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Case Report

Primary malignant melanoma in the pineal region treated without chemotherapy

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Abstract

Background: Primary pineal malignant melanomas are uncommon intracranial tumor.Here we discuss and review a case of primary pineal malignant melanoma over its feature of imaging studies, pathological findings, and management.

Case Description: A 49-year-old woman receiving renal dialysis underwent computed tomography due to a 4-month history of tinnitus and hearing disturbance. A high-density 35-mm diameter tumor was detected in the pineal region; there was obstructive hydrocephalus. The tumor was heterogeneously hyperintense on T1-weighted magnetic resonance images, iso- and low-mixed intense on T2-weighted images with hemorrhagic components, and very low-intense on T2* images. A tumor was subtotally removed via the occipital transtentorial approach. Histologically, it consisted of densely proliferated spindle-shaped or polygonal cells with rich cytoplasmic melanin. The neoplastic cells manifested cellular pleomorphism, nuclear atypia, and mitosis (3/10 high-power fields) and were immunopositive for HMB45, Melan-A, and S100 protein. The MIB-1 index was 17.4%. Whole-body 18-fluoro-deoxyglucose positron emission tomography did not demonstrate any sites with hyper uptake. Examination of the skin and mucosa identified no lesions suggestive of melanoma. She underwent treatment with the whole brain and extended local boost irradiation. Chemotherapy was not delivered due to renal failure. Follow-up imaging studies showed no recurrence or distant lesions 56 weeks after surgery.

Conclusion: We report a rare case of primary pineal malignant melanoma with prolonged survival of more than 56 weeks after subtotal tumor resection followed by whole-brain and extended local irradiation without chemotherapy.Radiotherapy without chemotherapy might be sufficient for the treatment of this tumor.

Key Words: Central nervous system, malignant melanoma, pineal, primary

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INTRODUCTION

Primary melanomas of the central nervous system (CNS) are rare but aggressive neoplasms; 3.6% of these tumors arise in the pineal region.[11] Primary intracranial melanomas are thought to develop from melanocytes, normal elements of the arachnoid covering the brain, spinal cord, and pineal gland, that originated at the neural crest and migrated during embryogenesis.[9,16]

To our knowledge, 16 pineal malignant melanomas have been reported since 1899. We now report a patient whose primary pineal malignant melanoma was treated without chemotherapy and discuss the imaging studies, pathological findings, and management of this rare case.

CASE REPORT

A 49-year-old Japanese woman on renal dialysis had a 4-month history of tinnitus and hearing loss. Computed tomography (CT) showed a high-density 35-mm diameter tumor in the pineal region and obstructive hydrocephalus [Figure 1]. The tumor was heterogeneously hyperintense on T1-weighted magnetic resonance imaging (MRI) scans and low- and iso-mixed intense on T2-weighted images. On T2* images, it contained very low intensity areas suggestive of hemorrhagic components [Figure 2]. No other intracranial lesions including lesions underlying her acoustic symptoms were identified. Her chronic renal failure ruled out enhanced imaging studies. On the basis of our neuroimaging findings, we made a preoperative diagnosis of pineal parenchymal tumor with hemorrhagic components and melanoma.

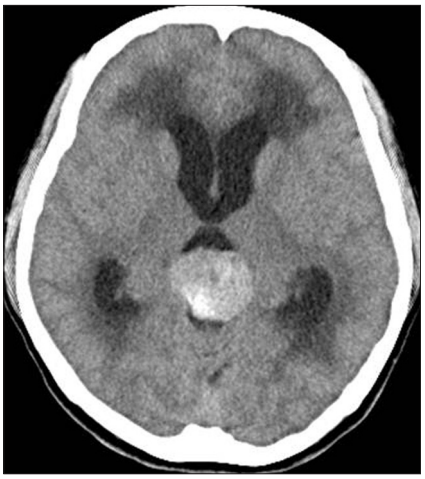

Figure 1: Computed tomography scan showing a high-density tumor in the pineal region accompanied by obstructive hydrocephalus

We used the left occipital transtentorial approach with the patient in the three-quarter prone position.[2] To reduce occipital lobe retraction, an operated side-down approach was used. The incision extended from the inion along the midline and then was curved in a horseshoe fashion back behind the ear. The craniotomy was performed to visualize the transverse and sagittal sinuses through extent in the operative field by rongeur or airdrill. Then, a catheter was placed in the left lateral ventricle. The dura mater was opened with two triangular flaps based on the superior sagittal sinus and the transverse sinus. The incision of the tentorium was made at an angle of 15° to the straight sinus, starting from a point, 15 mm lateral and 15 mm anterior to the junction of straight and transverse sinus, extending upto the tentorial free edge, and then the lateral flap was reflected laterally. After the dense arachnoid over the quadrigeminal cistern was opened, a dark red, easily bleeding solid tumor was found in the pineal region [Figure 3]. We successfully dissected the feeders arising from posterior choroidal arteries, removed the tumor subtotally. After 2 weeks later from first operation, endoscopic third ventriculostomy was performed due to persistent hydrocephalus. Her preoperative complaints of hearing disturbance and tinnitus gradually improved after two operations.

Hematoxylin and eosin (HE) staining showed the tumor to be composed of anaplastic spindle-shaped and epithelioid cells arranged in nests, fascicles, or sheets; they contained variable amounts of

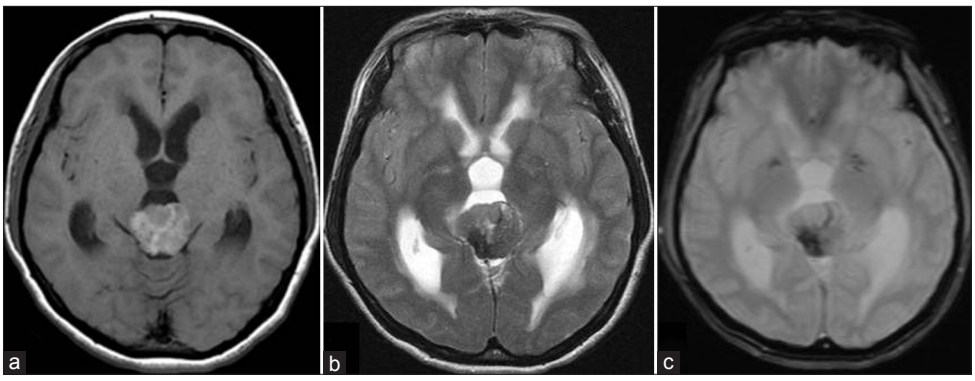

Figure 2: Preoperative magnetic resonance imaging. The tumor was heterogeneously hyperintense on T1- (a) and iso- and low-mixed intense on T2-weighted images (b). It contained hemorrhagic components of very low intensity on T2* images (c)

cytoplasmic melanin and manifested significant cellular pleomorphism, nuclear atypia, and mitosis (3/10 high-power fields; HPFs).The tumor cells were immunohistochemically positive for HMB45, Melan-A, and S100 protein. Additionally, the MIB-1 index was 17.4 ± 3.0% [Figure 4].

After surgery, the patient was treated with 36 Gy of whole-brain- and 18 Gy of extended local boost irradiation.Her coexisting renal failure ruled out chemotherapy. A whole-body 18-fluoro-deoxyglucose positron emission tomography (FDG-PET) scan showed no abnormally increased uptake [Figure 5]. Meticulous examination of her skin and mucosa by dermatologists found no lesions suggestive of melanoma.

The most recent MRI scans acquired 56 weeks after her initial treatment showed no evidence of recurrence or metastatic lesions [Figure 6].

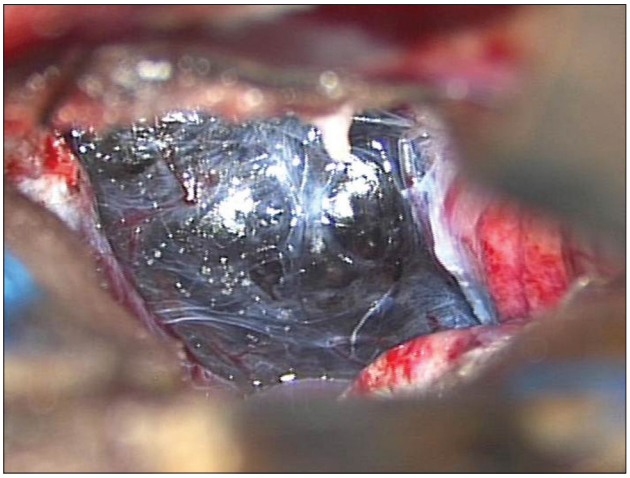

Figure 3: Intraoperative photograph (left occipital transtentorial approach) showing a dark red solid tumor in the pineal region

DISCUSSION

Most reported lesions of primary melanomas of the CNS were found in the spinal canal or the posterior fossa because of the higher concentration of melanocytes in the leptomeninges at the anterior and lateral surface of the spinal cord and ventrolateral to the medulla oblongata.

Primary pineal malignant melanomas are exceedingly rare; only 16 cases have been reported to date and of these, eight were detected by MRI [Table 1]. The mean age of these eight patients at presentation was 50.2 years (range, 20–73 years); five of the patients were female. On average, patients presented to the hospital 6.8 weeks (range, 2–16 weeks) after symptom onset and most manifested increased intracranial pressure (ICP). Lethargy, paralysis, aphasia, gait disturbance, and memory changes were also recorded. Only one patient presented with Parinaud's syndrome. Up to 20% of patients with pineal tumors experienced hearing loss and/or tinnitus that may be explicable by increased ICP and compression of the midbrain auditory pathways.[7,14] Gradual improvement of hearing loss and tinnitus after surgeries in the present case could be explained that similar mechanisms above may precede those symptoms.

CT scans of intracranial malignant melanomas usually show a homogeneously enhanced high-dense mass and MRI shows a characteristic signal. The melanin content of the tumor reflects the presence of free radicals; therefore, a paramagnetic effect responsible for a shortened T1 relaxation time is produced. Consequently, MRI reveals a mass that is hyperintense on T1- and iso/hyperintense on T2-weighted images. The shorter T1 relaxation time correlates with the amount of melanin in the tumor.[1] Gaviani *et al.* propose that there is no correlation between T2* intensity and melanin.[8] In our case, low intensity

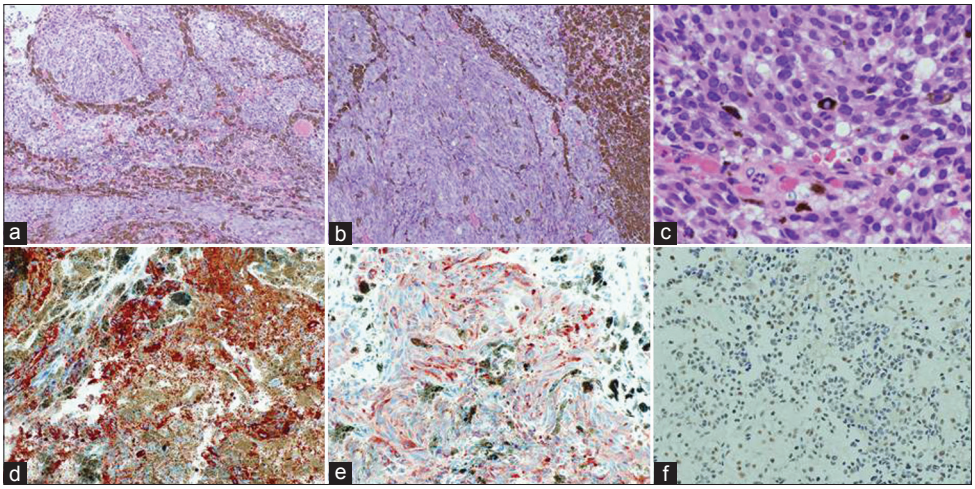

Figure 4: Photomicrographs of the excised tumor. Hematoxylin and eosin staining showed anaplastic spindled or epithelioid cells arranged in nests, fascicles, or sheets, displaying variable cytoplasmic melanin (a and b, ×100). These tumor cells exhibited significant cellular pleomorphism and nuclear atypia. Mitotic figures were seen occasionally (c, ×400). The tumor cells were positive for HMB45 (d, ×200) and Melan-A (e, ×200). The MIB-1 index was 17.4% (f, ×200)

areas on T2* images might describe tumor hemorrhage. These imaging findings help us to differentiate this rare tumor from other pineal parenchymal tumors arising in adults.

Melanocytic tumors are classified into well-differentiated melanocytomas, intermediate-grade melanocytic tumors, and malignant melanomas. Pathologically, malignant melanomas consist of spindle-shaped or epithelioid cells arranged in loose nests, fascicles, or sheets, with variable amounts of cytoplasmic melanin pigment. These tumors are densely cellular and manifest significant cellular pleomorphism and nuclear atypia associated with a high mitosis rate (mean 5.7/10 HPFs) and high MIB-1 labeling indices (mean 8.1%).[5] The cytoplasm is immunoreactive for HMB-45 and Melan-A, the hallmarks of melanoma, and the neoplastic cells are immunopositive for S-100 protein but not for GFAP or EMA. In our patient, the pathologic findings were compatible with malignant melanoma.

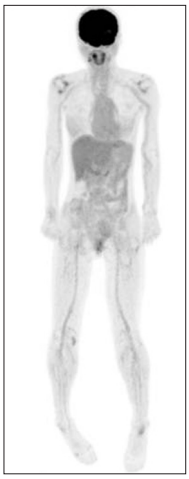

Figure 5: Whole-body 18-fluoro-deoxyglucose positron emission tomography showing no abnormal uptake

It is difficult to distinguish primary CNS melanoma from metastatic melanoma on neuroimages alone.[18] Hayward[10] proposed the following factors for establishing a diagnosis of a primary CNS melanoma: (1) no malignant melanoma outside the CNS, (2) leptomeningeal involvement, (3) intramedullary spinal lesions, (4) hydrocephalus, (5) tumor location in the pituitary or pineal gland, and (6) a single intracerebral lesion.Despite aggressive multimodality treatment, the reported median survival of patients with metastatic melanoma is only 3–6 months.[6,12] In contrast, appropriately treated patients with primary pineal melanoma can expect a long survival. Therefore, it is necessary to distinguish between primary CNS- and metastatic melanomas by systemic investigations including whole-body PET studies and scrupulous examination by dermatologists.

At present, there is no standardized treatment to address primary pineal malignant melanomas. As patients who did not receive adjuvant treatment survived no longer than 3 months,[13,16,17] surgical tumor resection and postoperative radio-chemotherapy have been recommended and reported to increase the length of survival.[1,3-5,13,15-17,19]However, as shown in Table 1, no difference was noted on the survival rate of patients who received radiotherapy alone or in combination with chemotherapy. In fact, Barron *et al.*[3] reported a patient with primary pineal gland melanoma who survived for 56 weeks after receiving only radiotherapy. In addition, the present case also survived more than 56 weeks after subtotal tumor resection and whole-brain and extended local irradiation without chemotherapy. Those suggest that radiotherapy without chemotherapy might be sufficient for the treatment of primary pineal malignant melanoma, especially over cases with renal failure in who are restricted to use anticancer agents.

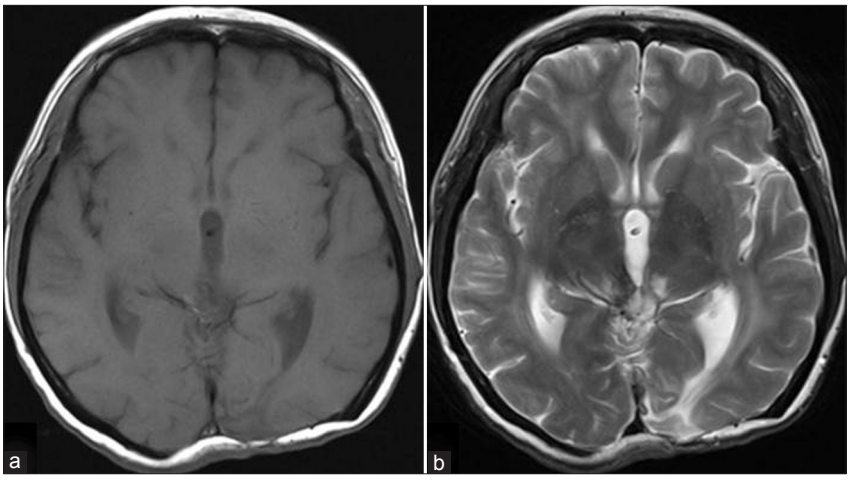

Figure 6: Magnetic resonance imaging after 56 months of surgery. Axial T1-weighted images (a) and T2-weighted images (b) showing no lesion in the pineal gland

Table 1: Reported cases of primary pineal malignant melanoma detected by magnetic resonance imaging

Author (year)	Sex/ age	Time to diagnosis	Symptoms	MRI (intensity)			Surgery	Adjuvant therapy	Immuno-positivity	Survival (weeks)
				T1 weighed image	T2 weighed image	Enhance-ment				
Rubino (1993)[14]	M/60	4	gait disturbance, lethargy, nystagmus	hyper	Hetero-geneous	+	total resection	whole brain radiation	HMB-45 S-100	>56
Mitchell (1998)[11]	M/49	3	increased ICP signs, dysarthria	hyper	NA	+	biopsy	NA	HMB-45 S-100	NA
Suzuki (2001)[15]	F/50	16	memory disturbance	hyper	hypo	±	subtotal resection	whole brain radiation	HMB-45 S-100	88
Yamane (2004)[17]	F/53	2	headache, Parinaud sign	hyper	hypo	+	surgical resection	dacarbazine, ACNU, vincristine, interferon	S-100	>280
Barron (2007)[3]	F/73	NA	headache, gait disturbance, diplopia, memory disturbance	hyper	iso	+	none	radiation	HMB-45 S-100 Melan-A	56
Bookland (2007)[4]	F/20	3	headache, amenorrhea	hyper	hypo	+	biopsy	whole brain radiation, gamma-knife, temozolomide	HMB-45 Melan-A	>37
Martin-Blond (2009)[12]	M/44	6	seizures, memory and gait disturbance	hyper	iso	+	biopsy	whole brain radiation	Melan-A	52
Arantes (2011)[1]	F/54	16	memory and gait disturbance, lethargy, incontinence	hyper	heterogeneous	+	subtotal resection	whole brain plus local radiation, temozolomide	HMB-45	>80
Present case (2012)	F/49	4	tinnitus hearing loss	hyper	iso-hypo mixed	NA	subtotal resection,	whole brain plus local radiation	HMB-45 S-100 Melan-A	>50

MRI: Magnetic resonance imaging, S-100: S-100 protein, HMB-45: A melanoma-associated antigen, ICP: Intracranial pressure, +: well enhanced, ±: slightly enhanced, NA: Not available

CONCLUSION

We report a rare case of primary melanoma of the pineal gland with prolonged survival of more than 56 weeks after subtotal tumor resection followed by whole-brain and extended local irradiation without chemotherapy. However, a long-term follow-up was needed to determine whether radiotherapy without chemotherapy is sufficient for the treatment of primary pineal malignant melanomas.

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