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Case Report

Primary Sellar Neuroblastoma in an Elderly Patient: Case Report

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A 71-year-old male presented with an isolated well-enhanced sellar lesion accompanied by hypopituitarism, diagnosed preoperatively as a pituitary adenoma, meningioma, or metastatic brain tumor. However, histological examinations yielded a diagnosis of neuroblastoma. Primary sellar neuroblastoma in the elderly is very rare. We therefore describe this case of primary sellar neuroblastoma, mimicking common pituitary tumor, and review the literature. There have so far been only nine reported cases of primary sellar neuroblastoma in the English literature. All reports like the present case, demonstrated similar neuroimaging of a "dumbbell-shaped extension in the sellar region." Moreover, the tumors may exhibit characteristic features, such as rapid tumor growth, hypopituitarism, or oculomotor nerve palsy, and these findings may represent helpful signs for the diagnosis of primary sellar neuroblastoma.

Keywords: elderly case, magnetic resonance imaging, neuroblastoma, pituitary tumor, sellar region

Introduction

Neuroblastoma arising in the sellar region is extremely rare, with only nine cases having been reported so far in the English literature.[1–9] A limited analysis of the pathogenesis has been given, and no therapeutic strategy has yet been established.

We report a case of primary sellar neuroblastoma, which was first diagnosed as pituitary adenoma. By reviewing the literature, we identified characteristic findings among the neuroimaging and clinical symptoms for differentiating sellar neuroblastoma.

Case Report

A 71-year-old male was admitted to another hospital complaining of general fatigue. Laboratory evaluations demonstrated hyponatremia. A computed tomography (CT) scan disclosed a sellar mass lesion. Under a diagnosis of pituitary tumor, the patient was referred to our hospital. His consciousness level was clear and neurological examinations revealed no abnormalities except for bitemporal hemianopsia and right oculomotor nerve palsy. Magnetic resonance (MR) imaging demonstrated a sellar mass with suprasellar extension and bilateral cavernous sinus invasion. The lesion was isointense on T_1-weighted and T_2-weighted MR images; slightly heterogeneous enhancement was evident after contrast medium administration (Fig. 1). Laboratory and endocrinological evaluations revealed hyponatremia and panhypopituitarism (Table 1). Hormone replacement therapy was initiated immediately after admission. The plasma sodium became normalized on the eighth day of hospitalization.

The patient underwent surgical removal via an endoscopic transsphenoidal approach on the fifteenth day of hospitalization. The intraoperative findings indicated that no contact existed between the tumor and the floor of the sella turcica or bone of the paranasal sinuses. It proved very difficult to remove the tumor, because it was rich in fiber components, and bled easily. Partial removal of the tumor was therefore carried out, excluding the suprasellar part and bilateral cavernous sinus invasion.

Pathological examinations of the tumor specimen showed that the tumor tissue was composed of small blue round cells arranged in a lobulated or "zellballen" pattern surrounded by a vascular connective tissue (Fig. 2a). The tumor cells were

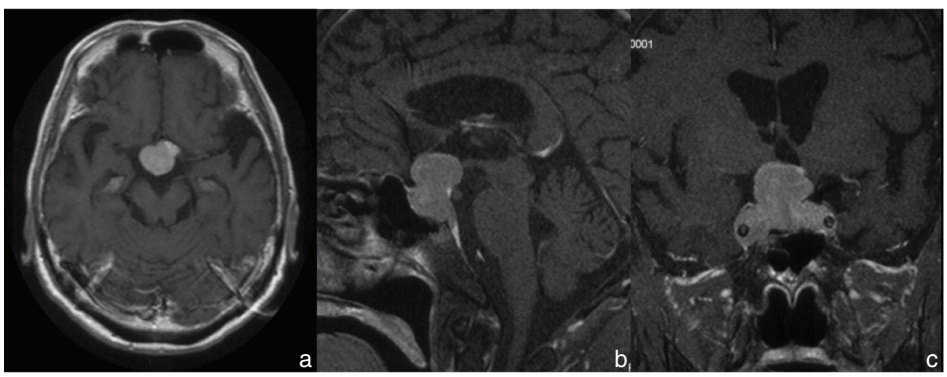

Fig. 1 Preoperative magnetic resonance (MR) imaging demonstrating a dumbbell-shaped form pituitary tumor with suprasellar extension and invasion of the cavernous sinus. There was heterogeneous enhancement after contrast medium administration (a: axial view, b: sagittal view, c: coronal view).

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Table 1 Laboratory data at the time of hospitalization

		(Normal values)
Plasma sodium	109 mEq/l	(136–148 mEq/l)
Plasma potassium	4.7 mEq/l	(3.6–5.0 mEq/l)
Plasma chloride	77 mEq/l	(98–109 mEq/l)
Thyroid stimulating hormone	0.12 μIU/ml	(0.34–3.80 μIU/ml)
Free triiodothyronine	1.45 pg/ml	(2.00–3.80 pg/ml)
Free thyroxine	1.04 pg/ml	(0.8–1.5 pg/ml)
Adrenocorticotropic hormone	3.0 pg/ml	(7.2–63.3 pg/ml)
Prolactin	8.65 ng/ml	(3.6–16.3 ng/ml)

The laboratory and endocrinological evaluations revealed hyponatremia and panhypopituitarism, at the time of hospitalization.

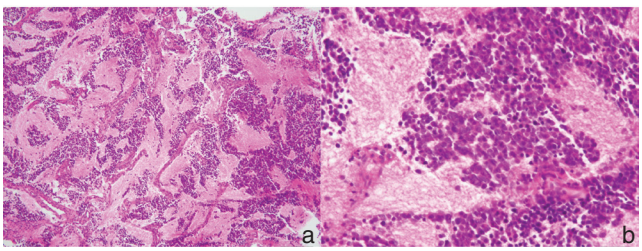

Fig. 2 Photomicrographs obtained by hematoxylin and eosin (H&E) staining. Histological examinations of the tumor revealed that it was composed of small cells with oval-round hyperchromatic nucleoli, accompanied by a surrounding vascular connective tissue (a: original magnification ×100, b: original magnification ×400).

round with oval-round hyperchromatic nucleoli and a sparse chromophilic, slightly acidophilic cytoplasm (Fig. 2b). Moderate cellular and nuclear pleomorphism and occasional mitoses were observed in some areas. Immunohistochemically, the tumor cells exhibited positive expression for S-100 protein, neuron-specific enolase, neurofilament, chromogranin A, and synaptophysin (Fig. 3a–d), whereas they were immunonegative for epithelial membrane antigen, glial fibrillary acidic protein, and pituitary hormones such as prolactin and adrenocorticotropic hormone (Fig. 3e–h). There was diffuse positivity for Ki-67; the MIB-1 labeling index for the proliferative activity was 12.6%. Immunostaining for TP53 was partially positive, although most cells were negative. These pathological findings were consistent with neuroblastoma.

The patient was discharged from our hospital on the fifteenth day after surgery, and his postoperative course was uneventful. His oculomotor nerve palsy was improved, and visual field deficit underwent slight improvement after the operation, but his panhypopituitarism and bitemporal hemianopsia persisted after the surgery. Laboratory examinations yielded a normal result for urinary vanillylmandelic acid (VMA): 3.1 mg/day (1.5–4.3 mg/day). A CT scan of the whole body revealed no other region with primary tumor or metastatic lesions. A second operation was performed at 3 months after the first operation to remove the suprasellar part of the tumor via a bi-frontal craniotomy. There was no contact of the

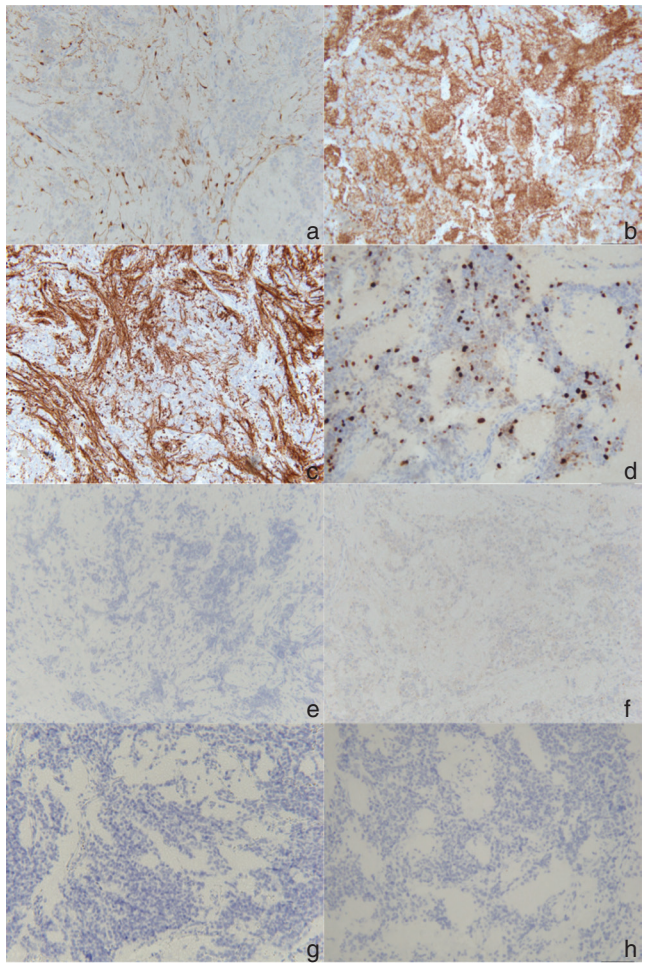

Fig. 3 Photomicrographs of immunohistochemical staining. The tumor cells showed positive expression for S-100 protein (a), synaptophysin (b), and neurofilament (c), and diffuse positivity for Ki-67 (MIB-1 labeling index: 12.6%, d); in the same time, the neoplasm was immunonegative for adrenocorticotropic hormone (e), prolactin (f), epithelial membrane antigen (g), and glial fibrillary acidic protein (h). Original magnification ×400.

tumor with the olfactory bulbs or ethmoidal aircells. These operative findings together with the neuroimaging data could exclude a diagnosis of esthesioneuroblastoma growing into the sella. Postoperative MR imaging indicated that the sellar and suprasellar parts of the tumor were mostly removed (Fig. 4a–c). Since tumor remained in the cavernous sinus, the patient underwent gamma-knife radiosurgery with a marginal isodose of 14 Gy, at 28 days after the second operation. Gadolinium scintigraphy at 7 months after the gamma-knife radiosurgery revealed no other region with primary tumor or metastatic lesions. At 18 months after the second operation, there was no apparent evidence of tumor recurrence (Fig. 4d–f).

Discussion

Cerebral neuroblastoma, a rare malignant tumor that commonly occurs in the cerebral hemisphere or paraventriclar region of children,[10,11] belongs to a group of central nervous system primitive neuroectodermal tumors (CNS PNETs) which represent embryonal tumors composed of

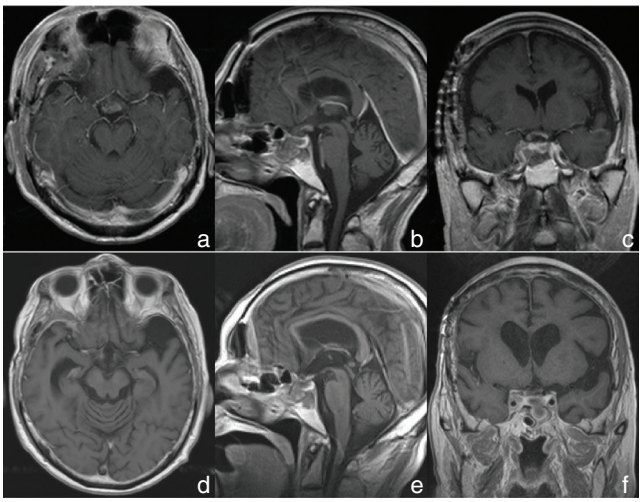

Fig. 4 Second postoperative magnetic resonance (MR) imaging. The sellar and suprasellar part of the tumor were mostly removed (a: axial view, b: sagittal view, c: coronal view). MR imaging was performed 1 year after gamma-knife radiosurgery. The tumor parts in the bilateral cavernous sinus had become shrunken and there was no recurrence of the tumor (d: axial view, e: sagittal view, f: coronal view).

undifferentiated or poorly differentiated neuroepithelial cells. Primary sellar neuroblastoma is extremely rare. There have so far been only nine reported cases in the English literature (Table 2).

Although the origin of primary sellar neuroblastoma remains unknown, several theories have been put forward in previous reports. Lin et al. suggested that diffusely scattered cells of the nervous terminalis, or olfactory placode neuronal cells which blocked migration, might represent the origin of the tumor.[2] Furthermore, there have been two additional suggestions for the origin of the tumor:neuronal transformation from the pituitary epithelium, and a ganglion of Locy which grows between the olfactory fossa and the telencephalic vesicle.[1,4,6,8,9] Oyama et al. reported the case of a 33-year-old male with sellar neuroblastoma who did not display an elevated urinary VMA. In this case, they suggested that the primary tumor could have arisen in the supradiaphragmatic region and extended into the sellar turcica, since catecholamine metabolites in the urine are usually elevated in peripheral neuroblastoma but not within tumor of the blood-brain barrier: primary cerebral neuroblastoma.[4]

Table 2 Cases of primary sellar neuroblastoma

Authors	Age	Neuroimaging		Neurological deficit	Pituitary function	Treatment	Follow-up
		DSF	BE				
Sarwar (1979)[8]	31	Yes	Yes	Bitemporal hemianopsia	Not mentioned	TCS (partial resection) Postoperative radiotherapy	5 years without progression
Lach et al. (1996)[1]	40	Yes	NM	Bitemporal hemianopsia	Hyperprolactinemia	TCS (partial resection)	NM
Roy et al. (2000)[6]	44	Yes	NM	Bitemporal hemianopsia	Hyperprolactinemia	TSS (partial resection) Postoperative radiotherapy	2 years without progression
Mariani et al. (2004)[3]	35	Yes	NM	Bitemporal hemianopsia	Hyperprolactinemia	TSS (complete resection)	25 months without recurrence
Sajko et al. (2005)[7]	57	Yes	NM	Left-side temporal hemianopsia	Hyperprolactinemia Increased levels of FSH	TSS (subtotal resection) Postoperative radiotherapy	NM
Oyama et al. (2005)[4]	33	Yes	Yes	Bitemporal hemianopsia Left oculomotor nerve palsy	Panhypopituitarism	TSS (finally, subtotal resection) TCS GKS (marginal dose: 15 Gy) Postoperative radiotherapy Radiotherapy for metastasis	Regrowth; 16 months after 1st surgery Surgery was performed 6 times Radiotherapy; after 6th surgery Cervical metastasis; 3 months after radiotherapy
Lin et al. (2009)[2]	40	Nm	Yes	No neurological deficit	Normal	TSS Postoperative radiotherapy	1 year without symptoms
Schmalish et al. (2009)[9]	43	Yes	NM	Bitemporal hemianopsia	Hyperprolactinemia	TCS (subtotal resection) Postoperative radiotherapy	7 months without progression
Radotra et al. (2010)[5]	29	Yes	Yes	Binocular visual loss	Hypopituitarism	TSS and TCS (partial resection) Postoperative radiotherapy	8 months without progression
Present case (2013)	71	Yes	Yes	Bitemporal hemianopsia Right oculomotor nerve palsy	Panhypopituitarism	TSS and TCS (partial resection) GKS (marginal dose: 14 Gy)	18 months without progression

Various common findings exist among these cases, such as age, tumor morphology, neurological deficit, and pituitary function. BE: bony erosion, DSF: dumbbell-shaped form, FSH: follicle stimulating hormone, GKS: gamma-knife surgery, NM: not mentioned, TCS: transcranial surgery, TSS: transsphenoidal surgery.

Based on the findings of neuroimaging, the differential diagnosis should include pituitary adenoma, craniopharyngioma, meningioma, paranasal cancer, and metastatic brain tumor. It is difficult to diagnose primary sellar neuroblastoma through preoperative radiological images. However, MR imaging did reveal a dumbbell-shaped form (intra- and suprasellar mass), and CT scan demonstrated osteolytic changes during tumor progression. These neuroradiological characteristics were closely similar to those described in previous reports (found in 8 of the 9 cases) as shown in Table 2. The dumbbell-shaped form might reflect rapid tumor progression in a malignant tumor. Further, the possibility of malignant tumor is greater if panhypopituitarism or oculomotor nerve palsy is found in addition to the neuroradiological characteristics. The presence of the above neuroradiological characteristics in the sellar region, especially with accompanying characteristic symptoms, might facilitate the differential diagnosis of primary sellar neuroblastoma.[4,7]

The primary treatment used for sellar neuroblastoma in all of the previous 9 patients was surgical resection. Adjuvant therapy, including radiation therapy, for primary cerebral neuroblastoma and especially sellar neuroblastoma has not yet been established. However, several studies have demonstrated the efficacy of radiation therapy for primary cerebral neuroblastoma and esthesioneuroblastoma.[10,12,13] The previous reports described the effectiveness of a combination of postoperative conventional radiotherapy in 7 of the 9 cases with primary sellar neuroblastoma, and they remained free from any recurrence, in spite of only a short follow-up period.[2–5,7–9] Stereotactic radiosurgery (SRS) may be effective for primary sellar neuroblastoma such as in previously reported cases with esthesioneuroblastoma.[14,15] SRS was actually effective in the present case, in spite of only a short follow-up period. Furthermore, some authors have recommended spinal radiation therapy in addition to conventional radiation therapy because patients with cerebral neuroblastoma, including sellar neuroblastoma, may exhibit metastatic spread within the spinal cord.[9,16] The effectiveness of chemotherapy for primary cerebral neuroblastoma including sellar neuroblastoma also remains unclear. Berger et al. advised that patients undergoing subtotal surgical resection for primary cerebral neuroblastoma and patients with tumor recurrence should receive adjuvant chemotherapy.[10] Yariş et al. also recommended that cerebral neuroblastoma be treated according to the same therapeutic strategy as for medulloblastoma because of their malignant behavior.[17] Further investigations are needed to establish an optimal program of chemotherapy for primary sellar neuroblastoma, since cerebral neuroblastomas display malignant features such as rapid recurrence and metastasis, and more detailed and careful observations by neuroimaging should be carried out.

In conclusion, the presentation of an elderly patient with primary sellar neuroblastoma is extremely rare. Neuroimaging showing a "dumbbell-shaped extension in the sellar region" with accompanying endocrinological and ophthalmological findings may point to the possibility of primary sellar neuroblastoma as the differential diagnosis. Further basic and clinical research on additional cases is needed, in order to establish a therapeutic consensus for primary sellar neuroblastoma in the future.

Conflicts of Interest Disclosure

The authors have no conflicts of interest to disclose. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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