

Case Report

Ectopic sphenoid sinus meningioma with huge hyperostosis: a rare case report and review of literature

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Abstract: Meningioma is a slow-growing and generally benign neoplasms occurring in the intracranial region, however, ectopic meningioma originating in sphenoid sinus (SS) are exceedingly rare. We reported a 49-year-old male of ectopic SS meningioma. This case is, to the best of our knowledge, the fourth case report of ectopic SS meningioma and the first case with huge hyperostosis in this location. The patient presented with 4-month history of dizziness and progressive blurred vision of right eye. Imaging studies showed a mass in the SS invading into posterior ethmoid sinuses, optic canal and cavernous sinus. There was a marked hyperostosis in the inferior wall of ethmoid sinuses. The tumor was almost completely removed via the endonasal endoscopic approach under navigation system, and the patient subsequently underwent stereotactic radiotherapy to control the tumor remnant. Pathological and Immunohistochemical examination established a transitional meningioma (Grade I WHO). No relapse was found at 5-year follow-up. Ectopic SS meningioma exhibits nonspecific symptoms, so the accurate diagnosis rests on the histological and immunohistochemical examinations. Total removal via the endonasal endoscopic approach is the treatment of choice for ectopic SS meningioma, with subsequent radiotherapy to help control any residual tumor.

Keywords: Ectopic meningioma, sphenoid sinus, diagnosis, endoscopic surgery

Introduction

Meningioma is the second-most common tumor in the central nervous system, accounting for 13-26% of all primary intracranial tumors [1, 2]. However, ectopic meningiomas are extremely rare, comprising less than 2% of all meningiomas [3, 4]. Ectopic meningiomas are defined as primary tumors located in sites without arachnoid cells, ruling out local extension or metastasis [5, 6]. Among these ectopic cases, meningiomas arising from sinonasal tract were reported to represent about 24% [6, 7]. Until now, a literature search revealed only three cases of ectopic SS meningioma [8-10]. Here, we present an unusual and intractable case of ectopic SS meningioma, extensively invading into posterior ethmoid sinuses, optic canal and cavernous sinus, and caused significant hyperostosis.

Case presentation

A 49-year-old man presented to our hospital complaining of progressive blurred vision of the

right eye and four months' dizziness. He had decreased right visual acuity and a pale optic disc. A computed tomography (CT) scan revealed a dense soft tissue mass in the SS, which had invaded the cavernous sinus, posterior ethmoid sinuses, and nasal cavity. Clinically significant hyperostosis was noted in the inferior wall of the ethmoid sinuses, and bone erosion was found around the SS, particularly in the anterior base skull, sellar floor, and clivus regions (**Figure 1A-D**). Magnetic resonance imaging (MRI) scans demonstrated an irregular solid lesion in SS measuring 3.44 cm × 4.78 cm × 4.56 cm. The neoplasm was hyperintense on T2-weighted MRI, T1-weighted MRI, and moderately enhanced with the invasion of the optic canal, cavernous sinus, and the wall of internal carotid artery (ICA) (**Figure 2A-F**). No vascular anomaly was found on MR angiography. Laboratory examination demonstrated normal levels of pituitary hormones (growth hormone, adrenocorticotropic hormone, sensitive thyroid-stimulating hormone, prolactin, follicle-stimulating hormone, and luteinizing hormone).

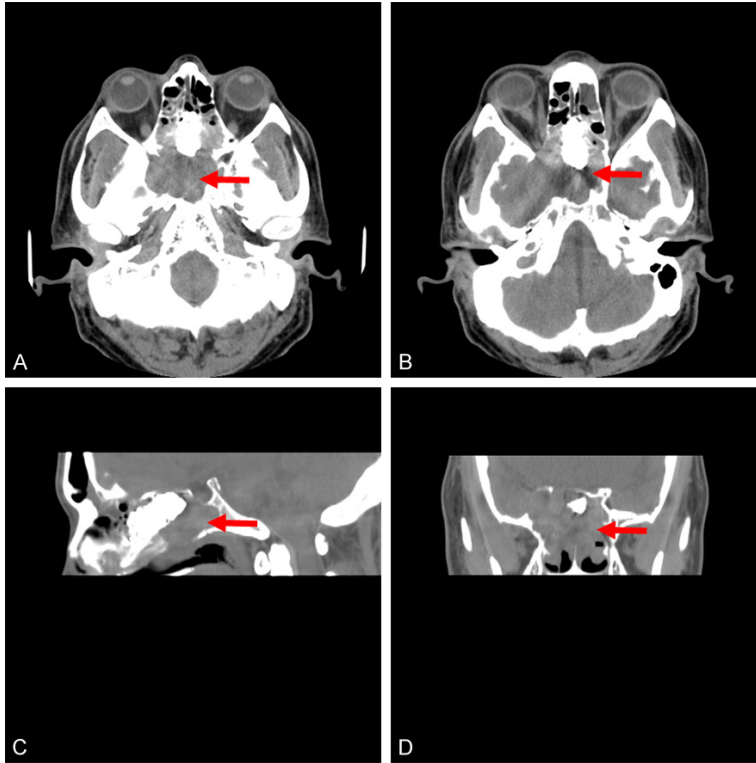


Figure 1. The pre-operative CT scans of the patient. (A, B) Axial, (C) Sagittal, and (D) coronal computed tomograms demonstrate a mass (red arrows) located in the sphenoid sinus that is invading the cavernous sinus, optic canal, and posterior ethmoid sinuses, causing reactive hyperostosis.

Endonasal endoscopic surgery was performed to remove the tumor with image-guided surgery control (Stealth Station, Medtronic, Inc., Minneapolis, Minnesota). Intraoperatively, the reddish-gray encapsulated vascular tumor was found to be elastic, firm, and well circumscribed in the SS, protruding from an SS aperture. The tumor had eroded the bony walls of the SS and was firmly attached to the anterior wall and roof of the SS. Notably, the tumor had also invaded the optic canal and cavernous sinus and was firmly adhered to the ICA. The inferior bony wall of the ethmoid sinuses was thickened and hard. Because of the hardness of the tumor, the tumor was resected in piecemeal to prevent iatrogenic cranial neurovascular injury. A tiny part of tumor that firmly adhered to the ICA was left in the cavernous sinus. Most of the thickened bone was drilled away until non-infiltrated bone structure was reached.

Histological examination of the tumor revealed monomorphic round, oval, and spindle cells arranged in a syncytial and whorled pattern, surrounded by a heavy deposition of fibrillary

pink collagen (**Figure 3A**). Immunohistochemical examinations showed marked positivity to vimentin and epithelial membrane antigen (EMA), focal positivity to S-100, and negativity to cytokeratin and glial fibrillary acidic protein (GFAP) (**Figure 3B-D**). Histological evidence was consistent with a transitional (mixed) meningioma (World Health Organization [WHO] grade I). The patient's postoperative course was uneventful, although his right visual acuity did not improve. Three weeks later, adjuvant stereotactic radiotherapy with a margin dose of 14 Gy was performed to control the small residual mass that remained in the cavernous sinus (**Figure 2G-I**). At 5-year follow-up, there was no recurrence of the tumor.

Discussion

Ectopic meningiomas comprise a mere 0.1% of all tumors of the nose or sinuses [6, 7]. Although most sinonasal ectopic meningiomas affect more than one sinus or the paranasal sinus and nasal cavity together, the most commonly affected sinus is the frontal sinus, followed by the maxillary sinus and then the ethmoid sinuses [12]. Ectopic meningiomas originating in the SS are rare, with only three documented cases reported in the medical literature (as found in a search of PubMed through 12/2016 using keywords "meningioma" and "sphenoid sinus") (**Table 1**) [8-10]. The present case also involves extensive invasion of the cavernous and ethmoid sinuses, including the ICA and optic canal, and sizable local hyperostosis. Given its attachment point, the absence of an intracranial lesion, and the lack of clinical or radiological connection with brain structures, the tumor in our patient was considered to be ectopic.

The pathogenesis of ectopic meningiomas in the nasal area is unknown. Arachnoidal cap cells are thought to be the most likely cell of origin, because of their cytological and functional similarities to meningioma cells [13]. In

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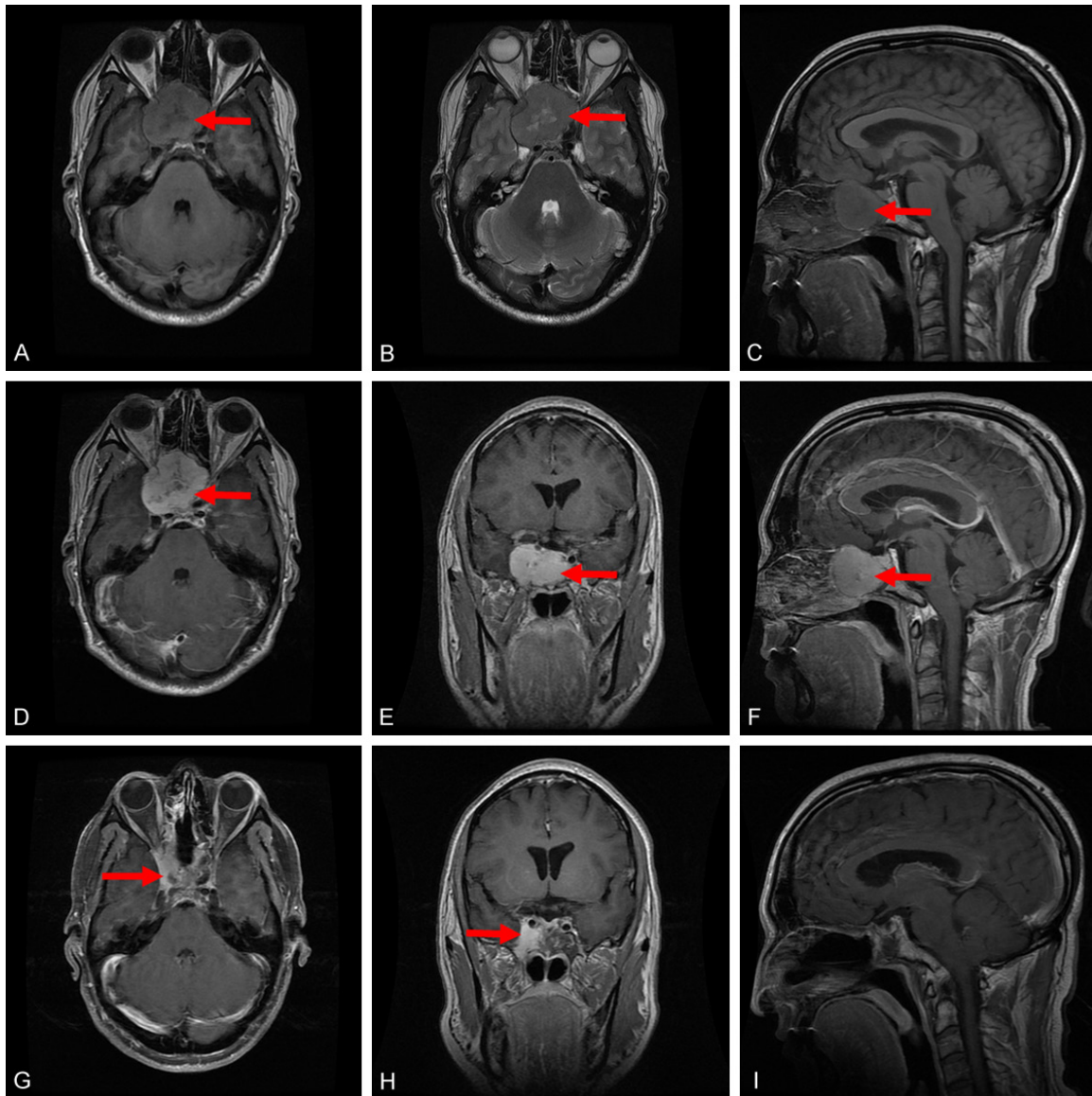


Figure 2. The pre-operative and post-operative MRI scans of the patient. (A, B, D: T1-/T2-weighted/ enhanced) Axial, (C, F: T1-weighted/enhanced) sagittal, and (E: Enhanced) coronal magnetic resonance images demonstrate an enhanced mass (red arrows) invading the cavernous sinus and involving the internal carotid artery and optic nerve, but the mass does not enter the cranium. (G) Axial, (H) Coronal, and (I) sagittal enhanced postoperative magnetic resonance images demonstrate a small residual tumor (red arrows) in the cavernous sinus.

normal physiological conditions, arachnoidal cap cells line the inner aspect of the arachnoid membrane and fill the cores of the arachnoid villi that project into the lumina of dural veins and venous sinuses, but these cells are not autochthonous to the SS. However, abnormal development or unexpected events could cause them to migrate extracranially. Arachnoid cells can be entrapped extracranially during embryologic development, or they may be present in the sheaths of nerves or vessels where

they emerge through the skull foramina, such as when arachnoid islets are displaced extracranially as the result of a traumatic event or cerebral hypertension. Moreover, undifferentiated or multipotent mesenchymal cells, such as fibroblasts and Schwann cells, exit the ectopic sites [14, 15]. These cells could proliferate and give rise to an ectopic meningioma after a discernible inciting event, such as trauma, hemorrhage, chemical irritation, inflammation, or radiation exposure. The ectopic meningioma

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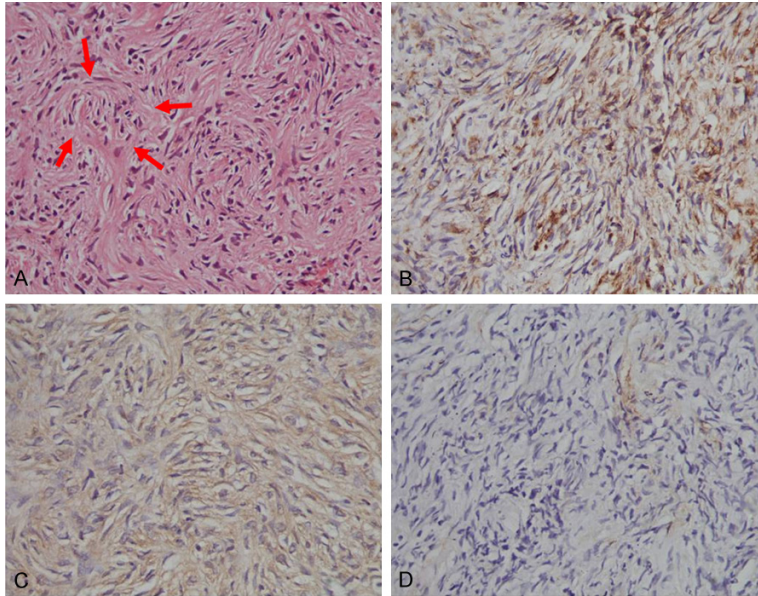


Figure 3. The histological results and Immunohistochemical staining of ectopic SS meningioma. (A) An H&E-stained section shows spindle cells arranged in a syncytial and whorled pattern surrounded by fibrillary pink collagen (red arrows) (original magnification $\times 200$). An immunohistochemical stain positive for (B) vimentin and (C) epithelial membrane antigen (original magnification $\times 200$). (D) An immunohistochemical stain locally positive for S-100 (original magnification $\times 200$).

in our patient may have arisen from arachnoidal cells trapped in the SS when the skull bones fused, or from undifferentiated or multipotent mesenchymal cells.

The primary diagnosis of ectopic SS meningioma is difficult because the presenting clinical symptoms are general, including signs and symptoms such as headache, dizziness, and evidence of compression of adjacent structures [9, 10]. Such evidence may include decreased visual acuity, diplopia, proptosis, exophthalmos (when the optic canal and orbit cavity are invaded), nasal mass and nasal obstruction, and epistaxis and sinusitis (when the tumor protrudes into the nasal cavity). Orbital apex syndrome and restricted eyeball movement and regulatory disorders may also be common at a later stage. CT and MR imaging may reveal only a dense soft tissue mass, without defining the tumor in relation to neighboring neurovascular structures. Definite diagnoses can be confirmed by characteristically microscopic morphology and immunohistochemistry [13, 16]. In our patient, light microscopy revealed characteristic findings of ectopic meningioma that included a syncytial and whorled pattern of polygonal tumor cells sur-

rounded by the heavy deposition of fibrillary collagen. Immunohistochemistry also indicated dual epithelial and mesenchymal characteristics (i.e., the strongly positive expression of EMA and vimentin) and focal immunoreactivity to S-100 protein.

Meningiomas are known to be associated with hyperostosis, as hyperostosis occurs in 25% to 75% of cases of meningioma [17]. However, the pathomechanism of hyperostosis in meningioma remains unclear and several hypotheses have been established including, preceding trauma, tumor irritation of the bone without invasion, osteoblast cells stimulated by humoral factors secreted from tumor cells, and vascular disturbances by the tumor and formation of bone by the tumor [18]. Recent

study has revealed matrix metalloproteinases (MMP) 1, MMP2 and MMP13 may be important for the formation of hyperostosis [19]. Neither preoperative imaging nor intraoperative pathological evaluation can definitively determine whether hyperplastic bone has been infiltrated by a tumor. Therefore, resection of the entire hyperostotic bone is usually recommended to prevent recurrence [20, 21]. In this case, the hyperostosis was so extensive in the inferior wall of the ethmoid sinuses that total resection was difficult to achieve via endonasal endoscopic surgery, during which endoscopically visible hyperplastic bone was drilled away.

Surgery is the treatment of choice for management of SS and sinonasal meningioma. The complex anatomy and the relationship of the SS with its vital neighboring structures, however, presents challenges for the neurosurgeon [22]. Three aspects of this case made removal of the tumor particularly difficult. First, the present case extended extensively into peripheral vital structures, including the skull base, ethmoid sinuses, cavernous sinus, optic canal, and carotid canal. The tumor was immediately adjacent to the optic nerve, cranial nerves III, IV, and VI, and the first and second branches of

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Table 1. Ectopic sphenoid sinus (SS) meningiomas reported in the literature

Reference, year	Age/ Sex	Clinical findings, history, and duration	Radiological findings	Treatment	Operative findings	Pathology	Follow-up duration (mo) and outcome in last follow-up
Wang et al., 2015 [8]	61/F	Vertigo, left eye blurred vision	Enhanced mass in SS; extending into ES and anterior cranial fossa	Total removal via microscopic transnasal transsphenoidal surgery	Gray, firm mass with rich blood supply; eroding SS bony walls	Meningothelial meningioma (WHO grade I)	0; Total resection
Mori et al., 2014 [9]	60/F	Decreased visual acuity, generally reduced retinal sensibility; 5 months	Enhanced mass in SS extending into ES; hyperostosis of SS roof and septum	Total removal via endonasal endoscopic approach	Reddish-yellow, elastic, firm, well-circumscribed tumor; invasion of ES	Meningothelial meningioma (WHO grade I)	3; No recurrence
Lee et al., 1979 [10]	26/F	Headaches, diplopia, nasal congestion, mild proptosis, ophthalmoplegia; 8 months	SS clouding; increased density in SS; no bony abnormality	Total removal via transsphenoidal microscopic surgery	Reddish-gray, encapsulated vascular tumor; limited to SS	Transitional meningioma (classification: not reported)	12; No recurrence
Current study	49/M	Dizziness, decreased visual acuity; 4 months	Enhanced mass in SS; hyperostosis of SS roof and anterior wall invasion of ES and CS; extensive bone destruction; ICA involvement	Subtotal removal via endonasal endoscopic approach; adjuvant radiotherapy	Reddish-gray, elastic, firm, encapsulated vascular tumor; eroding SS bony walls; invading ES and CS	Transitional meningioma (WHO grade I)	60; No recurrence

CS, cavernous sinus; ES, ethmoid sinus; F, female; ICA, internal carotid artery; M, male; mo, months; WHO, World Health Organization.

cranial nerve V. It firmly adhered to the wall of ICA. Thus, resection of the tumor involved the risk of morbidities (e.g., cranial nerve palsies) [23, 24]. More critically, radical removal of the tumor would introduce significant risk of mortality from catastrophic and uncontrollable bleeding of a ruptured ICA, even if bleeding from the cavernous sinus were controlled.

Second, the neurovascular structures that were attached to the tumor were located at the proximal end of the tumor. These structures could be identified only after the tumor was almost fully removed, so the lesion had to be carefully resected in piecemeal. Third, the rich blood supply to the tumor and the hardened texture of the tumor further hindered its resection. The endoscopic endonasal approach used in this case was minimally invasive and provided a wider field with multi-angled visualization [25]. Image guidance, which was also used in this procedure, helped us to accurately identify anatomic danger points, to outline the resection profile, and to reduce complications. We removed as much of the tumor as possible to minimize the likelihood of iatrogenic cranial neuropathy [26, 27]. Given these considerations, the tumor was removed in subtotal fashion without complications.

Radiotherapy and chemotherapy can help mitigate the risk of residual tumor and recurrence [28, 29]. SRT has demonstrated good rates of tumor control and low rates of postprocedural morbidity, particularly with regard to cranial nerve injury. Retrospective case series have described primary or adjunctive SRT that resulted in an overall local control rate of 98% for patients with meningioma in the cavernous sinus, and progression-free survival rates of 73% and 99% for patients with intracranial meningioma at 5-year and 10-year follow-up, respectively [30, 31]. Most studies also showed tumor shrinkage or obliteration in as many as 40% to 63% of treated meningiomas in the cavernous sinus [32]. Moreover, the incidence of chronic radiotherapy-induced injury was reported to be only 1% for meningioma of WHO grades I and II [33]. A study of 30 sinonasal meningiomas demonstrated 20% of cases developing local recurrence after the initial surgery, of which two cases invading the skull base died with disease at 0.1 and 3.5 years [12]. Other authors have reported the likelihood of recurrence of subtotally resected tumors for several

years after surgery [34, 35]. A considerable number of recent studies have found that ectopic meningioma treated with postoperative radiotherapy resulted in markedly reduced tumor remnants or no tumor recurrence at all, with neurosurgeons advocating for the use of operative adjunct radiotherapy to control the remnant [36-40]. We used postoperative MR imaging to verify the minimal residual tumor remaining in the cavernous sinus, and administered stereotactic radiotherapy to control the remnant, which resulted in no recurrence at 5-year follow-up.

Ectopic SS meningiomas are rare, slow-growing tumors that have nonspecific clinical manifestations. Accurate diagnosis depends on histological and immunohistochemical examinations. Total resection, including resection of the tumor attachment, is optimal; however, such cases can be surgically challenging. Radiotherapy is helpful to control any residual tumor.

Disclosure of conflict of interest

None.

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