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# Neuroanatomical insights into neuro-ophthalmic presentations of skull base meningiomas: Pathways to precision medicine – A meta-analysis

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ABSTRACT

Background: Skull base meningiomas are intricately related to neuro-ophthalmic functions and have been related to direct influences on both the afferent and efferent visual pathways due to close contacts with crucial neurovascular structures. The present article reviews the neuro-ophthalmic presentations of these tumors, necessitating the need for precise anatomic information for the delivery of customized diagnostic and therapeutic approaches.

Methods: A literature review was conducted using PubMed and Scopus, focusing on terms related to skull base meningiomas and their neuro-ophthalmic impacts. The review included recent and seminal articles to assess advances in understanding and managing these tumors from an anatomical perspective.

Results: The findings underscore the diversity in neuro-ophthalmic manifestations based on the meningioma's location, affecting visual pathways differently. For instance, meningiomas in the optic nerve sheath typically lead to isolated optic neuropathy and are often managed with radiation therapy. In contrast, those extending from the sphenoid wing require more aggressive approaches like open surgery. This review highlights how the tumor's location dictates the choice of treatment, ranging from conservative management to multidisciplinary surgical interventions.

Conclusion: Proper recognition of the sites of skull base meningiomas results in a treatment tailored to provide therapy aimed explicitly at neuro-ophthalmic outcomes related to the site of the tumors. This approach will not only help to treat effectively but also avoid a wide range of complications and, in turn, increase the effectiveness of the treatment results that a patient will receive. Future studies should aim to refine these anatomical insights toward further advancements in modes of treatment.

Keywords: Neuroanatomical classification, Neuro-ophthalmic presentations, Skull base meningiomas, Targeted therapy, Visual pathways

## **INTRODUCTION**

Neuro-ophthalmic manifestations represent a critical junction since they lie between neurosurgery, oncology, and neurology and demonstrate the complex relationship between suprasellar extension of the tumor and its involvement with the visual pathway. However, tumors of the skull base in general, and skull base meningiomas in particular, are associated with this condition. Those about the anterior visual pathways may present a multitude of

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neuro-ophthalmic symptoms by their proximity to both the afferent and efferent visual pathways. It represents a must-read paper by accounting for the difficulties faced in diagnosing and managing these effects and the considerable consequence on patient outcomes.

Meningiomas in the planum sphenoidale and tuberculum sellae, for example, often lead to visual acuity loss as one of the first presenting symptoms due to their direct effect on the optic chiasm and nerves.<sup>[11]</sup> Pediatric skull base meningiomas further exemplify this complexity, as they frequently involve the orbit and optic nerve sheath, presenting unique challenges due to the smaller anatomical structures and less matured neural pathways in children.<sup>[3]</sup> Moreover, the identification of aggressive midline meningiomas, which, despite being histologically benign, present with severe neuro-ophthalmic symptoms such as vision and hearing loss, underscores the variability in clinical presentations and outcomes based on anatomical location and tumor pathology.<sup>[9]</sup>

Treatment is based on the tumor's location with respect to the neurovascular structures, which includes type and method in surgery and regimens in radiotherapy. Fractionated radiotherapy and stereotactic approaches have been improving development in parallel with the promise of better outcomes to protect the quality of life and reduce long-term deficits in visual function. It, therefore, calls for an advancement in treatment modalities, alluding to the protection of not only the afferent but also the efferent aspects of the visual pathway.<sup>[1,4]</sup>

This paper seeks to briefly shed light on how the anatomical location of meningiomas at the skull base determines neuroophthalmic presentations along the visual pathways, with particular attention to the need to reach a precise diagnosis and targeted interventions to optimize outcomes in neuroophthalmic patients.

## MATERIALS AND METHODS

The search in databases (PubMed and Scopus) was carried out with the keywords "skull base meningiomas," "neuroophthalmic presentations," and the "visual pathways." It should be noted that PubMed emphasizes the most recent works of the authors. Specific important historical references have been included in the study. Inclusion criteria were set for studies examining the neuro-anatomical impacts on neuro-ophthalmic symptoms from skull base meningiomas, with a qualitative meta-analysis performed on selected articles to evaluate their insights into diagnosis and treatment advancements.

## RESULTS

The classification of the neuro-ophthalmic and ophthalmic presentations of the skull base meningiomas presented in

Table 1 considers the influence of the anatomical location on both the afferent and efferent visual pathways. It suggests that most of the manifestations, which range from optic neuropathy to ophthalmoplegia and lower cranial nerve (CN) palsies, are, in turn, the direct result of the proximity of the tumor to vital neurovascular structures. Such a wide diversity of symptomatology calls for a site-specific treatment approach that primarily includes neurosurgical intervention, except for a few cases in which involvement of the sheath of the optic nerve in the orbit is best treated by radiation therapy or simple observation. Examples of such explain that a better knowledge of a growing anatomical diagnosis is necessary for the development of proper treatment strategies for meningiomas of the skull base.

## DISCUSSION

This meta-analysis critically reviews neuro-ophthalmic presentations of skull base meningiomas about the anatomical classification and respective related clinical presentations concerning afferent and efferent visual pathways. We, therefore, emphasize in great detail how significantly the location of a tumor at the skull base corresponds with the vast differences seen in neuro-ophthalmic outcomes [Figure 1]. There is an extensive body of literature on the mapping of these outcomes to specific neuro-anatomic locations, which is mentioned herein and is usually related to clinicians to provide a nuanced understanding to assist in diagnosis and the delivery of targeted therapeutic management.

## Neuroanatomical classification of visual pathways

Meningiomas usually compromise the afferent visual pathway in the region of the optic nerves and chiasm. Those at the planum sphenoidale may be associated with early visual symptoms because this localization of the tumor will have a resultant impact on the optic chiasm, according to Sinaga *et al.*<sup>[11]</sup> Those in the tuberculum sellae are also known to cause bitemporal hemianopia, emanating from the direct compression of the optic chiasm.<sup>[1]</sup>

These, in addition, have a significant impact on the efferent pathway, the motor function of the eye, because they lie at the junction of the cavernous sinus and superior orbital fissure. This is important because between these areas lie very pertinent CNs, which control ocular motor function. Meningiomas in this region will result in some cases of ophthalmoplegia and ptosis, as is the case with our present rare work that involves CNs III, IV, and VI.<sup>[7]</sup>

## Neuro-ophthalmic manifestations

The different neuro-ophthalmic manifestations of diversity with varying presentations at every site inside the base of the skull underline the significance of accurate anatomical

Anatomical location	Afferent pathway manifestations	Efferent pathway manifestations	Treatment approach
Optic nerve sheath (orbit)	Optic neuropathy (disc edema or normal appearance)	Proptosis, optic neuropathy	Primarily radiation therapy; observation if no worsening
Sphenoid wing, clinoid (intracranial to intraorbital)	Optic neuropathy, vision loss	N/A*	A multidisciplinary approach often requires open neurological surgery to decompress intracranial components.
Sellae region	Vision loss, bitemporal hemianopia	N/A	Open surgery for tumor resection
Temporal, parietal, occipital regions	Homonymous hemianopia (from mass effect and edema)	N/A	Depends on the extent possible open surgery or radiotherapy
Cavernous Sinus	N/A	Ophthalmoplegia affecting CNs III, IV, V1, V2, and VI	Open surgery potential radiotherapy depending on tumor growth and symptoms
Cerebellopontine angle	N/A	Facial pain, hearing loss, vestibular dysfunction (CNs V, VI, VII, and VIII affected)	Open surgery, tailored to symptomatology and tumor size
Clivus	N/A	Abducens nerve palsy (CN VI)	Neurosurgical resection typically required
Foramen Magnum	N/A	Downbeat nystagmus, lower cranial neuropathies	Neurosurgical intervention is often necessary

Table 1: Neuro-ophthalmic and ophthalmic manifestations of skull base meningiomas by anatomical location.

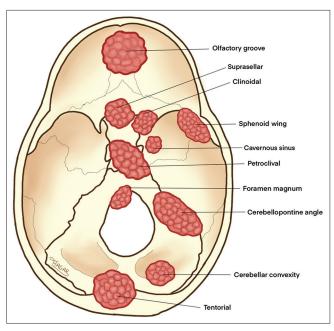


Figure 1: The anatomical locations of skull-based meningioma.

data in diagnosing and management of the skull base meningiomas. For instance, Rzehak *et al.*<sup>[10]</sup> also reported that meningioma of the optic nerve sheath frequently leads to pure optic neuropathy and can be managed conservatively by radiation when limited to the orbit. In clear contrast, the presence of meningioma from the sphenoid wing in the orbit will require aggressive surgical approaches due to complex anatomical involvement.<sup>[4]</sup>

All this is also of the essence in pediatric cases, where the size of the anatomical structures and variation in the behavior of the disease make this necessary.<sup>[3]</sup> The recognition that the meningioma subtypes bearing TRAF7 mutations tend to confer an aggressive phenotype has lent momentum to the push for targeted therapies to modulate these underlying genetic pathways.<sup>[9]</sup>

Integrating these insights, our review not only supports established clinical practices but also highlights emerging areas where further research could significantly impact patient outcomes. For instance, advancements in minimally invasive surgical techniques and radiosurgical interventions offer promising alternatives to traditional approaches, particularly in complex cases where conventional surgery poses significant risks.<sup>[6,8]</sup>

Specifically, about the management approach, what is essential is that meningiomas are localized to the intracranial and intraorbital compartments. Intracranial-type meningiomas, however, with further growth into the orbital compartment, such as in cases of sphenoid wing or clinoid processes as described by Tobias *et al.*<sup>[12]</sup> are tumors that, most of the time, require a more aggressive approach, even decompression of the intracranial and intraorbital components, by open surgery. On the other hand, intraorbital meningiomas, especially those that primarily involve the optic nerve sheath, can be well managed with radiation therapy alone, hoping to save the vision while keeping the surgical risks at a minimum.<sup>[10]</sup>

Furthermore, another feature that could be present is the involvement of numerous CNs by skull base meningiomas, which present complex neuro-ophthalmic syndromes. For example, meningiomas around the cavernous sinus will affect CNs III, IV, and VI, leading to multiple symptoms, such as diplopia and ptosis. In such cases, aggressive resection of the tumor and fine preservation of nerve functions should be balanced.<sup>[7]</sup> In contrast, meningioma at the cerebellopontine angle can involve CNs V–VII with the presentation of facial pain, hearing loss, and vestibular dysfunction – all significant baseline data for surgical planning.<sup>[5]</sup>

The importance of this to meningiomas involving visual and cognitive function in general cannot be overstated. Although primary visual symptoms are often recognized, the broader cognitive and neurological effects of these tumors, especially those with frontal and temporal lobe involvement, are also significant. There are reports of studies showing that cognitive and sensory post-surgery deficits are expected in the case of patients with larger tumors or those that occur close to critical brain structures.<sup>[2]</sup> The findings underline the necessity of preoperative planning and postoperative rehabilitation in the case of the occurrence of cognitive and sensory deficits.

The advent of radiological techniques has dramatically altered the approach to managing skull base meningiomas. Procedures such as Gamma Knife radiosurgery provide highly focused and, hence, minimally damaging procedures in critical locations where complications related to damage to adjacent normal tissues would be devastating – for example, the optic nerves. Such advancements have not only improved local control rates but also reduced complications associated with traditional surgery.<sup>[6]</sup>

Genetic studies have started showing some molecular ways that the development of meningiomas is initiated. New findings, like the identification of mutations, including TRAF7, raise new hopes for targeted therapies that could make a difference in patients with aggressive or recurrent meningiomas.<sup>[9]</sup> These advances, therefore, emphasize the prospect of using personalized medicine approaches for more effective and tailored treatment modalities to manage skull base meningiomas.

## CONCLUSION

Our review underscores the critical importance of understanding the neuro-anatomical locations of skull base meningiomas and their relationship to neuro-ophthalmic and ophthalmic manifestations. The findings from our analysis highlight that both afferent and efferent visual pathways are distinctly affected depending on the tumor's precise anatomical site. This delineation is crucial for tailoring diagnostic and therapeutic approaches to optimize patient outcomes. By integrating the latest advancements in surgical techniques, radiotherapy, and genetic insights, our paper contributes to a more nuanced comprehension of skull base meningiomas, paving the way for enhanced management strategies that align with the complex nature of these tumors.

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### **Ethical approval**

The Institutional Review Board approval is not required.

### Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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#### **Conflicts of interest**

There are no conflicts of interest.

## Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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