



Original Article

# Evidence-based treatment of cavernous sinus meningioma

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## ABSTRACT

**Background:** Cavernous sinus meningioma (CSM) causes gradual ophthalmoplegia and may eventually cause compression of the chiasma. The tumor is often histologically benign, slow growing, and seldom life threatening. Besides visual limitation, ophthalmoplegia causes emotional stress and disability. The tumor is commonly treated by operation, radiation, or both. While effective in varied degrees, the treatments, especially radical operation, are associated with unacceptable mortality and morbidity. The question remains as to what treatment approach is most conducive to longest survival with minimum disability.

**Methods:** In five patients, operation, radiotherapy, or both were based on presenting symptoms or delayed based on a doctor-patient decision, seeking the most desirable and suitable option that potentially offers longer life with less disability.

**Results:** Five patients were followed from over 2 to almost 5 decades: two patients are still alive, 25 and 28 years after craniotomy and radiation. One was treated conservatively for 15 years before requiring craniotomy and radiation. One was followed for 45 years without needing craniotomy or radiation, despite enlargement of the tumor. One was followed for 36 years after craniotomy. Patient did not have radiation. Craniotomy consisted of removing enough tumor to diminish symptoms without causing complications. There were no mortalities or complications.

**Conclusion:** The patient number is not large enough to make a broad conclusion. However, the individualized treatments and long follow-ups, together with detailed literature review, suggest that CSM requires individualized staged treatments based on each patient's condition. A period of "wait and see" before starting with either surgery or radiation treatment can benefit the patient.

**Keywords:** Cavernous sinus meningioma, Conservative treatment, Evidence-based treatment

## INTRODUCTION

The cavernous sinus is a crowded anatomic region. In addition to cranial nerves III, IV, VI, and the frontal branch of the V<sup>th</sup> nerve, it contains the carotid artery and receives venous drainage from the orbit and basilar plexus. Cavernous sinus meningioma (CSM) gradually compresses the above nerves and artery causing varied degrees of unilateral ophthalmoplegia. It may also cause compression of the chiasma over a long period of time. Histologically, the tumor is often benign and slow growing. The tumor is commonly treated by operation or radiation; while effective, both treatments have limited and partial therapeutic effects. Operation can be associated with death and disability; radiation can be associated with long-term complications.

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Meanwhile, without treatment, the tumor's spontaneous growth seldom threatens life and the ophthalmoplegia may take a long time to occur or become disturbing enough to limit the patient's daily activity. The question then remains as to what approach is most appropriate for each patient to potentially give a longer survival with less disability. This paper represents 2 to almost 5 decades of follow-up of five patients in whom operation, radiotherapy, and/or conservative management were done based on the evidence of presenting symptoms and a doctor-patient decision as to the best option to offer a longer life with less disability. Despite the small patient number, the results together with a review of pertinent available information from the literature may be of help in planning treatment measures.

## MATERIALS AND METHODS

In each patient, the potential treatment risks were assessed and presented to the patient, and a treatment plan was made for what was thought to likely offer the lowest chances for morbidity and mortality. Treatment was started based on presenting symptoms and their degree of impact on the patient's life, goals, and outlook. No specific routine or guideline was used, for at the time there was none. The patients were followed, so far for over 2 to almost 5 decades. A summary of each patient is presented, and the results are compared with those available in the literature.

### Presentations

#### Patient 1

A 55-year-old man presented in 1970 with mild diplopia caused by partial left VI<sup>th</sup> nerve palsy. Cerebral angiography showed no specific related abnormality. Due to no definite diagnosis, a plan was made for conservative management. The diplopia was corrected with glasses. Over a period of several years, he developed partial III<sup>rd</sup> nerve palsy with mild drooping of the eyelid, but retained normal vision.

The mild eyelid droop was corrected by a small attachment to his glasses and he was able to continue his work as a dentist. In 1976, what then was called an Electric and Musical Industries (EMI) scan showed a lesion lateral to the sella that could not be easily interpreted [Figure 1a], so conservative management was continued. Six years later, he had developed complete III<sup>rd</sup> nerve palsy together with closure of the left eye, and a computed tomography (CT) scan showed clear evidence for CSM [Figure 1b]. He also developed partial bitemporal loss of vision. While he did not mind the loss in the left eye since the eye was closed, conservative management no longer seemed reasonable. Despite the presence of some chronic lung disease, in 1983 an operation to remove just the part of the tumor compressing the chiasma



Figure 1: (a) 1976, (b) 1982.

and right optic nerve was recommended, and he accepted it. This returned the visual field in the right eye to near normal. To maintain his vision, radiation therapy was done. His vision remained stable until 5 years later when 28 years after the onset of diplopia, he died at age 83 from unrelated causes.

#### Patient 2

A 51-year-old woman began having slight diplopia in 1971 caused by the left VI<sup>th</sup> nerve palsy without much interference with her daily activities. In 1975, a CT scan showed a tumor in the cavernous sinus on the left side [Figure 2a]. Because the diplopia had not progressed much and did not cause any inconvenience, and because the patient did not want any complications, an operation was not done. Instead, she was followed with periodic CT scan assessments [Figure 2b-e].

Three years later, the diplopia did interfere with her daily activities, so the left lateral rectus muscle was shorted by an ophthalmologist, which corrected her diplopia. Her condition remained stable without the appearance of any related symptoms, despite enlargement of the tumor. She died 40 years after the onset of diplopia at age 91, from ovarian cancer. The histology of the tumor was never determined, but

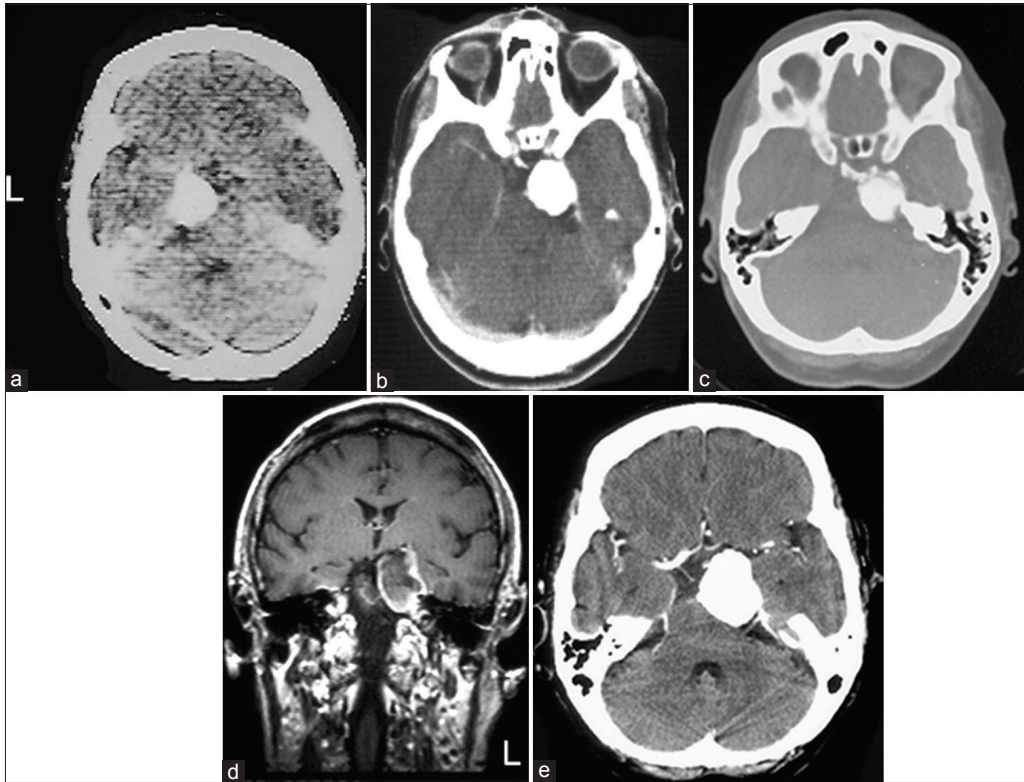


Figure 2: (a) 1975, (b) 1983, (c) 1984, (d) 1989, (e) 2002.

upon presentation of her scans on numerous occasions, no one doubted meningioma as the diagnosis.

**Patient 3**

A 38-year-old woman with mild proptosis, double vision from III<sup>rd</sup> nerve palsy, and decreased visual acuity in the left eye, was admitted for evaluation in 1981 [Figure 3a]. She was diagnosed with sphenoid wing meningioma and operated in 1982. At operation, a small portion of the tumor was removed. However, a radical removal was avoided. She did not have any radiation treatment. In follow-ups, except for the III<sup>rd</sup> nerve palsy, she did not develop any other complications despite the tumor growing slowly [Figure 3b-d]. Throughout the years, she remained active and healthy until she died in 2018 at age 88, of ovarian cancer.

**Patient 4**

A 48-year-old man presented in 1994 with diplopia caused by the left VI<sup>th</sup> nerve palsy. The scan showed CSM (scan no longer available). At operation, partial removal of the tumor was done without entering deep in the cavernous sinus and was followed by conventional radiation therapy. Postoperatively, his diplopia recovered and his scans show the residual tumor [Figure 4a-c]. The histology is presented in Figure 4d. The patient was able to return to work and a

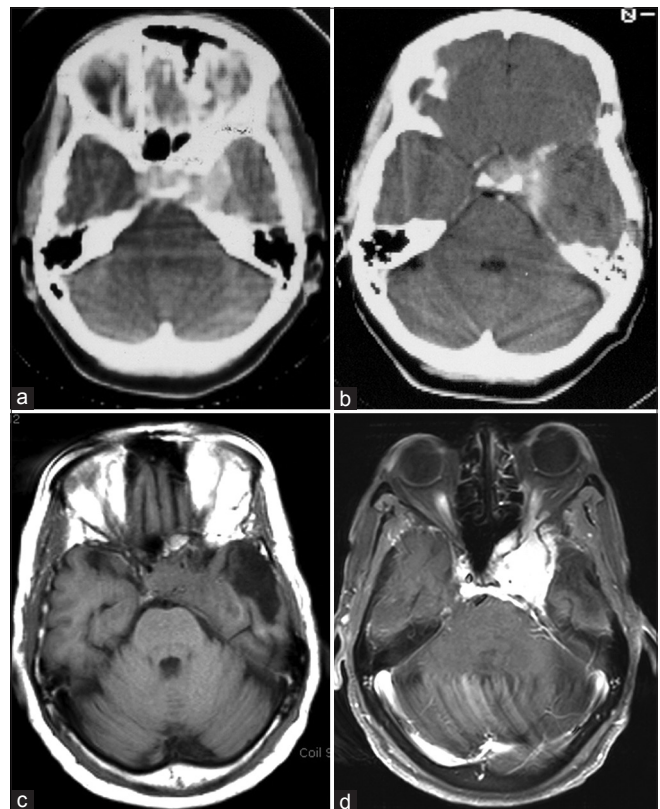


Figure 3: (a) 1981, (b) 1985, (c) 2006, (d) 2016.

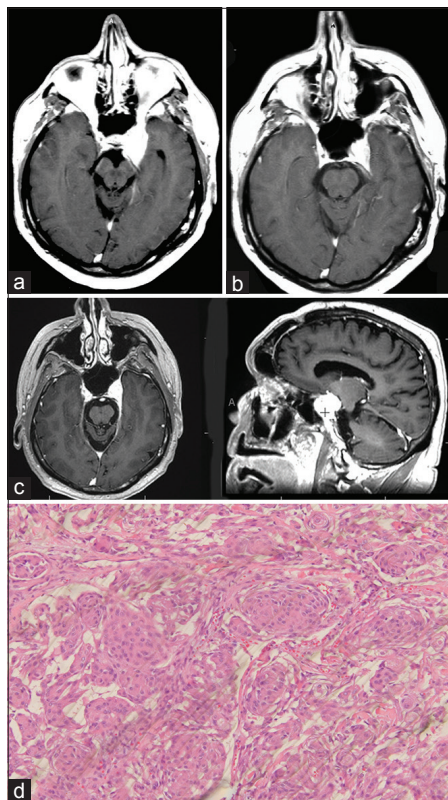


Figure 4: (a) 1995, (b) 1996, (c) 2017, (d) 1994.

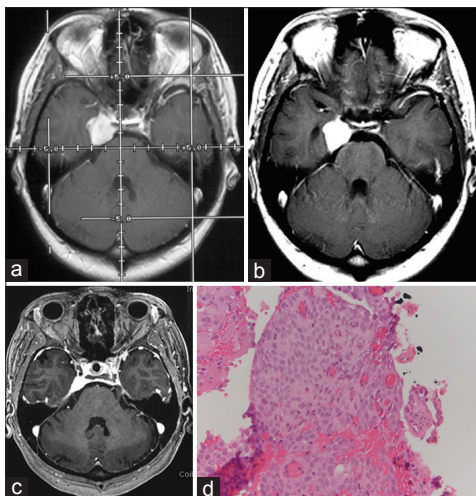


Figure 5: (a) 1997, (b) 1998, (c) 2017, (d) 1991.

scan from 2017 shows no significant enlargement of the tumor. The patient is still alive as of the date of writing this paper.

#### Patient 5

A 30-year-old woman presented in 1991 with diplopia, headaches, and right VI<sup>th</sup> nerve palsy. A magnetic resonance imaging (MRI) scan from an outside institution (not

available) showed a dense lesion lateral to the sella on the right side. She also had galactorrhea and due to that a pituitary tumor located in the cavernous sinus was considered. At operation, the tumor was a part of the cavernous sinus, hard in consistency, and unlike pituitary tumors, it was very solid. Part of the tumor was removed without entering deep into the cavernous sinus, and she received postoperative radiation treatment. The histology done in 1991 [Figure 5d].

Immediately, after the operation, the diplopia and the VI<sup>th</sup> nerve palsy recovered. Figures 5a and b show her 6- and 7-year follow-up, respectively. A year or two after the operation, she became pregnant with twins. Due to this history, multiple pathologists reviewed the histology and had mixed opinions. However, an MRI in 2017 shows the typical tail suggesting meningioma [Figure 5c].

Her galactorrhea recovered, her diplopia has not returned, and she is active, well and working at the writing of this paper 27 years postoperative.

#### DISCUSSION

The operative and radiological appearance of patients 4 and 5 are very similar. However, due to the elevated prolactin in patient 5 and somewhat different histology, it is of specific interest. For while the appearance of the tumor at operation and radiologic evaluations left no doubt for meningioma, several neuropathologists remained doubtful and could not make up their mind if the tumor was meningioma or pituitary adenoma. The outside preoperative scan for this case is not available, but the radiologist report on the angiogram states: “the finding of a blush which persists into the late venous phase without neurovascularity or early draining veins is compatible with a parasellar meningioma.” Such a flush is characteristic of meningioma and not pituitary adenoma. In addition, the meningeal tail in Figure 5c is typical for meningioma. Even after immunohistochemical and electron microscopic findings the neuropathologists remained in doubt. A report states: “while the light microscopic morphology is most suggestive of pituitary tumor, the lack of secretory vesicle calls that diagnosis into question.” Because the association of meningioma with elevated prolactin is not unusual<sup>[7,13]</sup> and the other indications explained above, we included the case as meningioma.

Operation and radiation treatment are the two most common treatments for CSM. Especially when radical or aggressive removal of the tumor is involved, these can be associated with relatively higher mortality and morbidity<sup>[4]</sup> than other intracranial tumors. Radiation treatment shrinks the tumor in some or slows the growth in others without mortality; yet, this too is associated with complications, as will be discussed later.<sup>[9]</sup> Ophthalmoplegia is the main complication of the tumor without and with treatments. Regardless of the cause,

however, its occurrence is a major consideration for choice of a treatment. Because aside from diminished visual capacity, the resulting facial disfigurement produces a major change in the mentation and social life of the patient. A review of literature supports the above statements, as does a detailed review of literature by Klinger *et al.*<sup>[6]</sup>

DeMonte *et al.*<sup>[4]</sup> reported that 31 (76%) of their 41 CSM patients had “total removal.” Three patients died; in the remaining 38 patients, preexisting cranial nerve deficits improved in 14%, remained unchanged in 80%, and worsened permanently in 6%. Furthermore, seven patients experienced a total of 10 new cranial nerves deficits. Out of the 10 patients who had total removal, one had recurrence 5 years after the operation. Cerebral ischemia occurred in three patients: in one, temporary and in two, residual hemiplegia. Nonetheless, the authors state that the “aggressive removal of CSMs can be performed with acceptable levels of morbidity and mortality.”

Blake *et al.*<sup>[3]</sup> analyzed this outcome and disagreed with their conclusion, commenting that it was not clear to them that aggressive surgical resection substantially improved either the natural history of the tumor or the prognosis after less radical treatment. They instead suggest that the morbidity and mortality of the procedure may not justify its use except in selected patients. In response, DeMonte *et al.*<sup>[3]</sup> emphasized that most of the patients in their study had shown signs of recent tumor growth, and all of the tumors extended outside of the cavernous sinus.

Radiation treatment is used as an alternative treatment for CSM. Hasegawa *et al.*<sup>[5]</sup> studied 150 CSM patients, excluding atypical or malignant meningiomas, in whom 111 could be followed with neuroimaging and for a median period of 62 months, and found that gamma knife radiation (GKR) was associated with progression-free survival rates of 87% and 73%, and tumor control rates of 94% and 92% at 5 and 10 years, respectively. The functional outcome in 43 (46%) patients was improved, 40 (43%) remained stable, and 11 (12%) had worse preexisting or newly developed symptoms. In another paper, Park *et al.*<sup>[9]</sup> found regression of tumor volume in 61%, unchanged in patients 25%, and worsened in 15% during a median follow-up 101 months.

Complications of GKR are certainly less than operative complications; nevertheless, they do exist. For example, Skeie *et al.*<sup>[11]</sup> in a study with a mean of 82 months follow-up of 100 patients observed 6.0% complications: optic neuropathy in two, pituitary dysfunction in three, worsening diplopia in one, and radiation-related edema in one patient. They found no mortality, and 88.0% of the patients were able to live independent lives at last follow-up. However, the complications of surgery usually present shortly after the operation, but with radiation, complications can occur long after. For example, al-Mefty *et al.*<sup>[1]</sup> described one case of a patient who developed a clival tumor 30 years postirradiation.

Sughrue *et al.*<sup>[12]</sup> analyzed 2065 cases of CSM through meta-analysis and found a rate of 3.2% recurrence treated with stereotactic radiosurgery (SRS) as compared with 11.1% in gross-total resection and 11.8% in subtotal resection. In addition, they found cranial neuropathy was markedly higher in patients undergoing resection (59.6%), as compared with 25.7% in those who underwent SRS treatment.

Meanwhile, Amelot *et al.*<sup>[2]</sup> treated 90 CSM patients symptomatically for 2–5 years. The patients had major symptoms such as impaired oculomotor function and minor symptoms such as intermittent diplopia. They found simple initial treatment such as short courses of corticosteroids and carbamazepine made 67.9% of patients with major symptoms and 80% of patients with minor symptoms “asymptomatic.” In addition, they found that 44 of 53 patients showed no significant growth over this time period and 42 were not symptomatic to begin with.

Emotional and social complications can also occur: aside from diminished visual capacity, the esthetic disfigurement of ophthalmoplegia has a profound impact on a patient’s life, especially in younger individuals. It diminishes self-image and makes it difficult to find employment despite all qualifications; it can hinder desired social life and personal relationships. It is difficult to understand the bias and stigma a person with even lesser facial disfigurement goes through. The impact stems from the way society perceives disfigurement and the way the person reacts to the way he is treated.

For example, Ryan *et al.*<sup>[10]</sup> performed a study where 98 participants were instructed to handle props previously handled by either a healthy confederate or by a confederate simulating medical conditions affecting the face—birthmark and influenza. The participants demonstrated strong behavioral avoidance to handle the prop when it had been handled by the influenza or birthmark confederates and showed “facial displays of disgust.” Ryan *et al.* write, “This implicit avoidance occur[ed] even when they know explicitly that such signs – the birthmark here – result from a noncontagious condition.” And in 2018, Newell and Marks<sup>[8]</sup> studied social fear in patients with facial disfigurement and found that their social phobia was similar to those with agoraphobia.

CSM is usually treated by operation, radiation, or both. The available literature, some of which is reported here, indicates that both treatments are effective. However, the degree to which each treatment contributes is difficult to measure; it is mostly assumed. The main goal of any treatment for CSM is to prevent growth of the tumor and to prevent occurrence of ophthalmoplegia. Because the tumor grows slowly over years, it is difficult to assess the degree of the prevention of growth due to radiation treatment. The actual therapeutic effect of radiation is also difficult to measure, unless the

ophthalmoplegia is eliminated or at least reduced. The results of an operation on reducing tumor volume and its therapeutic effects are immediately apparent, but the complication rate is higher and growth still can continue.

Furthermore, because the onset of diplopia is independent of the size of the tumor, we do not know when diplopia will occur. Moreover, if it does, shortening of the muscle as in the case of patient 2 or other noninvasive symptomatic treatments as reported by Amelot *et al.*<sup>[2]</sup> may be of help for a while and appropriate for certain patients. Like patient 1, one may prefer to wait until retirement or other events, or like patients 1 and 3, one may prefer not to take any risk of life. Thus, before recommending any treatment, an in-depth assessment of the patient's goals, desires, and physical condition is an essential part of the doctor-patient relationship.

Despite a detailed presentation of potential outcome, few patients can truly understand the impact of the physical disability and facial disfigurement caused by ophthalmoplegia before they actually undergo the operation. If a radical operation is recommended, patients often accept this option, despite the potential postoperative ophthalmoplegia, believing that in order to avoid death they must undergo the operation. However, even untreated, death seldom occurs. Or, a patient may accept operation hoping that an existing ophthalmoplegia recovers. Thus, recommendation for a treatment carries an awesome ethical responsibility. Discussion of blindness, paralysis, and death is not easy to hear. Patients seldom grasp what they will go through and accept the treatment based on trust.

Nevertheless, in the end, a patient needs to know why and for what reason a treatment is recommended and the doctor needs to know why the patient accepts or turns down a treatment. At times, one like patient 1 may be unreasonably hesitant to accept an operation due to older age or other reasons and suffers serious consequences of blindness. Without coercion, such a patient needs encouragement if the planned operation is not as risky as the patient perceives.

As a review by Klinger *et al.*<sup>[6]</sup> indicates, treatment of CSM has gone through an evolution, and radical operation is no longer favored. Perhaps, in occasional patients with malignant, aggressive, or fast-growing tumors, radical operation can be helpful. The patients presented here are too few to be able to come up with a general guideline; yet, they indicated that when spontaneous ophthalmoplegia occurs, it does so slowly and gradually. In addition, a review of literature indicates that death caused by spontaneous growth seldom occurs, unless the tumor is malignant. Therefore, the treatment of CSM is best based on evidence of the timing of the ophthalmoplegia.

Today, the trajectory of the growth of the tumor can easily be determined by clinical follow-up combined with radiologic studies such as MRI. Certainly, patients in this

study showed that disturbing diplopia may not occur for a long time. Thus, there seems to be no urgency in treating CSM with either operation or radiation treatment, especially if it is asymptomatic, or the symptoms are not disturbing to the patient and can be treated with noninvasive treatment. A certain period of "wait and see" can delay the potential complications of an operation and radiation until the evidence indicates their needs based on symptoms and the patient's desire. Nevertheless, in some patients, as in patients 4 and 5, diplopia can cause considerable limitation in their function to work; in such cases, a limited operation to relieve symptoms, followed by radiation, seems reasonable.

## CONCLUSION

- Ophthalmoplegia, whether spontaneous or resulting from treatments of CSM, is a serious complication. Facial disfigurement can cause adverse effects in the patient's self-image, social status, ability to find employment, and personal relationships.
- Treatment of CSM is seldom urgent. In most patients, it is preferable to wait until there is evidence for the need of operation, radiation, or both. Minor symptoms, such as slight diplopia of lateral gaze, can be treated with corrected eyeglasses or shortening of the lateral rectus muscle of the eye.
- Operations, especially radical or aggressive ones, are associated with high mortality and morbidity. Radiation treatment slows down and shrinks some tumors but can have some complications over a long time. Thus, in most patients, neither surgery nor radiation needs to be the starting treatment. A period of "wait and see" may be best, until, based on the evidence, operation, radiation, or both become needed.

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## Declaration of patient consent

The author certifies that he has obtained all appropriate patient consent forms.

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## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. al-Mefty O, Kersh JE, Routh A, Smith RR. The long-term side effects of radiation therapy for benign brain tumors in adults. *J Neurosurg* 1990;73:502-12.
2. Amelot A, van Effenterre R, Kalamarides M, Cornu P, Boch AL. Natural history of cavernous sinus meningiomas. *J Neurosurg* 2018;1:1-8.
3. Blake PY, Miller NR, Long DM. Treatment of cavernous sinus meningiomas. *J Neurosurg* 1995;82:702-3.
4. DeMonte F, Smith HK, al-Mefty O. Outcome of aggressive removal of cavernous sinus meningiomas. *J Neurosurg* 1994;81:245-51.
5. Hasegawa T, Kida Y, Yoshimoto M, Koike J, Iizuka H, Ishii D, *et al.* Long-term outcomes of gamma knife surgery for cavernous sinus meningioma. *J Neurosurg* 2007;107:745-51.
6. Klinger DR, Flores BC, Lewis JJ, Barnett SL. The treatment of cavernous sinus meningiomas: Evolution of a modern approach. *Neurosurg Focus* 2013;35:E8.
7. Michael AS, Paige ML. MR imaging of intrasellar meningiomas simulating pituitary adenomas. *J Comput Assist Tomog* 1988;12:944-6.
8. Newell R, Marks I. Phobic nature of social difficulty in facially disfigured people. *Br J Psychiatry* 2000;176:177-81.
9. Park KJ, Kano H, Iyer A, Liu X, Tonetti DA, Lehocky C, *et al.* Gamma knife stereotactic radiosurgery for cavernous sinus meningioma: Long-term follow-up in 200 patients. *J Neurosurg* 2018;1:1-0.
10. Ryan S, Oaten M, Stevenson RJ, Case TI. Facial disfigurement is treated like an infectious disease. *Evol Hum Behav* 2012;33:639-46.
11. Skeie BS, Enger PO, Skeie GO, Thorsen F, Pedersen PH. Gamma knife surgery of meningiomas involving the cavernous sinus: Long-term follow-up of 100 patients. *Neurosurgery* 2010;66:661-8.
12. Sughrue ME, Rutkowski MJ, Aranda D, Barani IJ, McDermott MW, Parsa AT, *et al.* Factors affecting outcome following treatment of patients with cavernous sinus meningiomas. *J Neurosurg* 2010;113:1087-92.
13. Yu E, Forghani R. Sellar, parasellar and clival region: Skull base cancer imaging. Thieme. *J Laryngol Otol* 2018;132:759.

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