# A Curious Diagnosis Causing Unilateral Proptosis

**Elyse Banister, OD**
The Villages VA Outpatient Clinic,
The Villages, FL

## ABSTRACT

*Background*: Sphenoid wing meningioma is one of the most common extraconal tumors and can present in various ways. Meningiomas tend to affect women more than men and tend to present in individuals over the age of 50. Sphenoid wing meningiomas usually do not need treatment, unless they threaten the optic nerve or rapidly invade surrounding brain structures. *Case Report*: A 48-yr-old woman presented with a complaint of headaches for the past three to four months, ocular pain, and a "yellow fluid pocket" in the left eye for the previous month. Ocular exam revealed unilateral proptosis of the left eye. Neuroimaging revealed a left sphenoid wing meningioma. Referral to neurology ultimately resulted in surgical removal of the intracranial lesion. The patient is currently being followed with yearly neurological and optometric exams. This case report will review the pathogenesis, prognosis, and management of sphenoid meningiomas. *Conclusion:* Meningiomas are considered to be benign lesions of the brain. They were once believed to be caused by hormonal variation, in part due to their predilection to affect women more than men. It is now believed that the genetic disorders neurofibromatosis type 2 and monosomy 22 are the culprits, as most meningiomas have been found to contain one or both mutations. Once stability of the surgical tumor resection has been established, management includes annual eye examination and neuroimaging (by magnetic resonance imaging (MRI) or computed tomography (CT) scans).

## INTRODUCTION

When a patient presents with unilateral proptosis, several alarming conditions including intra-orbital lesions can enter an optometrist's mind. Often, attentive listening to the patient's complaints and duration of symptoms can point toward a correct diagnosis.

The following case report will emphasize the importance of detecting and investigating unilateral proptosis before vision is severely impacted, and review the pathogenesis, treatments, and prognosis of orbital meningiomas.

## CASE REPORT

### History

A 48-year-old Caucasian woman presented emergently to the optometry department with complaints of increasing headaches over the past four months, accompanied by blurred vision, unilateral eye pain and the intermittent appearance of a "yellow fluid-filled sac" on the temporal conjunctiva, all in the left eye, over the past month. She also mentioned that her friend had noticed on several occasions that her left eye had a bulging appearance, accompanied by a swollen eyelid that would regress, only to return the next morning. Photos taken by her friend were shown to the provider at the exam to further clarify her varying appearance. The pain level was reported to be 7/10 and described as feeling like a "thumb is pushing on the back" of her eye. She denied double vision. Her last eye exam was also an emergency exam three months earlier with a different provider with similar complaints, resulting in a diagnosis of left preseptal cellulitis. One month prior to that appointment, another provider noted

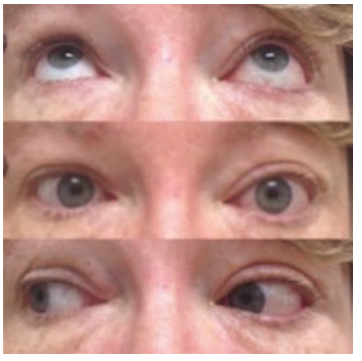
trace left periorbital edema due to presumed internal hordeolum. Her complaints at that visit included the left upper lid becoming intermittently "puffy" with a constant pressure sensation.

Her medical history was positive for post-traumatic stress disorder (PTSD), bipolar disorder, chronic obstructive pulmonary disease (COPD), depression, cutaneous melanoma, and anxiety. She had a previous history of substance abuse and current history of daily tobacco use. Her family history was positive for glaucoma in her maternal grandmother.

**Clinical Examination**

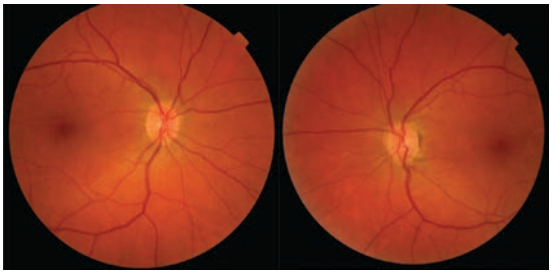
At presentation, habitual refraction was OD -1.25-1.25x 087 (20/20) and OS -0.75-1.25x 111 (20/30) . Subjective refraction and best corrected visual acuity was OD -1.25-1.00 x 092 (20/20) and OS -1.00-0.50 x 110 (20/20). Pupils were round and reactive to light without afferent defect. Versions were smooth with 10% restriction on lateral and medial gaze in the left eye, with no diplopia or pain on eye movement. Confrontation visual field testing was full to finger-counting in both eyes. Goldmann applanation tonometry (GAT) yielded pressures of 12mmHg OD and 12mmHg OS. Gross external examination revealed visible proptosis with lid lag of the left eye (Fig. 1). Color vision was normal. A slight decrease (5%) was noted on red desaturation testing of the left eye. Lid crease was measured at 6mm OD and 9mm OS. Hertel exophthalmometry measured 18mm OD and 23mm OS with a base of 104.

Figure 1: *Initial presentation shows slight proptosis of the left eye (center) with medial gaze restriction (lower). The right eye appears esotropic (center). The left bulbar conjunctiva appears slightly injected compared to that on the right, which is most obvious in right gaze (lower) and up gaze (upper).*



Biomicroscopy was unremarkable, except for mild bilateral meibomian gland dysfunction and conjunctivochalasis temporally OS (there was no visible "yellow" sac observed on the temporal bulbar conjunctiva OS). Dilated fundus exam revealed small and symmetric C/D of 0.20/.20 OD and OS. Both discs were perfused, flat, and without edema, hemorrhage, or pallor (Fig. 2). A spontaneous venous pulse was noted to be present OD, and absent OS. The macula was flat and intact OU. There were no peripheral retinal breaks or detachments in either eye.

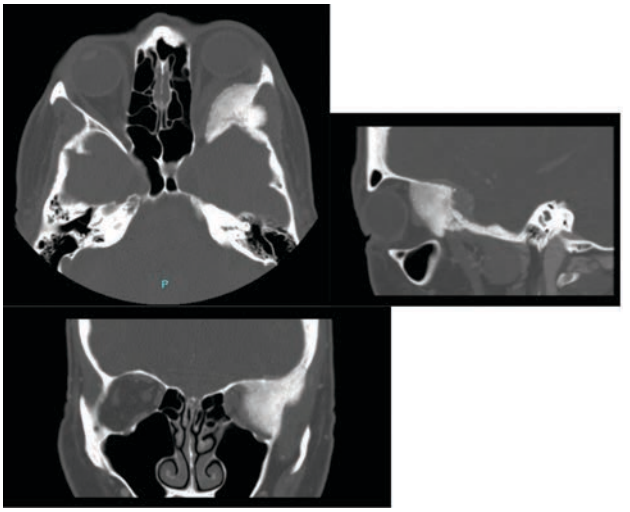
Figure 2: *(left) The right optic nerve appears healthy and well-perfused with distinct margins. (right) The left optic nerve is well-perfused but shows subtle blurring of the inferior and superior nasal margins. Paton's lines were not present in either eye and there was no detectable spontaneous venous pulse in the left.*



**Diagnosis**

Due to the asymmetric Hertel readings, lack of spontaneous venous pulse in the left eye, and complaint of headache, CT of the orbits was ordered urgently (less than two weeks) with radiology. The radiology report diagnosed an intraosseous meningioma of the left greater and lesser sphenoid wing. Radiology also noted that "osteoblastic metastatic lesions can occasionally result in similar findings". The mass sat in the anterior aspect of the temporal bone and the floor of the middle cranial fossa, and extended to the anterior clinoid process. It measured approximately 3 cm in transverse diameter by 1 cm in thickness. There was no apparent narrowing of the superior orbital fissure or optic canal. The left optic nerve was displaced medially from the lesion, while the left lacrimal gland was displaced anteriorly. The lateral rectus was directly affected. Visible proptosis of the left globe was also apparent in the CT scan (Fig. 3 and Fig. 4a,b)

Figure 3: *Pre-operative CT scans without contrast revealed visible proptosis of the left globe (upper left). The left-wing sphenoid wing meningioma is hyperintense, similar to surrounding bone structures (all three images) and appears to show early invasion of the left temporal bone (most obvious in the upper left and lower images). The optic nerve is impinged upon and shifted medially (upper left) due to reduction of the extraconal and lateral intraconal space.*



**Treatment and Follow Up**

Upon receipt of the radiology reports, the patient was referred to a neuro-ophthalmologist for further evaluation and exploration of treatment options, and was seen three weeks after the CT scan. At that exam, vision remained stable. However, early left optic neuropathy was suspected. A trace left afferent pupillary defect was noted, although there was no pallor, hemorrhage, or elevation of the left optic nerve. 24-2 visual field testing was normal in both eyes. Due to the possibility of permanent damage to the left optic nerve, the patient was referred to a neurologist with a recommendation of surgical removal of the meningioma. At the neurology exam two weeks later, a sensory-related deficit of the left trigeminal nerve (CN5) was noted in the cheeks and mandible. The patient was informed that, due to optic nerve displacement, surgical resection was recommended over observation or radiation. She was educated on the possible risks of intracranial and intraorbital surgery, including blindness, stroke, brain damage, weakness, or >>>and<<< cerebrospinal fluid (CSF) leakage. After providing informed consent, the patient underwent surgical resection. A pre-operative MRI was scheduled two weeks after the neurology appointment, and a pre-operative exam was scheduled one month after the MRI. Surgery was performed four days after the pre-operative examination. Surgery involved left craniotomy with left orbiotomy. Porex® and titanium mesh were used for reconstruction of the orbital roof and cranioplasty. Biopsy was not performed prior to lesion removal (Fig. 4: Pre- and post-operative MRI images).

**Post-Surgical Results**

The lesion was graded as a WHO-I meningioepithelial tumor. The patient returned for her first post-operative exam with a complaint of vertical and lateral double vision (Fig. 5): this was felt to be secondary to resolving periorbital and intraorbital edema and resolved spontaneously over subsequent examinations with the surgeon. Following surgery, best-corrected visual acuity remained 20/20 in both eyes with stable refractive error. Red desaturation and afferent pupillary defect were no longer present. Optical coherence tomography (OCT) has shown no signs of nerve

fiber loss attributed to previous optic nerve impingement (Fig. 6). The patient continues to be followed annually by both neurology and optometry, and has experienced no reoccurrence over the past six years.

Figure 4: *(upper left) Pre-operative axial T2-weighted MRI (without fat suppression). There is visible intrusion of the lesion into the lateral orbital space of the left eye. The lateral rectus is not visible. The optic nerve is free of tumor but is being compressed by the lesion. Compared to the CT scan, the MRI provides a better view of the extent of invasion of the lesion into the temporal extraconal and intraconal space. (upper right) Pre-operative axial T1 weighted after contrast without fat suppression. The extent of the sphenoid wing meningioma invasion is more evident. (center left) One-month post -operative axial T2-weighted MRI (without fat suppression). (center right) One-month post-operative axial T2-weighted MRI (with fat suppression). The surgical resection has reduced the optic nerve compression and the lateral rectus is now slightly visible. There is some post-operative swelling around the implant. Proptosis is still evident. (lower) Four-year post-operative axial T2-weighted MRI (without fat suppression). The orbital structures have returned to their normal positions. Proptosis has reduced. The lateral rectus is fully visible. The post-operative swelling around the implant has fully resolved.*

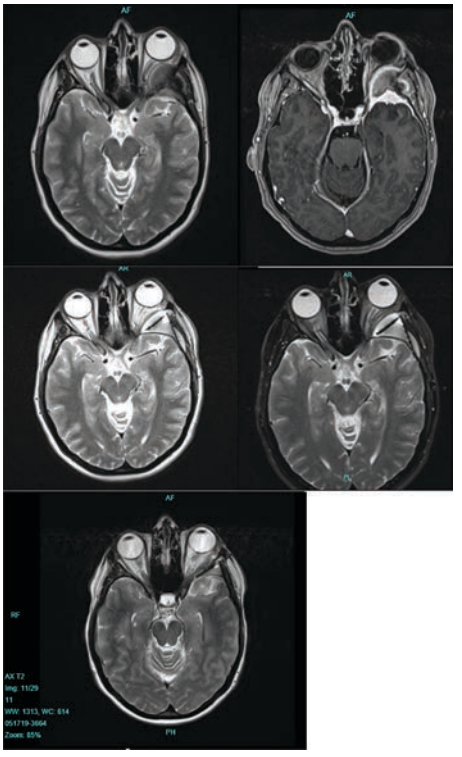


Figure 5: *Post-operative images show retro-positioning of the left globe resulting in narrowing of the palpebral fissure (center). Medial gaze has recovered (lower), but left hypotropia (most obvious in the lower image) resulted in temporary vertical diplopia.*

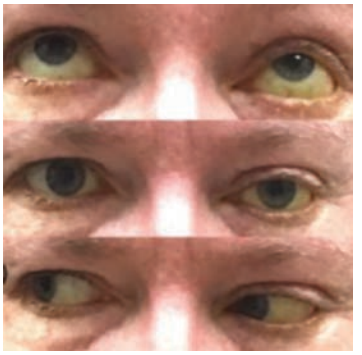
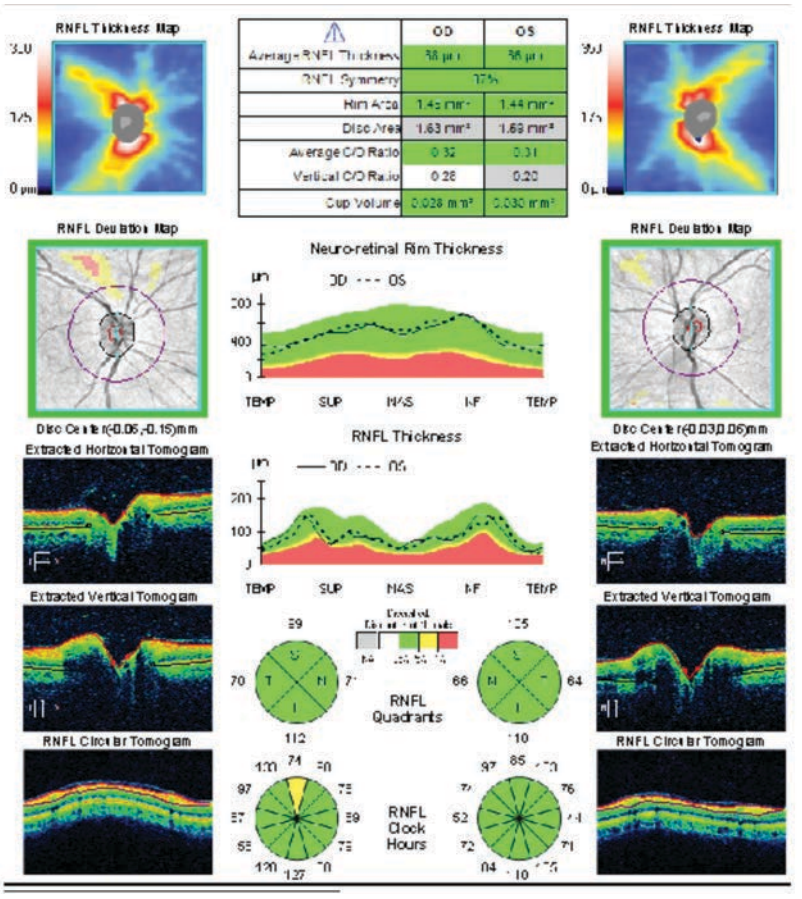


Figure 6: *Optical coherence tomography (OCT) four years post-operative shows no sustained left optic nerve damage following previous optic nerve impingement.*

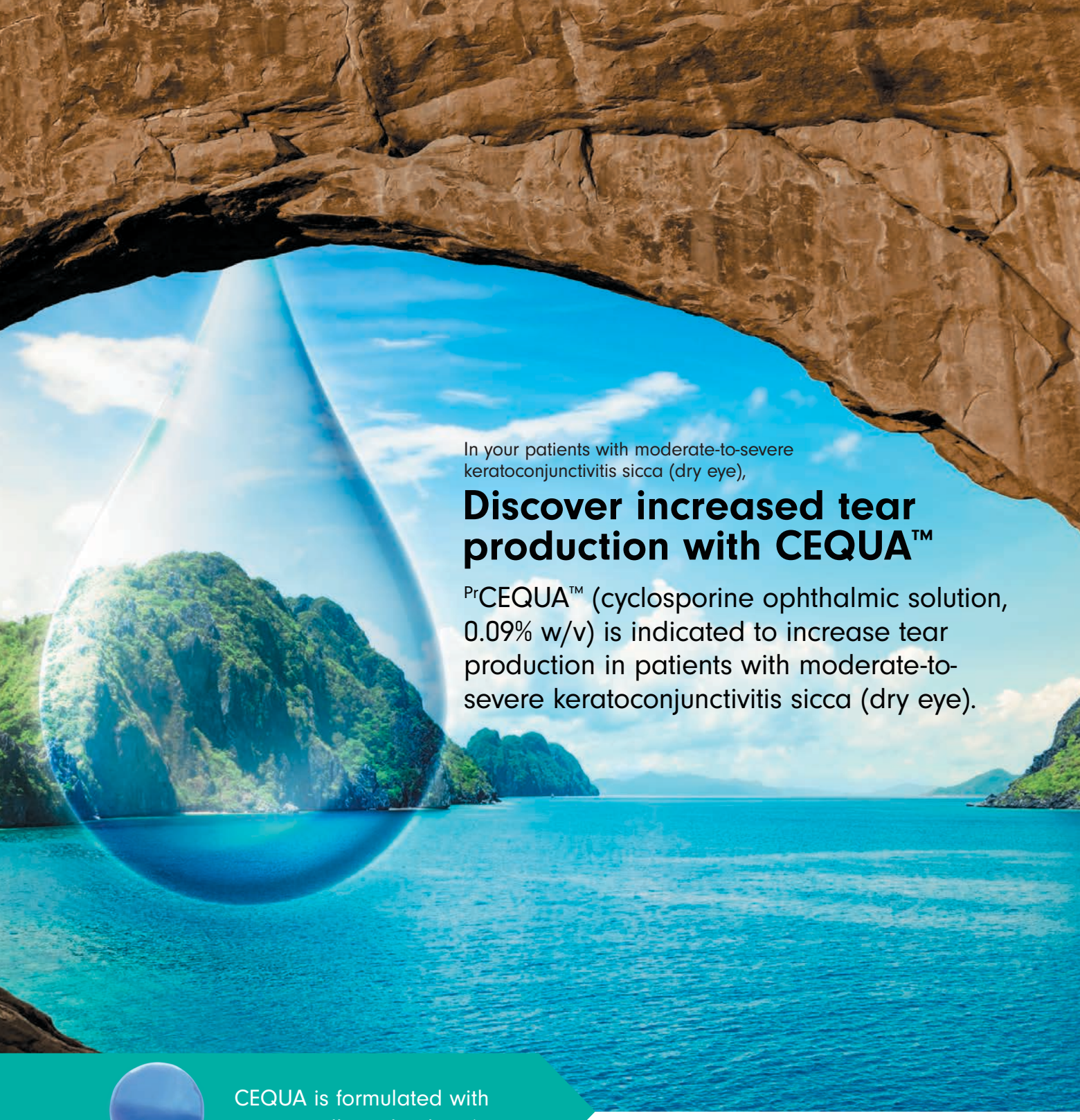



## Epidemiology and Classification

Meningiomas can occur in many locations within the brain. This review will focus exclusively on sphenoid meningiomas, the most common intracranial tumor to invade the orbital space, with an incidence of 2 cases per 100,000 people per year. Caucasians are affected more than any other ethnicity, and women (most often those over the age of 50) are affected more than men. Sphenoid meningiomas account for nearly 20% of all meningiomas. The World Health Organization (WHO) has a tumor classification system which pathologists use when describing the tumor in their formal diagnosis. Lesions are divided into three classifications (I- Benign, II- Atypical, and III- Malignant) and further described by their microscopic shape and composition (Table 1). Approximately 90% of sphenoid meningiomas are found to be WHO classification 1- benign.[1,2]

Table 1: *WHO Meningioma Classifications*

| WHO tumor classification – Meningiomas (*) = most common | |
|---|---|
| I – Benign | *Meningioepithelial, *Fibrous, *Transitional, Psammomatous, Angiomatous, Microcytic, Secretory, Lymphoplasmacyte, Metaplastic |
| II –Atypical | Choroid, Clear cell |
| III – Malignant | Papillary, Rhabdoid, Anaplastic |



In your patients with moderate-to-severe keratoconjunctivitis sicca (dry eye),

# Discover increased tear production with CEQUA™

PrCEQUA™ (cyclosporine ophthalmic solution, 0.09% w/v) is indicated to increase tear production in patients with moderate-to-severe keratoconjunctivitis sicca (dry eye).

CEQUA is formulated with nanomicelle technology*

*Clinical significance is unknown

Cequa™
(cyclosporine ophthalmic solution) 0.09%

SUN PHARMA

Sphenoid wing meningiomas are also commonly described as globoid or en plaque tumors based on their radiologic shape. While globoid tumors are nodular in appearance, en plaque meningiomas are flat and follow the contour of the sphenoid bone. Globoid tumors can be further sub-classified by their location on the lesser sphenoid wing: medial, middle, and lateral. Meningiomas that occur in the middle sphenoid wing are more likely to affect the optic nerve and invade the orbit, while medial meningiomas are most likely to invade the optic canal. Lateral meningiomas are the least likely to affect orbital structures.[1]

### Presenting Signs and Symptoms

The most common signs and symptoms associated with sphenoid meningiomas that optometrists should be aware of are unilateral proptosis, headache, and blurred vision. Other common findings include diplopia, swelling around the eye, facial pain or numbness, altered mental status, and seizures. Similar to other ocular and intracranial tumors, sphenoid meningiomas that begin to invade the cavernous sinus can present with lateral double vision secondary to impingement of the abducens nerve (CN6), which is usually the first nerve to be affected. Additionally, if the trigeminal (CN5) nerve is affected, the patient will report ipsilateral facial pain or numbness. Horner's syndrome can be the presenting sign of a meningioma by compressing the ophthalmic division of the internal carotid artery within the orbit.[3] In rare cases, intracranial inflammatory pseudotumor can masquerade as a sphenoid meningioma, with similar presenting symptoms of unilateral proptosis and vision decline. It is often difficult to differentiate inflammatory pseudotumor from a sphenoid meningioma by imaging alone. Surgical decompression, biopsy, and histopathological evaluation is the main way to rule out inflammatory pseudotumor, as the radiological and clinical appearances closely resemble those of a sphenoid meningioma.[4]

### Pathogenesis

Meningiomas are slow-growing CNS tumors arising from cap cells of the outer arachnoid layer. The genetic disorder neurofibromatosis type 2 (NF2, an autosomal dominant tumor-forming disease of the nervous system characterized by bilateral acoustic neuromas) confers a high risk for developing meningiomas; this is not to be confused with neurofibromatosis type 1 (NF1), which correlates with skin melanoma. The NF2 locus on chromosome 22 encodes the tumor-suppressing protein merlin (also known as schwannomin or neurofibromin 2). A deletion or mutation at the NF2 locus causes neurofibromatosis type 2. This is the most commonly found mutation within the tumor, and patients with this mutation are also at an increased risk for WHO classification III-malignant meningioma. Monosomy 2 (specifically accompanied by the deletion of NF2 locus) is present in almost 50% of all meningiomas. In one study, NF2 mutation-containing meningiomas were found in menopausal women with monosomy 22.[5] WHO-III classification malignant meningiomas have also been found to have deletions or insertions on chromosomes 9,10,14, and 18.[6]

**Risk Factors**

There are several risk factors for developing a meningioma. Greater age, especially over the age of 65, carries an increased risk. Women are affected two times more often than men. Alternatively, men are three times more likely to have a malignant meningioma. Children are rarely affected. Exposure of the cranium to high-dose radiation increases the risk of intracranial tumors. Meningiomas in women have been found to contain estrogen, progesterone, and androgen. Therefore, meningiomas have historically been thought to be influenced by hormones. However, recent studies investigating hormone-related causes, such as oral contraceptive use or hormone replacement therapy, have remained inconclusive.[7-9] Interestingly, recent research actually suggests a small decrease in the occurrence of meningiomas in female smokers and a small increased occurrence in male smokers, and the relation between smoking and meningiomas remains inconclusive.[7,8]

Meningiomas can show accelerated growth in the third trimester of pregnancy. Studies have suggested that this increased growth rate results from hemodynamic (blood flow) changes, whereas hormone-mediated tumor cell proliferation is not believed to play a role. The most common symptoms that these patients experience are changes in vision (CN2) and facial paralysis (CN5), although other cranial nerves can also be affected.

**Prognosis and Management**

Meningiomas are not known to metastasize, but medial sphenoid meningiomas do carry a high risk of morbidity and mortality due to their proximity to important vascular and neurologic structures. Tumor growth is usually slow and can go undetected without imaging. Permanent visual loss has been reported in up to 35% of cases, but the visual outcome is usually excellent for patients whose vision has not yet been affected.[2,3,10] Benign meningiomas respond better to treatment.[10] Surgical resection with microsurgery is the preferred treatment for sphenoid meningiomas due to the low rate of tumor reoccurrence, but various radiation treatments, such as stereotactic radiosurgery, can also be used in certain cases. Re-growth can occur in 1 out of 10 patients who undergo complete surgical removal, compared with 1 out of 5 patients who have an incomplete removal. Lower-grade lesions have a lower rate of recurrence. Medial meningiomas carry the highest risk of regrowth: 50% over 10 years.[1,2,11] Surgical removal of the tumor during pregnancy is not recommended, as the tumor often regresses naturally postpartum. Due to the risk of uterine and fetus hypoperfusion under anesthesia, surgery is reserved for cases with progressive neurological deficit, hydrocephalus, or brainstem herniation.[12,13] Radiosurgery is safe for skull-based meningiomas and should be used when patients are not good surgical candidates, but should be avoided if the lesions are close to radio-sensitive neurological structures, which include the optic chiasm, prefrontal cortex, and hippocampus.[14] Radiation therapy is most commonly used for recurrent lesions but has historically been reserved for inoperable, malignant or progressive meningiomas. It is no longer recommended as it minimally impacts tumor regression and carries a high rate of toxicity.[15]

Due to the slow growth of meningiomas, yearly eye examination after surgical resection is likely adequate, providing that stability has been established by neuroimaging or the patient has been discharged from neuro-ophthalmology into optometric care. Examinations should pay close attention to any changes in the patient's extraocular motility, visual acuity, visual field deficits, and OCT RNFL. Patients with higher-grade tumors should be followed more frequently and advised to return immediately if headaches, diplopia, blurred vision, or facial pain/numbness occurs. The patient should also be followed by neurology for yearly imaging to detect re-growth.

## CONCLUSION

Optometrists are likely to be the first providers to encounter a patient with symptoms related to a sphenoid meningioma. Although sphenoid wing meningiomas are not considered a metastatic risk, they are locally invasive, and cause varying degrees of morbidity. Patients should be monitored at least annually, paying close attention to eye asymmetry with exophthalmometry, changes in acuity, return of headaches, and optic nerve changes using OCT or photos. Proptosis should be assumed and further ruled out with exophthalmometry in cases where there is inferior scleral show in the presence of eyelid edema and gaze restriction. Consequently, this case demonstrates the importance of looking directly at patients at each exam, being sure to annotate any asymmetric facial and ocular features, while also evaluating potential causes for a complaint of intermittent preseptal, periorbital or conjunctival edema. ●

**CORRESPONDING AUTHOR:**
Elyse Banister – Elyse.banister2@va.gov

## REFERENCES


1. Sughrue ME, Ritkowski MJ, Chen J, et al. Modern surgical outcomes following surgery for sphenoid wing meningiomas. J Neurosurg 2013 Jul;119(1):86-93.
2. Verma SK, Sinha S, Sawarkar DP, et al. Medial sphenoid wing meningiomas: Experience with microsurgical resection over 5 years and a review of literature. Neurol India. 2016 May-Jun;64(3):465-75.
3. Chaichana KL, Jackson C, Patel A, et al. Predictors of visual outcome following surgical resection of medial sphenoid wing meningiomas. J Neurol Surg B Skull Base. 2012 Oct; 73(5):321-326.
4. Kasliwal MK, Suri A, Gupta DK, et al. Sphenoid wing inflammatory pseudotumor mimicking a clinoid meningioma: case report and review of the literature. Surg Neurol. 2008 Nov;70(5):509-13.
5. Tabernero M, Jara-Acevedo M, Nieto AB, et al. Association between mutation of the NF2 gene and monosomy 22 in menopausal women with sporadic meningioma. BMC Med Genet. 2013 Oct 30;14:114.
6. Choy W, Kim W, Nagasawa D, et al. The molecular genetics and tumor pathogenesis of meningiomas and the future directions of meningioma treatments. Neurosurg Focus. 2011 May; 30(5):E6.
7. Fan Z, Ji T, Wan S , et al. Smoking and risk of meningioma: a meta-analysis. Cancer Epidemiol. 2013 Feb; 37(1):39-45.
8. Claus EB, Walsh KM, Calvocoressi L, et al. Cigarette smoking and risk of meningioma: the effect of gender. Cancer Epidemiol Biomarkers Prev 2012 Jun;21(6):943-50.
9. Claus EB, Calvocoressi L, Bondy ML, et al. Exogenous hormone use, reproductive factors, and risk of intracranial meningioma in females. J Neurosurg. 2013 Mar;118(3):649-56.
10. Nakamura M, Roser F, Jacobs C, et al. Medial sphenoid wing meningiomas: clinical outcome and recurrence rate. Neurosurgery. 2006 Apr;58(4):626-39.
11. Ouyang T, Zhang N, Wang L, et al. Sphenoid wing meningiomas: surgical strategies and evaluation of prognostic factors influencing clinical outcomes. Clin Neurol Neurosurg. 2015 Jul;134:85-90
12. Kurdoglu Z, Cetin O, Gulsen I, Dirik D, Bulut MD. Intracranial Meningioma Diagnosed during Pregnancy Caused Maternal Death, Case Rep Med. 2014;2014:158326.
doi:10.1155/2014/158326
13. Saha S, Lata I, Gupta D. Management of pregnant female with meningioma for craniotomy. J Neurosci Rural Pract. 2010 Jan-Jun; 1(1): 35-37.
14. Combs SE, Ganswindt U, Foote RL, et al. State-of-the-art treatment alternatives for base of skull meningiomas; complementing and controversial indications for neurosurgery, stereotactic and robotic based radiosurgery or modern fractionated radiation techniques . Radiat Oncol. 2012 Dec; 7:226
15. Sherman WJ, Raizer JJ. Chemotherapy: What is its role in meningioma?. Expert Rev. Neurother. 2012 Oct; 12(10);1189-1195.