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Case Report

A sellar neuroblastoma showing rapid growth and causing syndrome of inappropriate secretion of antidiuretic hormone: A case report

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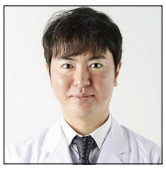

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ABSTRACT

Background: Sellar neuroblastoma is a very rare entity. We report a rare case of arginine vasopressin (AVP)-producing sellar neuroblastoma presumed to have originated from the lower part of sellar turcica, which grew very rapidly.

Case Description: A 33-year-old woman was found to have a sellar lesion with a diameter of 18 mm invading into the bilateral cavernous sinus on magnetic resonance imaging (MRI) performed for dizziness. Six years later, when she visited the clinic due to bilateral visual disturbance, MRI showed a rapid growth of the tumor, with a maximal diameter of 56 mm at the current state, strongly compressing the optic nerve and chiasm. Transsphenoidal decompression of the optic chiasm revealed an intact pituitary gland on the top of the tumor. The tumor was composed of neoplastic cells that were immunohistochemically positive for neuronal markers and arginine vasopressin (AVP), but negative for all anterior pituitary hormones, glial fibrillary acidic protein, or thyroid transcription factor-1; these findings were suggestive of sellar neuroblastoma. She underwent 50-Gy radiation therapy, which has controlled the growth for the past 3 years.

Conclusion: Awareness of rare sellar neuroblastomas will allow the accumulation of clinicopathologic information that may facilitate the understanding of their origin, clinical features, neuroimaging characteristics, and pertinent adjuvant treatment.

Keywords: Neuroblastoma, Rapid growth, Sellar, Syndrome of inappropriate antidiuretic hormone secretion

INTRODUCTION

Neuroblastomas are the most common extracranial solid tumors occurring in infants and children. They originate from the sympathetic ganglion and adrenal medulla.[9] Intracranial neuroblastomas are infrequent and may involve the supratentorial brain parenchyma, mainly in children, and the anterior skull base as an invasion from an olfactory neuroblastoma in adults.[12,17,19] Primary sellar neuroblastoma, not an extension of an olfactory neuroblastoma,

is extremely rare. Only ten cases have been reported in the English literature to date.[4-8,12-17,19] We report a case of sellar neuroblastoma invading into the bilateral cavernous sinuses at the initial visit, which had grown very large over 6 years. We also discuss the origin, imaging features, and biological nature of this unusual tumor.

CASE REPORT

A 33-year-old woman with the dizziness as a chief complain. Magnetic resonance imaging (MRI) found a sellar lesion with a diameter of 18 mm invading into the bilateral cavernous sinus [Figure 1]. The physician suspected it to be a pituitary adenoma. A normal pituitary gland was seen on top of the tumor. The posterior gland was found superoposterior to the tumor. Despite the tumor's lack of impingement to the optic apparatus, she was recommended to have regular visits but were lost to follow-up later. Six years later, she noticed bilateral visual disturbance and visited the clinic. MRI showed an extensive growth of the tumor.

On admission to Kagoshima University Hospital, the patient had clear consciousness. Her vision was 0.3 in the right and 0.7 on the left. Bitemporal hemianopia was found on perimetry. Her serum sodium (Na) level was 127 meq/L. MRI showed a large tumor with a maximal diameter of 56 mm, involving the sellar, suprasellar, retroclival, and bilateral cavernous sinus regions and strongly compressing the optic nerve and optic chiasm [Figure 2]. The tumor was slightly hypointense on T1-weighted MRI and hyperintense on T2-weighted MRI compared to white matter. The bilateral internal carotid arteries were completely encased. A postgadolinium scan showed a heterogeneous enhancement. The relatively well-enhanced thick bundle suggested that the pituitary gland was located in the upper left part of the tumor. A computed tomography (CT) scan showed that the tumor was slightly hyperdense [Figure 3]. Neither bleeding nor calcification was seen. The sellar floor was remarkably thickened.

The assessments of the anterior pituitary hormonal function showed hyperprolactinemia (53.9 ng/mL) and growth hormone deficiency, but the other four hormonal axes showed normal secretory functions. There was no manifestation of diabetes insipidus.

Decompression surgery of the optic chiasm was conducted through an endoscopic transsphenoidal approach. The removal of the thickened sella and thinned fibrous tissue presumed to be a remnant of the dura mater revealed the

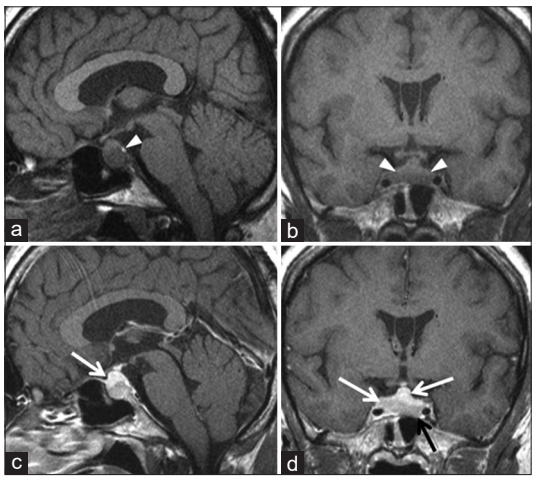

Figure 1: Magnetic resonance imaging (MRI) at the first visit showing an incidentally found sellar tumor. The posterior pituitary gland was located superoposterior to the tumor (open arrowhead in a). The pituitary gland seemed to be on top of the tumor (arrows in c and d). Cavernous sinus invasion is indicated by arrowheads (b and d) (a) Sagittal T1-weighted image (WI). (b) Coronal T1WI. (c) Sagittal gadolinium-enhanced image (GEI). (d) Coronal GEI.

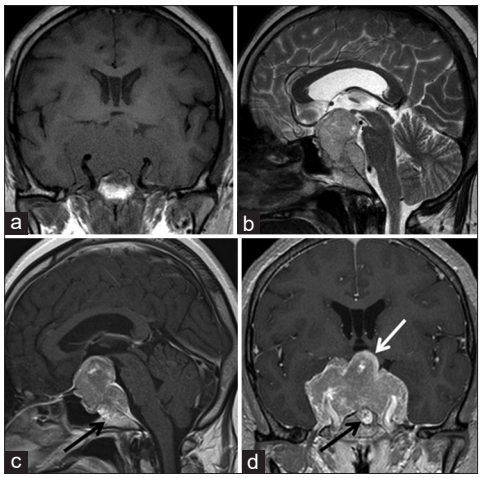

Figure 2: A magnetic resonance imaging (MRI) study for 6 years after the first visit demonstrated an extensively grown tumor occupying the sellar and wide juxtasellar regions (a-d). The white arrow indicates a relatively well-enhanced area, supposed to be the pituitary gland, on top of the tumor (d). The black arrow indicates an invasion of the front of the tumor into the clivus (c and d). (a) Coronal T1WI, (b) sagittal T2WI, (c) sagittal GEI, (d) coronal GEI.

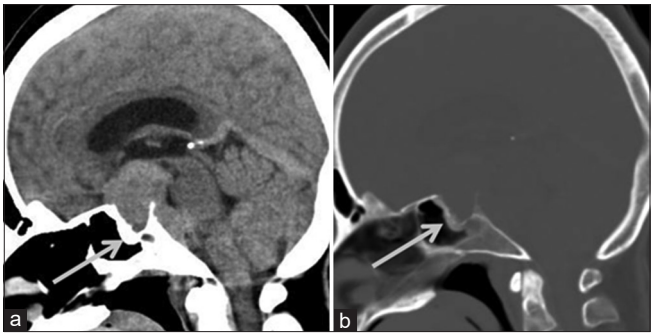

Figure 3: A sagittal computed tomography (CT) scan the tumor was isodense to the brain parenchyma (a). The sellar floor was extensively thickened (arrows in a and b). (a) Brain window. (b) Bone window.

tumor, which was basically fibrous and easy to bleed. Tumor removal was continued until the suprasellar arachnoid membrane and tough tissue consistent with a pituitary gland appeared, leaving the tumor in the cavernous sinuses. Postoperative MRI demonstrated the sufficient decompression of the optic chiasm and an intact pituitary gland [Figure 4]. Postoperatively, a significant improvement of visual field deficit and normalization of vision (1.2 in both) was noted. The anterior pituitary function did not worsen. The blood prolactin level normalized (11.2 ng/mL).

Pathologically, the tumor was composed of a proliferation of round to oval neoplastic cells with scant to moderate cytoplasm and chromatin-rich short rod-like nuclei against a background of intercellular neuropil-like fibrillary matrix [Figure 5a]. Cellular pleomorphism was mild. There were a few ganglion cells accompanied by elongated cells. These cells were partly packed, showing a lobular arrangement separated by a fibrovascular stroma [Figure 5b]. The neoplastic cells and fibrillary matrix were immunohistochemically positive for neuronal markers, including synaptophysin [Figure 5c], neurofilament protein [Figure 5d], neuron-specific enolase, and NeuN [Figure 5e] chromogranin A [Figure 5f]. The neoplastic cells were also positive for arginine vasopressin (AVP) [Figure 5g]. The S-100 protein [Figure 5h] and vimentin were positive, mainly in spindle cells surrounding the fibrovascular stroma. They were negative for any anterior pituitary hormones, epithelial membrane antigen (EMA), glial fibrillary acidic protein (GFAP), or thyroid transcription factor-1 (TTF-1). These pathologic findings were suggestive of sellar neuroblastoma. The MIB-1 index was 6%.

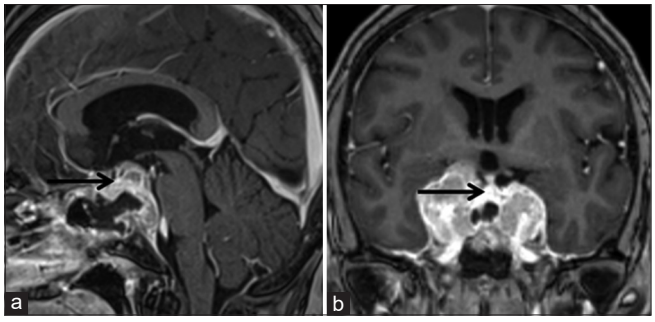

Figure 4: A magnetic resonance imaging (MRI) scan immediately after the surgery showing sufficient decompression of the optic chiasma. The pituitary gland was well preserved (arrows in a and b). (a) Sagittal GEI and (b) coronal GEI.

A postoperative whole-body CT scan revealed a right ovarian cyst, which was later pathologically proven to be a simple cyst; otherwise, no other abnormalities were found. She underwent 50-Gy of intensity-modulated radiation therapy to the residual tumor due to hospital's standard operating procedure, which has controlled its growth for the 3 years [Figure 6]. The serum Na levels remained low postoperatively at 126–130 meq/L, which did not cause any disturbance in consciousness. She was diagnosed with the syndrome of inappropriate secretion of antidiuretic hormone (syndrome of inappropriate antidiuretic hormone secretion [SIADH]) at 12 months after surgery. The laboratory results were as follows: serum Na: 130 meq/L, osmolarity: 259 osmo/kg, AVP: 18 pg/mL, urinary Na: 96 meq/L, and urinary osmolarity: 507 osmo/kg. The patient had no hypoadrenocorticism, kidney dysfunction, and cardiac failure. She is currently working in a factory without neurological impairment or hormonal replacement.

DISCUSSION

This is an unfortunate case, in which the recommendation of regular follow-up was ignored, but, ironically, the natural course of the sellar neuroblastoma still occurred in 6 years. [Table 1] shows a summary of the previously reported ten cases of sellar neuroblastoma:[6-8,12-17,19] five of those were diagnosed as ectopic esthesioneuroblastomas in the previous reports.[7,8,14-16]

Lach *et al.* assumed that the tumor was attributable to the transformation of the pituitary epithelium into neuronal cells

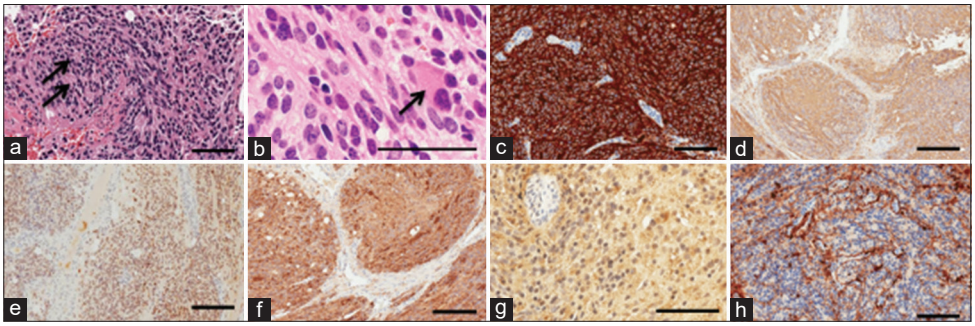

Figure 5: Histologic features of the specimen obtained by transsphenoidal surgery. The tumor was composed of neoplastic cells with scant to moderate cytoplasm and chromatin-rich oval or short rod-like nuclei. The neoplastic cells partly formed a lobular arrangement (×200, a). A few ganglion-like cells were seen (×600, b). On immunohistochemistry, the tumor was diffusely positive for synaptophysin (×200, c), neurofilament protein (×200, d), NeuN (×200, e), chromogranin A (×200, f), and arginine vasopressin (×400, g). S-100 protein was positive mainly in the spindle cells surrounding a fibrovascular stroma (×200, h). Bar = 100 μm.

based on the colocalization of prolactin-immunopositive granules in the neoplastic neuronal cells.[6] Roy *et al*.[14] and Sarwar[16] speculated that the ganglion of loci grows between the olfactory fossa and the telencephalic vesicle as the origin of the tumor, which is also considered to be the origin of an esthesioneuroblastoma. According to the terminal nerve system theory regarding embryologic development of the olfactory system, the terminal nerve neurons spread diffusely in the lamina cribrosa, nasal mucosa, and hypothalamus at around 50 days postconception. The persistence of these cells beyond fetal life may provide the origin of the tumor.[3,18]

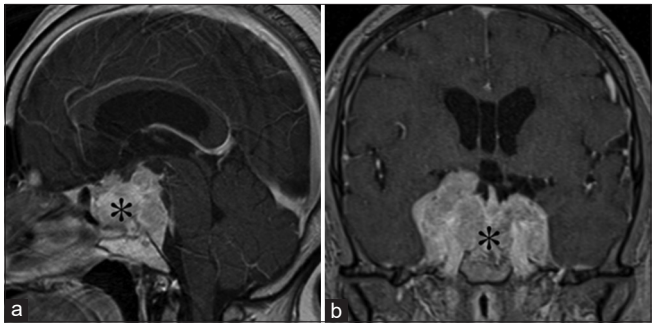

Figure 6: A magnetic resonance imaging (MRI) scan studied at 34 months after the surgery showed the control of the tumor growth. The surgically debulked area was occupied by fibrous tissues (* in a and b) (a) sagittal GEI. (b) Coronal GEI.

The unstretched pituitary gland located on top of the tumor, relatively preserved anterior pituitary function, thickened sellar floor, and tattered dura mater on the sellar floor in our case hinted that the tumor arose from the lower part of sella turcica, including the dura mater, subdural space, and base of the pituitary gland.

The median age of patients with similar cases reported previously was 40 years (range: 29–71 years). These patients were much younger than the patients with nonfunctioning

Table 1: Reported cases of the primary sellar neuroblastoma.

Author (year)	Age/ sex	Extension	Multilobar	Manifestation	Clinical course before diagnosis	Pituitary function	Treatment	Follow-up
Sarwar (1979)[8]	31/f	SS, bilateral CS	Yes	BTH, numbness in the left cheek	NA	NA	TCS, radiotherapy	5 years without progression
Lach (1996)[1]	40/f	SS, unilateral CS	Yes	BTH, infertility	NA	Hyper-PRL	TCS	NA
Roy (2000)[6]	44/f	SS	Yes	BTH	NA	Hyper-PRL	TSS, rad	2 years without progression
Mariani (2004)[3]	35/f	SS	No	BTH, oligomenorrhea	Rapid growth in 3 years	Hyper-PRL	TSS	25 months without recurrence
Sajko (2005)[7]	57/f	SS, unilateral CS	No	Left temporal hemianopia	NA	Hyper-PRL	TSS, rad	NA
Oyama (2005)[4]	33/m	SS, clival, cervical spinal	Yes	BTH left oculomotor palsy	Rapid growth despite 5 surgeries and GK	Panhypo	TSS, rad	Remarkable shrinkage
Lin (2009)[2]	40/m	Bilateral CS, sphenoid, clival	No	CSF rhinorrhea, meningitis	NA	None	TSS, rad	1 year without progression
Schmalish (2009)[9]	43/f	SS	Yes	BTH, amenorrhea	NA	Hyper-PRL	TCS, rad	7 months without progression
Radotra (2010)[5]	29/m	SS, bilateral CS, sphenoid, clival	Yes	Bilateral visual loss, hyponatremia	NA	Hypopituitarism, SIADH	TCS and TSS, rad	8 months without progression
Yamamura (2013)[10]	71/m	SS, bilateral CS	Yes	BTH right oculomotor palsy	NA	Panhypo	TCS and TSS, GK	18 months without progression
Present case	39/f	SS, bilateral CS, sphenoid, clival	Yes	BTH	Rapid growth in 6 years	Hyper-PRL, GH deficiency	TSS, rad	3 years without progression

f: Female, m: Male, CS: Cavernous sinus, SS: Suprasellar, BTH: Bitemporal hemianopia, TH: Temporal hemianopia, NA: Not available, Hyper-PRL: Hyperprolactinemia, GH: Growth hormone, Panhypo: Panhypopituitarism, SIADH: Syndrome of inappropriate antidiuretic hormone secretion, Rad: Radiation, GK: Gamma-knife, TCS: Transcranial surgery, TSS: Transsphenoidal surgery

adenomas (*n* = 166, mean age: 62 years, and range: 19–84 years), who we treated for the last 10 years. The major manifestation was visual impairment, including temporal hemianopia. Cavernous sinus symptoms were seen in three out of the 11 cases, which are rarely seen in pituitary adenomas even with cavernous sinus invasion.[6-8,12-17,19]

Hyperprolactinemia, due to the stalk effect, was recorded in six cases. However, the impairment of other hormones was relatively low, which was recorded in only four cases. The anterior pituitary provocation test, in our case, found a well-preserved secretory function, considering the large tumor volume; only the GH secretion was compromised.[6-8,12-17,19]

SIADH, by definition, is a condition of excessive secretion or action of AVP irrespective of hyponatremia and inappropriate urinary concentration. There are various causes of SIADH: central nervous system disease such as meningitis, brain tumor, and cerebral hemorrhage; lung diseases such as pneumonia, lung tumor, and tuberculosis; iatrogenic such as vincristine, clofibrate, and carbamazepine drug adverse effects; and ectopic ADH-producing tumors such as small cell lung carcinoma and pancreatic cancer.[11] Interestingly, esthesioneuroblastoma or olfactory neuroblastoma case reports frequently showed SIADH as paraneoplastic syndromes with the positive result of AVP by immunohistochemistry.[1,11] Our case is the second reported case of a sellar neuroblastoma manifesting SIADH, in which the production of AVP was proven by immunohistochemistry.[12] Due to the lack of neurological abnormality, probably due to the slow progression of hyponatremia, a specific treatment, other than mild fluid restriction, has not been given. In esthesioneuroblastoma, it was assumed that the tumor expressing AVP,[11] otherwise deeper study should be performed to explain more its pathophysiology either in the sellar neuroblastoma cases.

In general, MRI revealed the aggressive nature of the disease. Among the 11 reported cases (including the present case), the suprasellar extension was seen in ten, cavernous sinus invasion in seven with five bilateral cases, clival involvement in four, sphenoid sinus involvement in three, and cerebrospinal fluid dissemination in one case. Eight cases showed multiple lobar appearances. Calcification was noted in only two cases.[6-8,12-17,19]

As in the previously reported cases, our case displayed immunohistochemical positivity for neuronal markers, including neurofilament protein, chromogranin, and synaptophysin, but negativity for all anterior pituitary hormones.[3,4] It was also negative for EMA, GFAP, or TTF-1, excluding the possibility of posterior pituitary tumors, such as pituicytoma, ependymoma, and granular cell tumors.[10]

The natural course of the pituitary neuroblastoma remains not well known. In our case, the tumor had grown rapidly in 6 years, showing an aggressive nature of this tumor. Mariani *et al.*[8] also reported the rapid growth of the tumor in 3 years before its diagnosis. The clinical and neuroimaging characteristics, such as the relatively young age of a patient, more aggressive features than commonly seen in benign sellar tumors on MRI, and relatively preserved pituitary function may lead to the suspicion of this rare entity.

At present, there has been no consensus established regarding the treatment of sellar neuroblastomas. Postoperative radiation, including gamma-knife, was conducted in the ten reported cases, which provided good control of the tumor during the 5-year follow-up period, except for one case [Table 1]. Although adjuvant chemotherapy after utmost safe surgical removal has been recommended for cerebral neuroblastoma,[2,3,20] chemotherapy has not been provided for the previously reported sellar neuroblastoma cases.

In conclusion, although sellar neuroblastomas seem extremely rare, awareness of this special entity will promote the accumulation of clinicopathologic information, which may facilitate the understanding of its origin, clinical features, neuroimaging characteristics, and pertinent adjuvant treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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