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Primary Malignant Melanoma of the Sphenoid Sinus as a Crucial Differential Diagnosis of Skull Base Tumors: A Case Report

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Abstract

A 79-year-old man presented with progressive ptosis, diplopia, and headaches, which led to the diagnosis of a rare primary malignant melanoma of the sphenoid sinus. Imaging revealed extensive bone destruction and aggressive tumor behavior. The rarity of primary malignant melanoma in the sphenoid sinus complicates early detection. Despite undergoing surgical decompression, immunotherapy, and radiation therapy, the tumor rapidly recurred, necessitating supportive care. This case highlights the need for neurosurgeons to include primary malignant melanoma in the differential diagnosis of skull base tumors, particularly in the sphenoid sinus, due to its potential for aggressive local invasion and significant impact on critical neurovascular structures. Early recognition and intervention are crucial for managing this rare and aggressive malignancy effectively.

Keywords: skull base, melanoma, sphenoid sinus, pituitary, case report

Introduction

Primary malignant melanoma of the sphenoid sinus is an extremely rare condition, with less than 15 cases reported since 1986. Its nonspecific initial symptoms, such as headaches and diplopia, often lead to a delayed diagnosis. However, the disease can progress rapidly, causing severe visual deficits and functional decline.[1,2] The prognosis largely depends on early detection and the extent of surgical resection, although complete removal is challenging due to the tumor's proximity to critical structures. Given its resistance to radiotherapy, early surgical intervention is crucial.[1,2] This case report contributes to the limited body of knowledge, highlighting the need for early recognition of tumors near the sella turcica.

Case Report

A 79-year-old man with no prior history of tumorous lesions presented with left ptosis as the initial symptom. Ten days later, he developed diplopia, which was followed by the onset of headache and vomiting 4 days later, leading to hospitalization at a local hospital. Imaging studies, including X-ray, computed tomography (CT), and magnetic resonance imaging (MRI), revealed a tumorous lesion extending from the sphenoid sinus with significant bone destruction affecting the sella turcica and clivus. The lesion demonstrated strong contrast enhancement (Fig. 1).

Three weeks after the onset, the patient developed bilateral ptosis, with preserved pupillary light reflexes in both eyes, yet experienced a nearly complete loss of voluntary eye movements, resulting in functional blindness. laboratory evaluation of the hypothalamic-pituitary axis revealed partial hypopituitarism, indicated by the following values: free T3 at 1.84 pg/mL (normal range: 2.4-4.0 pg/mL), thyroid-stimulating hormone at 0.09 mIU/L (normal range: 0.610-4.230 mIU/L), and prolactin at 30.6 ng/mL (normal range: <15.0 ng/mL).

One month after the onset of symptoms, the patient became unable to eat due to persistent headaches and repeated vomiting. Suspecting metastasis to the pituitary gland or sphenoid sinus from a malignant tumor, lymphoma, or chordoma, an endonasal surgical approach was performed. Intraoperatively, the tumor was highly vascular-

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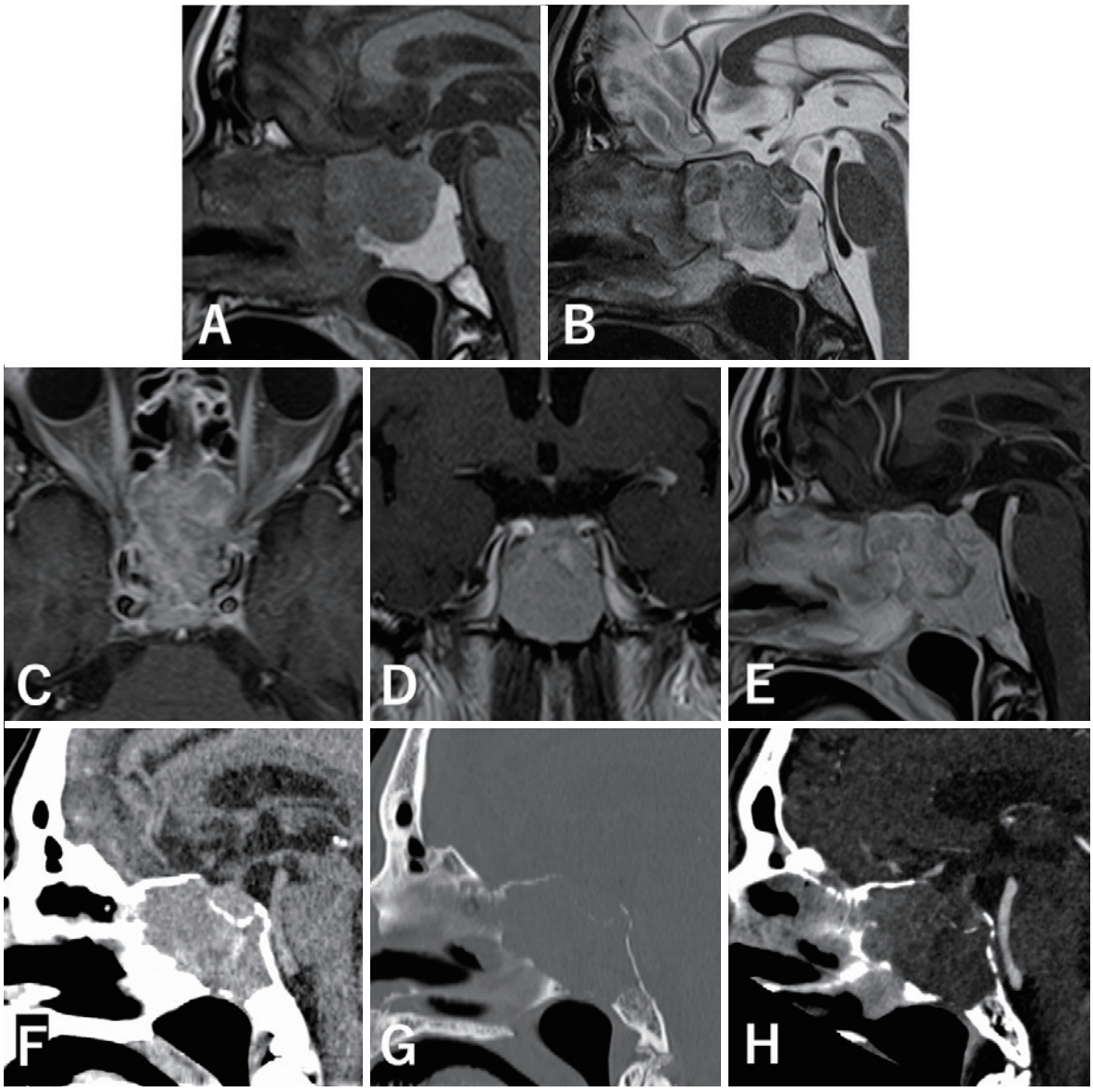

Fig. 1 Preoperative imaging.
Preoperative magnetic resonance imaging (MRI) and computed tomography (CT) images are presented. Image A is T1-weighted (T1WI), B is T2-weighted (T2WI), and C-E are T1-weighted with gadolinium contrast (T1-Gd) in axial, coronal, and sagittal images. The tumor shows isointensity on T1WI and slightly low intensity on T2WI. It forms lobulations while filling the sphenoid sinus and extends to the sella turcica and clivus. The tumor demonstrates heterogeneous contrast enhancement, with areas in the posterior portion appearing cystic, showing isointensity on both T1 and T2 but with enhancement. Image F is non-contrast CT, G is contrast-enhanced CT, and H is the bone window. The isodense tumor fills the sphenoid sinus, with minimal residual bone at the base of the sella. However, parts of the anterior wall of the sphenoid sinus and the posterior clinoid process are destroyed, and the cortical bone of the clivus is significantly thinned.

ized and predominantly composed of dark, hemorrhagic tissue suggestive of intratumoral hematoma (Fig. 2).

The anterior wall of the sphenoid sinus was destroyed and could not be identified. Two samples were sent for intraoperative rapid pathology, both of which suggested lymphoma. Therefore, the surgery was limited to mild tumor decompression. Postoperatively, there was a temporary, mild improvement in ocular movement, and the headache and nausea subsided, allowing oral intake. However, within 2 weeks, the patient experienced a recurrence of headache and nausea, and imaging revealed rapid regrowth of the tumor, filling the resection cavity (Fig. 3).

Permanent histopathology revealed diffuse proliferation of large atypical cells with a high nucleus-to-cytoplasm ratio against a background of fibrotic nasal or paranasal sinus mucosa. Some atypical cells exhibited nuclear pleo-

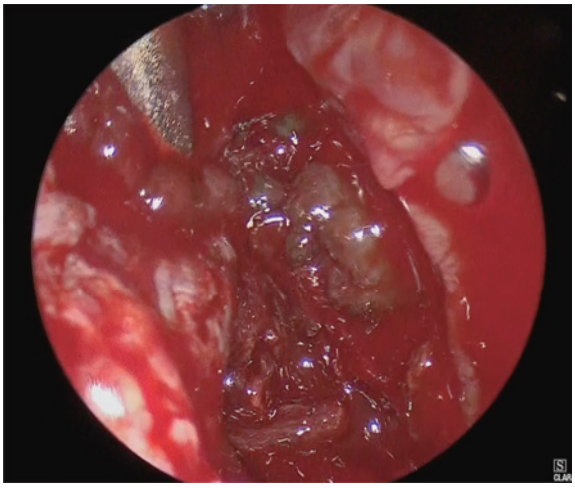

Fig. 2 Intraoperative findings.
Intraoperative images are presented. The incised mucosa of the sphenoid sinus was highly vascularized and prone to bleeding. The anterior wall of the sphenoid sinus could not be identified, and a highly vascular, hemorrhagic tumor was found beneath the mucosa. The tumor was friable and dark in color, resembling a blood clot during surgery.

morphism, with melanin deposits in both the cytoplasm and stroma. Numerous mitotic figures and apoptotic bodies were observed, consistent with a small round-cell tumor (Fig. 4A). The atypical cells were positive for S-100 and HMB-45 (Fig. 4B and C), negative for cytokeratin (AE 1/AE3) and leukocyte common antigen (CD45), and retained integrase interactor 1 staining; *BRAF* p.V600E was negative (not shown).

Based on these findings, a diagnosis of malignant melanoma was made. Whole-body examination, including upper and lower endoscopy and whole-body positron emission tomography-CT, ruled out a primary lesion in the trunk, leading to a diagnosis of primary malignant melanoma of the sphenoid sinus. Although a second surgery for maximal tumor resection was considered, the dermatology-oncology team advised against it, and the patient was transferred to a specialized hospital for chemotherapy with immune checkpoint inhibitors, molecular targeted therapy, and radiotherapy. Despite these efforts, the disease continued to progress, and the patient is currently receiving the best supportive care 4 months postoperatively.

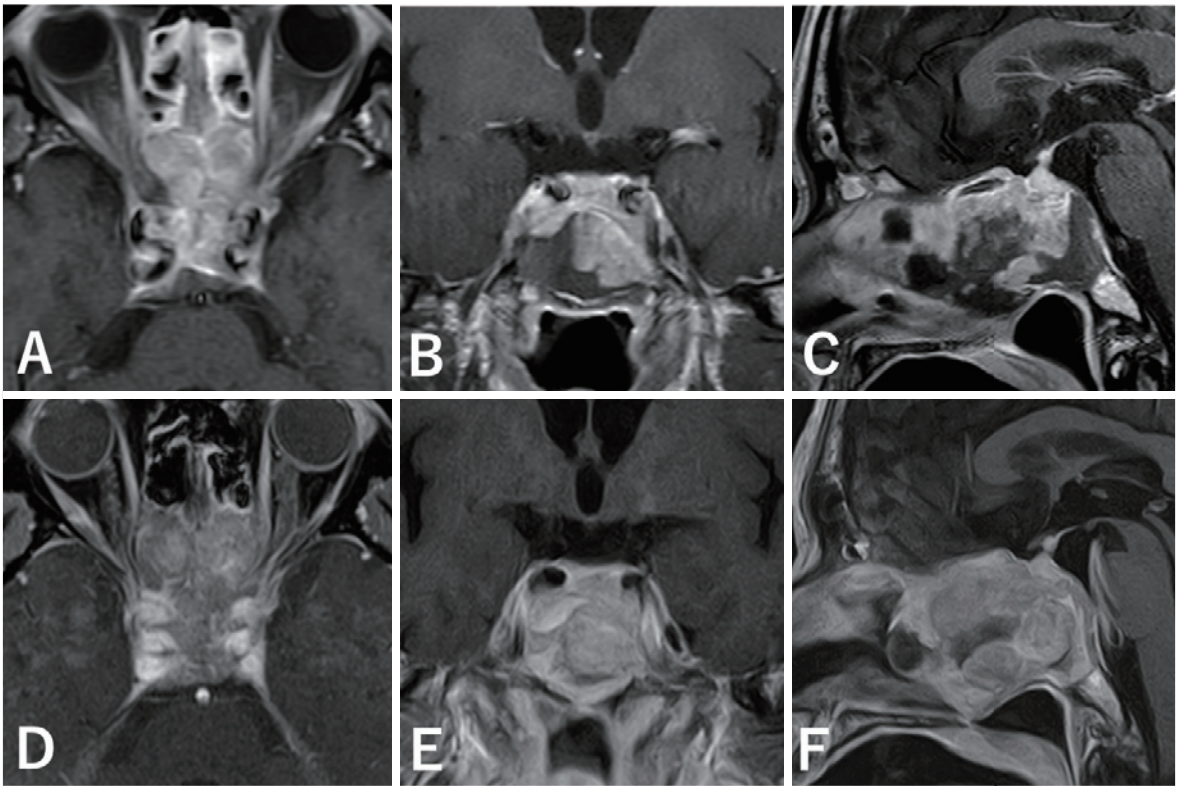

Fig. 3 Postoperative imaging.
Postoperative images are shown. A-C: The contrast-enhanced magnetic resonance imaging (MRI) taken on postoperative day 3 shows decompression of the tumor cavity, with communication established between the cystic component posterior to the tumor. D-F: The contrast-enhanced MRI taken on postoperative day 28 shows that the resection cavity has been replaced by fluid accumulation, and rapid tumor growth has led to nasal cavity obstruction.

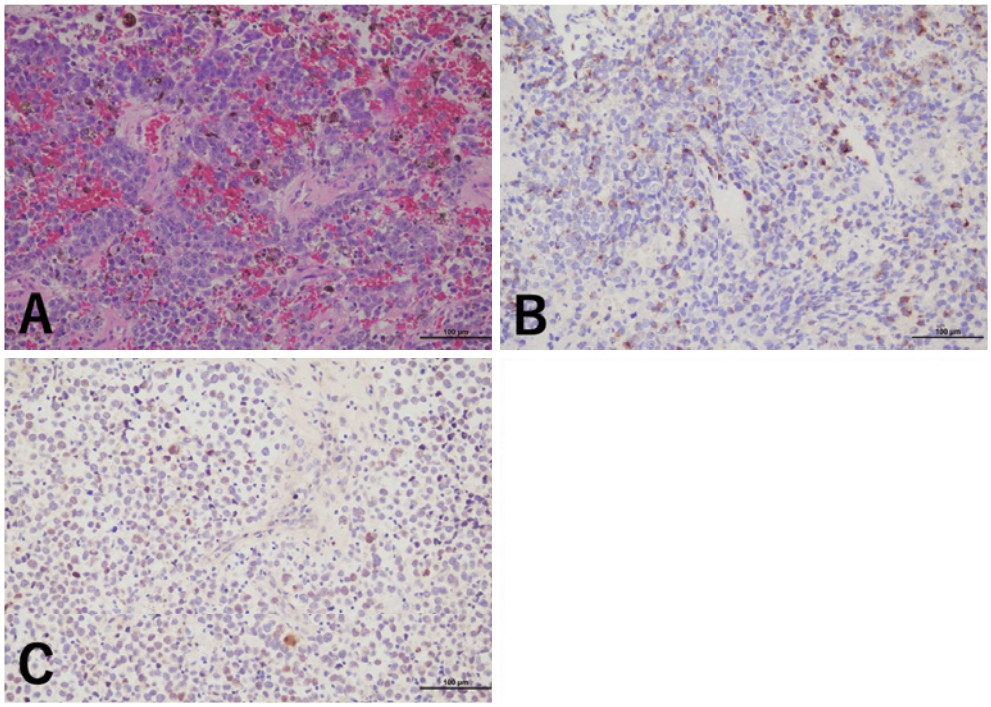

Fig. 4 Histopathological findings.
Histopathological findings are presented. A: Large atypical cells with a high nucleus-to-cytoplasm (N/C) ratio show diffuse proliferation, with some cells exhibiting nuclear pleomorphism. Melanin is observed within the cytoplasm and stroma. Numerous mitotic figures and apoptotic bodies are present.
B, C: The atypical cells are positive for S-100 protein and HMB-45 markers in immunohistochemistry.

Discussion

Melanoma is an aggressive malignancy arising from melanocytes, typically found in the skin, mucosal surfaces, and eyes. It is characterized by rapid progression and a high potential for metastasis.[1] Advances in immunotherapy and targeted treatments have improved outcomes for some subtypes, but treatment resistance and poor prognosis remain significant challenges, particularly in rare forms such as mucosal melanoma.[2] Specific genetic abnormalities in malignant melanoma are known to be associated with treatment resistance and poor prognosis. *NRAS* mutations are linked to aggressive disease and limited responses to immune checkpoint inhibitors.[3] Similarly, *KIT* mutations, frequently observed in mucosal melanomas, exhibit resistance to radiotherapy and variable responses to molecularly targeted therapies.[4] Furthermore, *CCND1* amplifications and *CDKN2A* deletions, commonly found in mucosal melanomas, complicate treatment strategies.[5] These findings highlight the critical role of genetic profiling in guiding therapeutic decisions. Malignant melanoma is predominantly a disease of the skin and mucosa, with primary sinonasal melanomas accounting for only 0.5%-1.5% of all cases.[6] Among these, primary melanomas originating in the sphenoid sinus are extremely rare, with only 11 cases reported in the literature since the first case was described by Carter et al. in 1986.[6-17] This case represents the 12th reported instance. In addition to our report, we have reviewed previous case reports to summarize the initial symptoms, treatment approaches, and outcomes (Table 1).

The symptoms of primary sphenoid sinus malignant melanoma often begin with nonspecific signs such as headache, nasal obstruction, and epistaxis, making early detection challenging. As the disease progresses, patients may rapidly develop symptoms resembling orbital apex syndrome, including visual field deficits, diplopia, facial pain, and ptosis. The prognosis of malignant melanoma is closely associated with the extent of the primary lesion, the completeness of surgical resection, and the occurrence of distant metastases. Early and appropriate surgical intervention is crucial for symptom relief and improving prognosis.[11]

Reports of primary malignant melanoma of the sella turcica,[18] metastatic melanoma to the pituitary gland,[19] and metastatic melanoma to pituitary adenomas[20] highlight the increasing prevalence of endonasal surgeries. Reporting such rare cases of malignant melanoma in this region is significant for expanding the knowledge of neurosurgeons and for considering the still undefined treatment strategies.[11,21] Mucosal-origin melanoma is known to be resistant to radiotherapy and follows an aggressive course among si-

Table 1

No.	Sex	Age	Ethnicity	Initial symptoms	Range of progress	Period to definitive diagnosis	Symptoms before surgery	Treatment	Outcome	Year
1	F	67	White	Nasal stuffiness, epistaxis	N/A	2.5 year	Nasal stuffiness, epistaxis	Excision, radiation therapy	Alive at 2.5 year	Carter et al., 1986
2	F	67	N/A	Diplopia, right lacrimation, vision impairment of right eye	Sella turcica	Autopsy case	Diplopia, right lacrimation, headache, V1 trigeminal neuralgia, ptosis, bilateral visual disturbance	Radiation therapy	Died 3 months later	Shinbori et al., 1988
3	F	87	N/A	Headache, diplopia	Optic canal, cavernous sinus, middle fossa	2 months	Headache, diplopia, dysopia	Biopsy, primary photon-beam external radiation (46 Gy)	Died 1 year later	Busaba et al., 2000
4	F	83	Japanese	Headache	Sella turcica	4 months	Headache, nasal bleeding, anosmia, dysopia, anisocoria, median fixation of the eyeball, partial hypopituitarism	Surgery	Died 6 Months later	Asano et al., 2000
5	M	56	Spanish	Headache	Cavernous sinus	Several months	Headache, diplopia, ptosis	Biopsy, radiotherapy (70 Gy)	Alive at 4 years	Pino Rivero et al., 2004
6	F	83	N/A	N/A	Cavernous sinus	Several weeks	Trigeminal paresthesia, ptosis, diplopia	Surgery, radiation therapy (60 Gy)	Alive 15 months after presentation	Lynch et al., 2005
7	M	75	Black	N/A	Cavernous sinus, middle fossa	Several weeks	Headache, diplopia, ptosis	Biopsy, radiation therapy, chemotherapy	N/A	Batra et al., 2005
8	F	74	N/A	Visual disturbance of the left eye	Sphenoid sinus, ethmoid sinus, left middle fossa	N/A	Bilateral visual disturbance, headache, ophthalmalgia, paresis of cranial nerveIII	Biopsy	Died 3 months later	Tsukahara et al., 2013
9	M	70	N/A	N/A	Nasal septum, sella turcica	Several weeks	Headache, lightheadedness, lassitude, bilateral blurry vision, diplopia, tonic seizure	Surgery, radiation therapy, chemotherapy	Died 7 months later	Smith SM et al., 2015
10	M	57	N/A	N/A	Left side of ethmoidal sinus, left optic foramen	Several weeks	Nasal congestion, epistaxis	Surgery, radiation therapy (60 Gy), chemotherapy, immunotherapy, interferon therapy	Died 1 year later	Zhao et al., 2015
11	F	50	N/A	N/A	Right side of sphenoid sinus	2 months	Headache, epistaxis	Surgery, radiation therapy (70 Gy), Chemotherapy	Alive 10 months after presentation	Mandal et al., 2022

Table 1 (continued)

No.	Sex	Age	Ethnicity	Initial symptoms	Range of progress	Period to definitive diagnosis	Symptoms before surgery	Treatment	Outcome	Year
12	M	57	N/A	N/A	Right side of cavernous sinus, clivus, sella turcica	2 months	Headache, trigeminal paresthesia, ptosis	Surgery, radiation therapy (60 Gy)	Died 2 years later	Liu et al., 2024
13	M	79	Japanese	Left ptosis	Sella turcica, clivus	1 month	Left ptosis, headache, nausea, partial hypopituitarism bilateral oculomotor paresis, visual disturbance	Surgery, radiation therapy, immunotherapy	Alive 4 months after presentation	Present case

F: female; M: male; N/A: not applicable; No., number

nonasal tumors.[22] Given the involvement of critical structures such as cranial nerves and the internal carotid artery within the cavernous sinus and the favorable outcomes of stereotactic radiotherapy for intracranial melanoma,[18] it is imperative to continue accumulating case reports of melanoma in the skull base region.

Primary malignant melanoma in the sphenoid sinus is an uncommon and challenging condition. Although case reports are gradually expanding our understanding, it remains a diagnosis that neurosurgeons should consider, especially in patients presenting with symptoms like headaches or double vision. Due to the rapid progression of symptoms, which can significantly impact daily living, it is important to include this rare disease in the differential diagnosis of sella turcica-related tumors requiring timely treatment.

Involving an otolaryngologist is highly recommended in such scenarios, as their expertise can aid in early and precise diagnosis, particularly when the disease has progressed. In this case, the tumor was thought to originate within the sella turcica, so only neurosurgical intervention was performed. However, reflecting on the situation, seeking input from an otolaryngologist could have provided a more thorough evaluation and treatment plan. Endoscopic assessments by an otolaryngologist may have identified potential sinonasal involvement, contributing to more targeted imaging and biopsy efforts. This interdisciplinary approach can enhance diagnostic accuracy, expedite intervention, and improve overall patient outcomes.

Informed Consent

A written informed consent form was provided by the patient for the use of the data for the present manuscript.

Disclaimer

Author Takakazu Kawamata is one of the Editorial Board members of the Journal. This author was not involved in the peer-review or decision-making process for this paper.

Conflicts of Interest Disclosure

There are no conflicts of interest.

References

1) Miller AJ, Mihm MC. Melanoma. N Engl J Med. 2006;355(1):51-65. doi: 10.1056/NEJMra052166
2) Schadendorf D, Fisher DE, Garbe C, et al. Melanoma. Nat Rev Dis Primers. 2015;1(1):15003. doi: 10.1038/nrdp.2015.3
3) Garcia-Alvarez A, Ortiz C, Muñoz-Couselo E. Current perspectives and novel strategies of NRAS-mutant melanoma. Onco Targets Ther. 2021;14:3709-19. doi: 10.2147/OTT.S278095
4) Carvajal RD, Antonescu CR, Wolchok JD, et al. KIT as a therapeutic target in metastatic melanoma. JAMA. 2011;305(22):2327-34. doi: 10.1001/jama.2011.746
5) Vízkeleti L, Ecsedi S, Rákosy Z, et al. The role of CCND1 alterations during the progression of cutaneous malignant melanoma. Tumour Biol. 2012;33(6):2189-99. doi: 10.1007/s13277-012-0480-6
6) Batsakis JG, Regezi JA, Solomon AR, et al. The pathology of head and neck tumors: mucosal melanomas, part 13. Head Neck Surg. 1982;4(5):404-18. doi: 10.1002/hed.2890040509
7) Asano K, Sobata E, Yamazaki K, et al. Malignant melanoma arising from the sphenoidal sinus--case report. Neurol Med Chir (Tokyo). 2000;40(6):329-34. doi: 10.2176/nmc.40.329
8) Batra K, Chhabra A, Rampure J, et al. CT and MRI appearances of primary sphenoid melanoma: a rare case. AJNR Am J Neuroradiol. 2005;26(10):2642-4.
9) Busaba NY. Primary melanoma of the sphenoid sinus. Otolaryngol Head Neck Surg. 2000;123(6):748-9. doi: 10.1067/mhn.2000.110724
10) Carter TR. Pathologic quiz case 1. Malignant melanoma. Arch Otolaryngol Head Neck Surg. 1986;112(4):450-3. doi: 10.1001/archotol.1986.03780040090019
11) Liu J, Wang P, Wang J, et al. Malignant melanoma of the sphenoid sinus: case report and literature review. Ear Nose Throat J. 2024;1455613241256520. doi: 10.1177/01455613241256520

12) Lynch SC, Lee AG, Graham SM, et al. Primary melanoma of the sphenoid sinus presenting with a third cranial nerve palsy. J Neuroophthalmol. 2005;25(4):289-92. doi: 10.1097/01.wno.0000189825.62010.93
13) Mandal G, Yadav V, Arora V, et al. An unusual case report of malignant melanoma of the sphenoid sinus with review of literature. Indian J Otolaryngol Head Neck Surg. 2022;74(suppl 2):752-4. doi: 10.1007/s12070-019-01787-8
14) Pino Rivero V, Keituqwa Yánez T, Marcos García M, et al. [Melanoma of sphenoid sinus. Case presentation and review of literature]. Acta Otorrinolaringol Esp. 2004;55(1):45-8. doi: 10.1016/s0001-6519(04)78482-4. Spanish.
15) Shinbori T, Uyama E, Eto K, et al. [An autopsy case of malignant melanoma possibly originating in the sphenoid sinus]. Rinsho Shinkeigaku. 1988;28(6):636-42. Japanese.
16) Smith SM, Schmitt AC, Carrau RL, et al. Primary sinonasal mucosal melanoma with aberrant diffuse and strong desmin reactivity: a potential diagnostic pitfall! Head Neck Pathol. 2015;9(1):165-71. doi: 10.1007/s12105-014-0553-5
17) Tsukahara K, Nakamura K, Motohashi R, et al. A case report of malignant melanoma of the sphenoid sinus. Case Rep Otolaryngol. 2013;2013:613472. doi: 10.1155/2013/613472
18) Tüttenberg J, Fink W, Back W, et al. A rare primary sellar melanoma. Case report. J Neurosurg. 2004;100(5):931-4. doi: 10.3171/jns.2004.100.5.0931
19) Lamorie-Foote K, Rangwala SD, Kammen A, et al. Melanoma metastasis to a nonfunctioning pituitary macroadenoma: illustrative case. J Neurosurg Case Lessons. 2021;1(23):CASE2167. doi: 10.3171/CASE2167
20) Mattogno PP, Giordano M, D'Alessandris QG, et al. Solitary metastatic melanoma of the pituitary gland: report of two cases and literature review. World Neurosurg. 2020;139:378-81. doi: 10.1016/j.wneu.2020.04.138
21) Salari B, Foreman RK, Emerick KS, et al. Sinonasal mucosal melanoma: an update and review of the literature. Am J Dermatopathol. 2022;44(6):424-32. doi: 10.1097/DAD.0000000000002157
22) Koto M, Demizu Y, Saitoh JI, et al. Definitive carbon-ion radiation therapy for locally advanced sinonasal malignant tumors: subgroup analysis of a multicenter study by the Japan carbon-ion radiation oncology study group (J-CROS). Int J Radiat Oncol Biol Phys. 2018;102(2):353-61. doi: 10.1016/j.ijrobp.2018.05.074

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