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Case Report

Primary intrasellar melanotic ependymoma successfully treated by combined transsphenoidal and gamma knife surgeries: case report and review

Yoshikazu Ogawa[1], Mika Watanabe[2], Hidefumi Jokura[3], Teiji Tominaga[4]

[1]Department of Neurosurgery, Kohnan Hospital, Sendai, Miyagi, Japan; Departments of [2]Pathology, [4]Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan; [3]Jiro Suzuki Memorial Gamma House, Furukawa Seiryo Hospital, Osaki, Miyagi, Japan

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Abstract: Ependymoma accounts for 6-12% of all intracranial tumors, but only 6 cases of melanotic ependymoma have been reported. Sellar ependymomas are also extremely rare, with only 5 cases reported in the pituitary fossa. A 26-year-old man presented with an extremely rare case of primary intrasellar melanotic ependymoma manifesting as consistent frontalgia. Magnetic resonance imaging showed a sellar lesion slightly compressing the optic chiasm upwards with various sizes and shapes of significant hypointense areas, initially suspected to be flow voids, in and on the surface of the lesion. Transsphenoidal surgery was performed, resulting in gross total removal of the tumor. Postoperative histological examination disclosed that the tumor cells had round to semioval nuclei without specific structures. Nucleoli were distinct, and frequent brown pigmentations were seen in the cytoplasm. Immunohistochemical examinations revealed diffuse positive reactions to vimentin, glial fibrillary acidic protein, and CAM5.2, and focal positive reaction to HMB-45. Type IV collagen was negative, and epithelial membrane antigen showed dot-like positive reaction at the perinuclear area. Gamma knife surgery was applied, and the patient has been healthy without tumor recurrence for 24 months. This extremely rare variant of ependymoma should be included in the differential diagnosis if melanin production is suspected.

Keywords: Intrasellar, melanotic ependymoma, pituitary, primary

Introduction

Glioma rarely occurs at the sella turcica, either as primary tumor, or by secondary invasion from the nearest parenchyma around the hypothalamus. Primary glioma includes granular cell tumor and pituicytoma as differential diagnoses, and pituicytoma includes pilocytic astrocytoma and various types of infiltrative astrocytoma [1]. Ependymoma is extremely rare in the sella turcica, with only 5 clinical cases [2-5]. The World Health Organization classification of 2007 proposed rare variant ependymomas as giant cell ependymoma, ependymoma with extensive tumor cell vacuolization, signet-ring cell ependymoma, ovarian ependymoma, ependymoma with neuropil-like islands, and melanotic ependymoma [6]. However, establishment of diagnoses for these rare variants could be extremely difficult in the absence of typical perivascular pseudorosettes and/or ependymal rosettes. Signet-ring cells and cells with cytoplasmic vacuoles could raise controversies in the differential diagnosis from metastatic brain tumors, and the presence of cytoplasmic brown pigmentation requires diagnostic exclusion from malignant melanoma.

We experienced a unique case of primary melanotic ependymoma in the sella turcica with an unusual appearance on magnetic resonance (MR) imaging, which was successfully treated by combined transsphenoidal and gamma knife surgeries.

Clinical summary

A 26-year-old man was introduced to our department suffering from consistent frontalgia. His familial and past histories included no

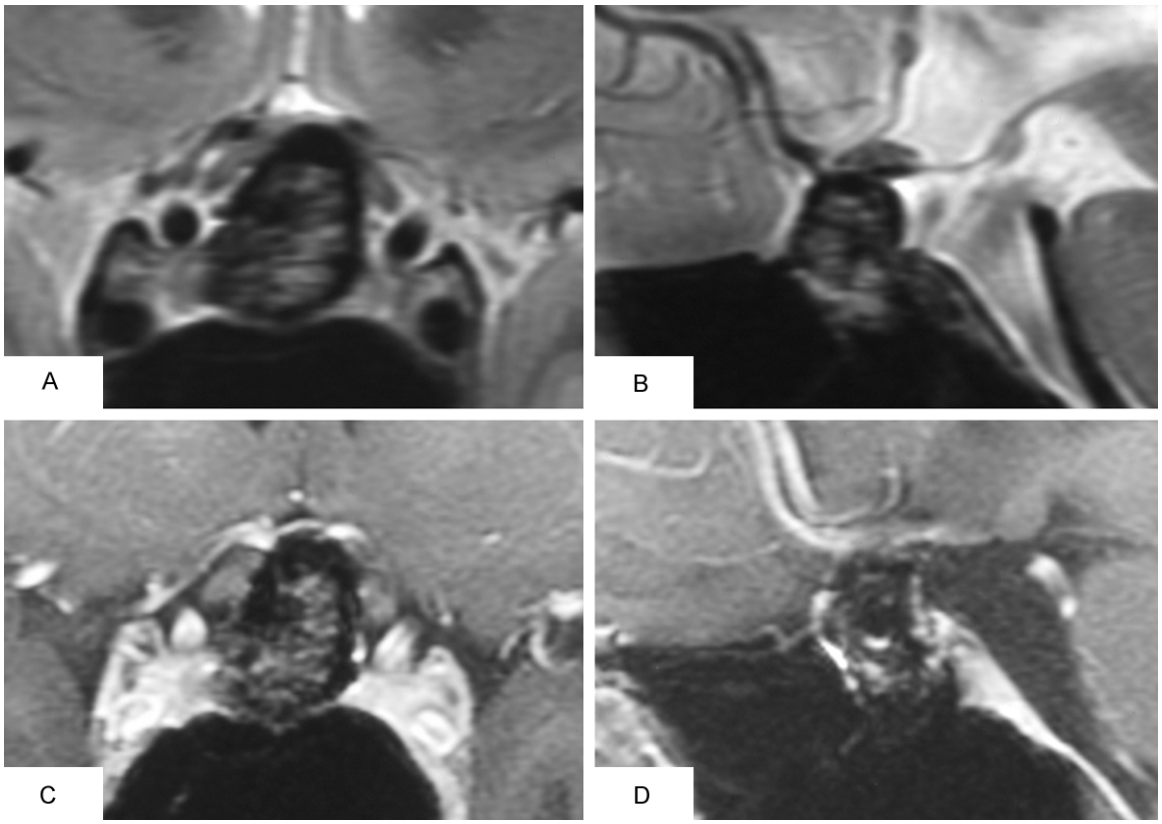

Figure 1. Magnetic resonance images showing a sellar tumor slightly compressing the optic chiasm upwards. Various sizes and shapes of significant hypointense areas, initially suspected to be flow-voids, are seen in and on the surface of the lesion. The tumor appears hyperintense on the T2-weighted images (A: Coronal image, B: Sagittal image), and heterogeneously enhanced with gadolinium (C: Coronal image, D: Sagittal image).

abnormal events. On admission, neurological examinations and endocrinological screenings discovered no abnormal findings. MR imaging showed a sellar lesion slightly compressing the optic chiasm upwards, and appearing as isointense on T1-weighted images and hyperintense on T2-weighted images. Various sizes and shapes of significant hypointense areas, which were initially suspected to be flow-voids, were seen in and on the surface of the lesion (**Figure 1**). Cerebral angiography showed faint tumor staining from the bilateral inferior hypophyseal arteries but no obvious vascular lesions. The differential diagnosis included metastatic brain tumor or occult and preclinical Cushing's disease, and transsphenoidal surgery was performed. Intraoperative findings disclosed soft tumor spotted with black pigmentary deposits like Indian ink, which was easily collapsed with slight manipulations, and the tumor bulk was totally removed by piecemeal. Normal pituitary gland and the arachnoid plane were preserved with pigmented deposits. The postoperative course was uneventful, and he was discharged 12 days after the operation without neurological or endocrinological deficits.

Pathological findings

The surgical specimens were immediately fixed for histological and immunohistochemical examinations with 10% buffered formalin and embedded in paraffin, and serial sections were cut to 3-μm thickness. Hematoxylin and eosin staining showed tumor cells with round to semioval nuclei without specific structures. Nucleoli were distinct, and cytoplasm were basophilic (**Figure 2A**). Frequent brown pigmentations were seen in the cytoplasm (**Figure 2B**). Immunohistochemical staining using the avidin-biotin peroxidase complex method was negative with all the following anti-pituitary hormone antibodies r: polyclonal anti-growth hormone (Dako Denmark A/S, Glostrup, Denmark), polyclonal anti-adrenocorticotropic hormone

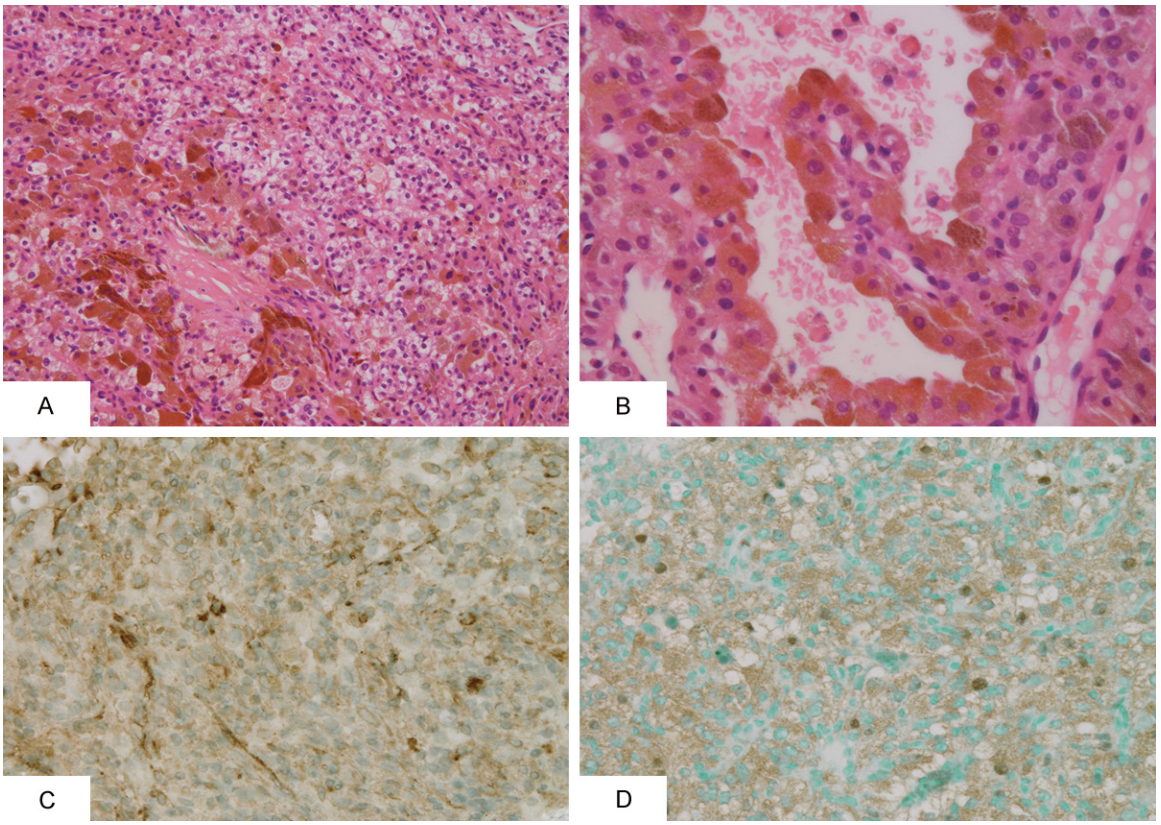

Figure 2. Photomicrographs of the surgical specimen showing tumor cells with round to semi-oval nuclei without specific structures. Nucleoli are distinct, and cytoplasms are basophilic (A), with frequent brown pigmentations in the cytoplasms (B). Hematoxylin and eosin, original magnification a: × 100, b: × 400. Photomicrographs of the surgical specimen showing diffuse positive reactions for vimentin (C), glial fibrillary acidic protein (D). Original magnification × 100.

(Dako Denmark A/S), polyclonal anti-prolactin (Dako Denmark A/S), monoclonal anti-thyroid-stimulating hormone (SPM104, Lab Vision, Fremont, CA; 1:100), monoclonal anti-luteinizing hormone (LH01, Lab Vision; 1:500), monoclonal anti-follicle-stimulating hormone (FSH03, Lab Vision; 1:500), and polyclonal anti-alpha-subunit hormone (CELL MARQUE, Rocklin, CA). Ki-67 (MIB-1, autoclave for antigen retrieval, Dako Denmark A/S; 1:300) labeling index was 2%.

A provisional diagnosis of malignant melanotic tumor was made. Whole body screening was introduced to exclude metastases from malignant melanoma including dermatological examination, ophthalmology, esophagogastroduodenoscopy, colonoscopy, and whole body scanning by computed tomography with contrast medium and positron emission tomography using [^{18}F] fluorodeoxyglucose, but all these examinations were negative. Additional immunohistochemical examinations revealed diffuse positive reactions for vimentin (clone V9, diluted, microwave for antigen retrieval, Dako Denmark A/S) (**Figure 2C**), glial fibrillary acidic protein (clone 6F2, Dako Denmark A/S; 1:100) (**Figure 2D**), and CAM5.2 (clone 5D3, diluted, autoclave for antigen retrieval, Nichirei, Tokyo, Japan) (**Figure 3A**), and focal positive reaction for HMB-45 (clone HMB45, trypsin for antigen retrieval, Dako Denmark A/S; 1:100) at almost the same locations as melanin granules (**Figure 3B**). Staining was negative for Type IV collagen (clone CIV22, trypsin and pepsin for antigen retrieval, Dako Denmark A/S; 1:100) (**Figure 3C**), so this tumor was thought to have no basal membrane. Dot-patterned positive reactions were seen in the cytoplasm with anti-epithelial membrane antigen antibody (clone E29, Nichirei; 1:2) (**Figure 3D**). The final diagnosis was established as primary intrasellar melanotic ependymoma.

The patient thereafter received gamma knife surgery as adjuvant therapy to treat possible

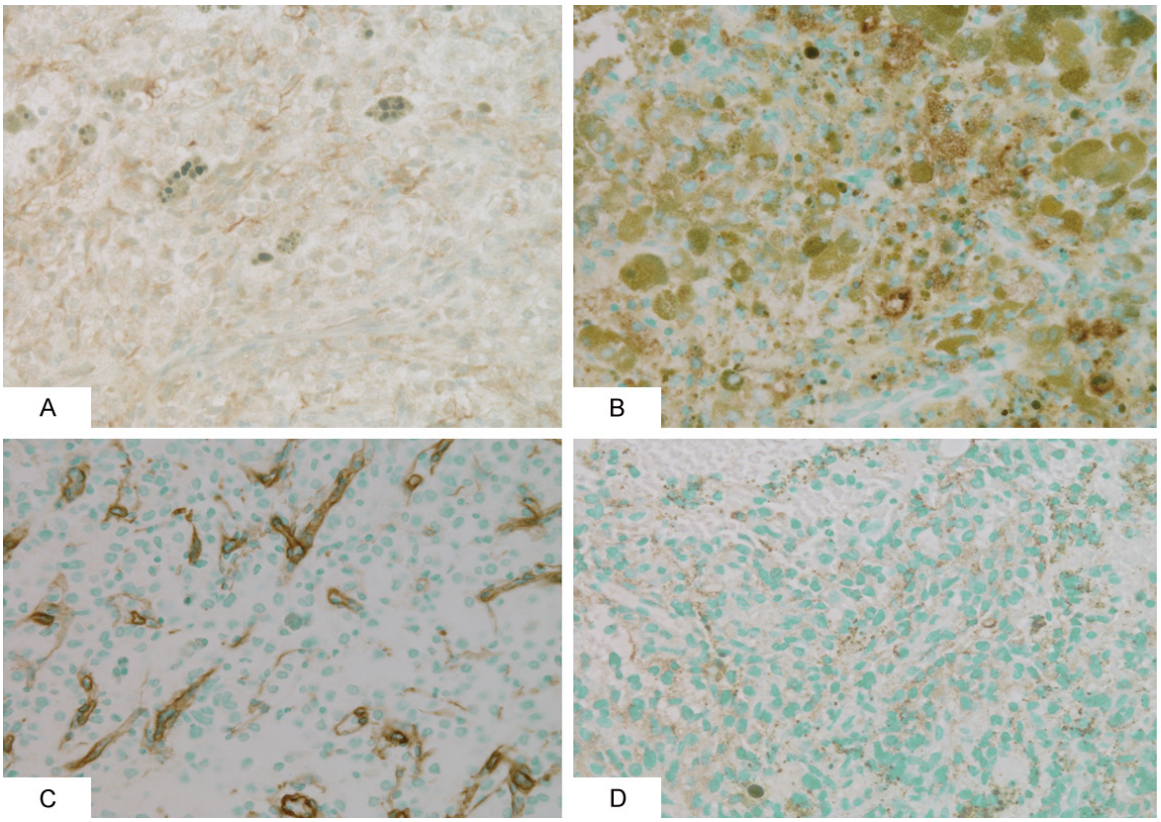

Figure 3. Photomicrographs of the surgical specimen showing diffuse positive reactions for CAM5.2 (A), and focal positive reaction for HMB45 (B). Type IV collagen is negative (C), but epithelial membrane antigen shows dot-like positive reaction (D). All original magnifications × 100.

Table 1. Summary of reported cases of melanotic ependymoma

Authors & Year	Age (yrs)/Sex	Location
McCloskey et al., 1976	30/woman	Posterior temporal lobe
Rosenblum et al., 1990	13/woman	Frontoparietal region extending from lateral ventricle to cortical surface
Rosenblum et al., 1990	52/man	Fourth ventricle (subependymoma, autopsy case)
Russel and Rubinstein, 1989	36/man	Fourth ventricle
Chan et al., 2003	45/man	Fourth ventricle
Ertan et al., 2010	35/woman	Fourth ventricle
Present case, 2015	26/man	Sella turcica

Table 2. Summary of reported cases of ependymoma of the sella turcica

Authors & Year	Age (yrs)/Sex	Symptom	Outcome
Sarkisian & Schltz, 1956	31/woman	Amenorrhea and galactorrhea	Uneventful bitemporal hemianopsia
Winer et al, 1989	81/man	Visual loss, headache	Died 3 days, sepsis oculomotor nerve palsy
Thompson et al, 2001	64/man	Visual decrease, atrophy, left hypopituitarysm	Improved 3 mons residual hemianopsia
Mukhida et al, 2006	43/man	Decreased libido, weight loss, hypopituitarysm	Improved 12 mos
Scheithauer et al, 2009	71/man	Migrane, bitemporal hemianopsia	Unchanged 15 mos
Present case, 2015	26/man	Frontalgia	Total removal, 24 mos

infiltration of the tumor cells to the meninges and normal pituitary gland. He has remained healthy and continued working without local tumor recurrence or developing any other lesions for 24 months.

Discussion

Ependymoma accounts for 6-12% of all intracranial tumors, but only 6 cases of the rare variant melanotic ependymoma have been report-

ed (**Table 1**) [7-11]. These cases arose with connections to the ventricular system; the fourth ventricle in 4 cases, the lateral ventricle in 1, and the posterior temporal lobe in 1. The diagnoses were established by confirming typical ependymal rosettes. Sellar ependymomas are also extremely rare, with only 5 reported cases in the pituitary fossa (**Table 2**) [2-5]. Four of these 5 cases had typical perivascular pseudorosettes and/or ependymal rosettes, but monomorphous histology without typical pseudorosette formation was reported in 1 case with resultant difficulties in identifying these rare and atypical findings [1].

The origin of these tumors remains unknown. Intrasellar ependymomas may develop from neoplastic transformation of remnants of the ependymal cleft, which consists of undifferentiated ependymal precursors that form the pituitary infundibulum and normally recede by 16 weeks gestation [3]. Aberrant migration may also be involved based on rare examples in the soft tissue, eye, ovaries, broad ligament, mediastinum, and lung [5]. Recent evidence has raised the possibility of so-called ependymal pituicytes, a type of cell uncommon in mammals but frequently seen in lower vertebrates [1, 12]. Accumulation of more experiences and gene researches are expected to solve this enigma.

Conclusion

The present extremely rare case of primary intrasellar melanotic ependymoma indicates that preoperative diagnosis is almost impossible to establish, but this rare variant should be included in the differential diagnosis if melanin production is suspected. Multidisciplinary treatment including gamma knife may be effective.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Yoshikazu Ogawa, Department of Neurosurgery, Kohnan Hospital, 4-20-1 Nagamachiminami, Taihaku-ku, Sendai, Miyagi 982-8523, Japan. Tel: +81-22-248-2131; Fax: +81-22-248-1966; E-mail: yogawa@kohnan-sendai.or.jp

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