predominated among patients presenting initially with ocular complaints. Visual loss, transient visual obscurations, and visual-field defects represented the most frequent manifestations, while pituitary macroadenomas and meningiomas constituted the principal tumor groups identified. These findings emphasize the close anatomical relationship between intracranial neoplasms arising near the anterior visual pathways and the development of early visual dysfunction [1], [2].

Anatomical localization proved essential for interpreting neuro-ophthalmological findings. Sellar and suprasellar lesions were predominantly associated with visual-field abnormalities, whereas tumors involving the anterior cranial base or optic apparatus more frequently produced optic-disc alterations. Posterior or anatomically remote intracranial lesions could manifest through papilledema, retrochiasmal field defects, or ocular motor abnormalities. Consequently, the pattern and combination of visual findings can provide valuable information regarding the probable location of the intracranial lesion before definitive imaging.

The study also demonstrated the importance of combining functional, structural, and radiological assessment. Automated perimetry provides information regarding visual-field integrity, while OCT offers objective measurements of retinal ganglion cell and retinal nerve fiber structure. Evidence showing abnormal macular ganglion cell complex thickness in patients with MRI-confirmed chiasmal compression despite normal visual fields indicates that structural damage may be detectable before conventional functional deterioration becomes evident [10]–[12]. MRI remains fundamental for confirming and anatomically characterizing the underlying intracranial lesion.

Diagnostic timing was another relevant finding. Although a considerable proportion of patients received a diagnosis shortly after the onset of visual symptoms, more than one third remained symptomatic for over six months, with extreme cases reaching several years before definitive tumor identification [2]. This variability illustrates the potential for slowly progressive visual manifestations to delay recognition, particularly when symptoms resemble more common ophthalmological disorders.

The findings therefore support the central hypothesis of this study: **recognizable neuro-ophthalmological patterns can function as sentinel signs of intracranial neoplasms and may contribute to earlier diagnostic investigation when systematically evaluated.** The presence of progressive unexplained visual loss, neurological visual-field defects, optic atrophy without an evident ocular cause, papilledema, persistent binocular diplopia, or acquired ocular motor palsies should increase suspicion for intracranial pathology and justify timely neurological assessment and appropriate neuroimaging.

Early recognition is especially important because prolonged compression of the optic pathways may progress from potentially reversible dysfunction to irreversible retinal ganglion cell and optic nerve axonal loss. Once advanced optic atrophy has developed, complete visual recovery may remain limited even after successful treatment of the underlying lesion [13], [18]. Thus, the objective of early diagnosis extends beyond identifying the tumor itself and includes preservation of visual function and prevention of permanent neurological disability.

In conclusion, neuro-ophthalmological assessment represents a valuable component of the early diagnostic pathway for intracranial neoplasms. Integrating detailed clinical examination with automated perimetry, OCT, funduscopy evaluation, ocular motility assessment, and magnetic resonance imaging can improve anatomical localization and recognition of clinically significant visual pathway involvement. Greater awareness of these manifestations among ophthalmologists, neurologists, neurosurgeons, endocrinologists, oncologists, emergency physicians, and primary-care clinicians may reduce diagnostic delay and promote earlier multidisciplinary management. Future studies with larger and more diverse populations should further define the predictive value of specific neuro-ophthalmological patterns and establish standardized diagnostic algorithms for patients presenting with unexplained visual abnormalities.

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