

Subarachnoid hemorrhage caused by an undifferentiated sarcoma of the sellar region

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Abstract

Background: It is rare for patients with pituitary apoplexy to exhibit concomitant subarachnoid hemorrhage (SAH). Only a handful of patients with pituitary apoplexy have developed such hemorrhagic complications, and histopathological examination revealed pituitary adenoma as the cause of SAH.

Case Report: A previously healthy 35-year-old woman was brought to our institution after complaining of severe headache and left monocular blindness. Brain computed tomography showed a diffuse SAH with a central low density. Subsequently, the brain magnetic resonance imaging revealed an intrasellar mass with heterogeneous contrast enhancement. The patient was presumptively diagnosed with SAH secondary to hemorrhagic pituitary adenoma and underwent transcranial surgery to remove both the tumor and subarachnoid clot. A histological evaluation of the surgical specimen revealed malignant cells with strong predilection for vascular invasion. Following immunohistochemical evaluation, the tumor was negative for the majority of tumor markers and was positive only for vimentin and p53; thus, a diagnosis of undifferentiated sarcoma was established.

Conclusions: This case was informative in the respect that tumors other than pituitary adenoma should be included in the differential diagnosis of patients with pituitary apoplexy.

Key Words: Pituitary apoplexy, sella turcica, subarachnoid hemorrhage, undifferentiated sarcoma

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INTRODUCTION

Pituitary apoplexy is a rare cause of hemorrhage in the pituitary gland. In most circumstances, bleeding does not expand beyond the pituitary gland due to the presence of the surrounding membranes, such as the arachnoid membrane and diaphragma sellae, which function as a barrier.^[10] Consequently, it is rare for patients with pituitary apoplexy to exhibit concomitant subarachnoid hemorrhage (SAH). Only a handful of patients with pituitary apoplexy have developed such hemorrhagic complications,^[8,12,14,16] and histopathological examination revealed pituitary adenoma as the cause

of hemorrhage.^[3-5,13,15] Herein, we report a rare case of fatal SAH caused by an undifferentiated sarcoma of the

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sellar region, which posed a diagnostic and therapeutic challenge to neurosurgeons.

CASE REPORT

A previously healthy 35-year-old woman who had no history of radiation exposure was brought to our institution after complaining of severe headache and left monocular blindness. Her consciousness level on arrival was E1V4M5 on Glasgow Coma Scale. Brain computed tomography (CT) revealed a diffuse SAH with a central low density [Figure 1a], and on the sagittal reconstructed view, no enlargement of the sella turcica was observed [Figure 1b]. There were no brain aneurysms on the brain CT angiography [Figure 1c], and thus, brain magnetic resonance imaging with gadolinium was subsequently performed. The intrasellar mass was depicted as a low-intensity signal on nonenhanced T1-weighted sequence [Figure 2a], with strong, heterogeneous contrast enhancement after gadolinium administration [Figure 2b and c], and the posterior pituitary lobe appeared to have been displaced posteroinferiorly by the tumor. On a T2-weighted image, the mass is depicted as heterogeneous high intensity, and a dense subarachnoid clot was also observed in the prepontine cistern [Figure 2d]. Based on the clinical history and imaging studies, a presumptive diagnosis of SAH occurring secondary to hemorrhagic pituitary adenoma was made. The blood levels of the anterior lobe hormones collected preoperatively were mostly below the normal range, except for prolactin (63.9 ng/mL) which was mildly elevated.

For removal of the tumor, we chose a transcranial approach via frontotemporal craniotomy rather than a

transsphenoidal approach, with a hope of reducing the amount of SAH in the basal cistern, and the patient was brought to the operation room following administration of intravenous hydrocortisone. During surgery, the tumor was found to be soft and was easily aspirated. However, the tumor could only be partially removed due to profuse bleeding from the tumor and swelling of the surrounding brain tissue as a result of SAH. The interface between the tumor and the diaphragma sellae could not be fully inspected, and the position of the pituitary stalk could not be confirmed. Postoperative management included administration of intravenous vasopressin, hydrocortisone, and oral levothyroxine, and the patient was maintained normovolemic/normotensive to prevent delayed vasospasm. Despite transient mild improvement in the consciousness level following surgery, the patient sustained a large cortical infarction secondary to the vasospasm [Figure 1d]. Her family did not consent to our recommendation to perform decompressive craniectomy for the infarction, and she died 8 days after admission. An autopsy was not performed. Permission for publication was granted by her family.

Pathological examination

On hematoxylin and eosin staining, the tumor cells were found to be densely proliferated either in a medullary or in a trabecular pattern. Densely arranged tumor cells with large, irregular nuclei and many mitotic figures were observed [Figure 3a]. In another area of the specimen, tumor invasion into the venous wall was observed [Figure 3b]. An extensive immunohistochemical workup was conducted to identify the histological origin of the tumor, with a list of the evaluated markers [Table 1]. The tumor was negative for the majority of epithelial, neuroendocrine, glial cell, germ cell, lymphocytic, and

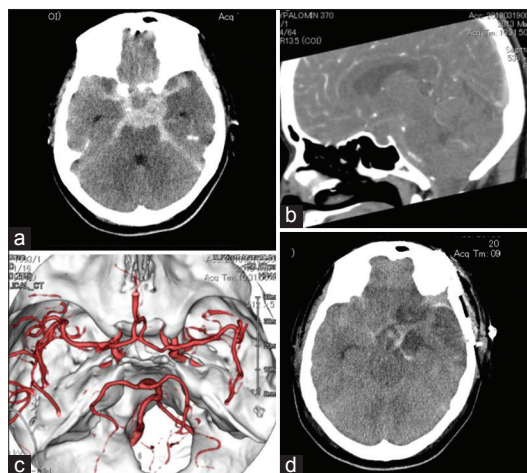


Figure 1: Computed tomography of the brain showing subarachnoid hemorrhage with a central low density (a). No substantial sellar enlargement is observed with a sagittal reconstructed view (b). Brain computed tomography angiography showing the absence of a ruptured aneurysm (c). Computed tomography obtained 7 days postoperatively showing extensive cerebral infarction due to vasospasm (d)

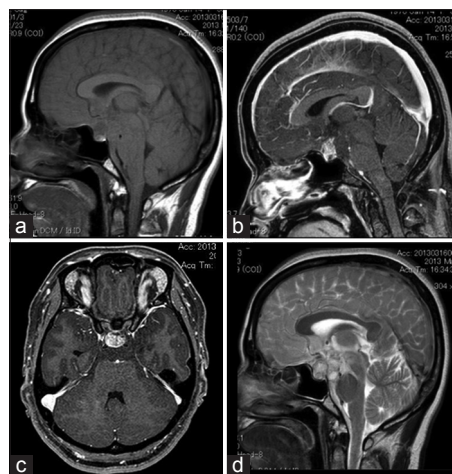


Figure 2: Magnetic resonance imaging showing an intrasellar mass which is depicted as low-intensity on a nonenhanced T1-weighted image (a). With gadolinium, the mass exhibits strong enhancement (b, sagittal view; c, axial view). On a T2-weighted image, the mass is depicted as heterogeneous high intensity, and a dense subarachnoid clot was also observed in the prepontine cistern (d)

mesenchymal markers [Table 1] and was positive only for vimentin [Figure 3c] and p53. The MIB-1 labeling index was 63.6%, indicating potent proliferative activity of the tumor [Figure 3d]. Based on the histopathological findings, the patient was diagnosed with undifferentiated sarcoma; pituitary adenoma was considered unlikely due to the lack of immunoreactivity to synaptophysin, chromogranin A, and CD56.

DISCUSSION

Although the precise pathological mechanism of pituitary apoplexy has not yet been fully elucidated, the great majority of patients have underlying pituitary adenomas which often remain silent. Pituitary adenoma cells have a higher energy demand/consumption than the surrounding brain tissue, and episodes of hypoxia and/or hypoglycemia are known to result in necrotic cell death and subsequent bleeding from the degenerated adenoma cells.^[4,9,13] Tumors other than pituitary adenoma rarely causes pituitary apoplexy, except Rathke cleft cysts.^[13] In a recent study on 68 surgically treated pituitary apoplexy cases, histopathological examination revealed that 64 had pituitary adenoma and the remaining 4 had Rathke cleft cyst.^[13] Aside from the two tumors, only a few tumors, such as craniopharyngiomas and metastatic cancers, have been reported as the cause of pituitary apoplexy.^[3,4] Due to the presence of the arachnoid membrane and diaphragma sellae, the membrane complex surrounding the pituitary gland functions as a natural barrier, and intratumoral bleeding usually does not expand beyond the pituitary gland.^[10] As a result, occurrence of SAH or

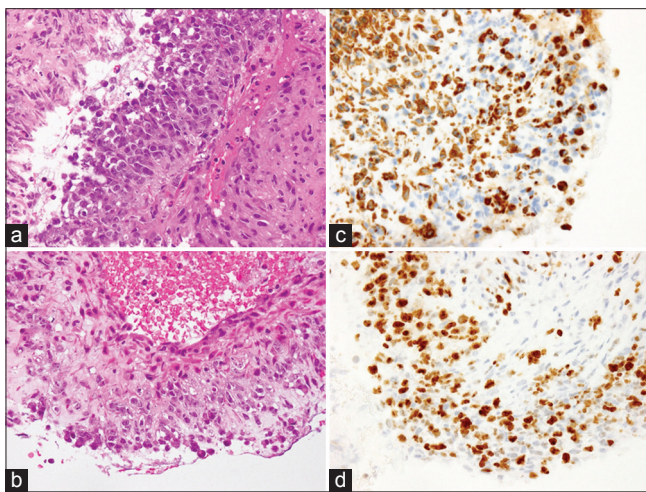


Figure 3: On H and E staining, the tumor cells are seen to have proliferated densely, either in a medullary or trabecular pattern, and densely arranged tumor cells with large, irregular nuclei and many mitotic figures are observed (a). In another area, tumor invasion to the venous wall is observed (b). Although an extensive immunohistochemical study was performed to identify the histological origin of the tumor, it is positive only for vimentin (c) and p53. The MIB-1 labeling index is 63.6%, indicating potent proliferative activity of the tumor (d)

Table 1: A list of tumor markers evaluated histochemically to identify the origin of the tumor

Category	Epithelial	Neuroendocrine		Germ cell	Glial cell	Lymphocytic		Metastatic		Mesenchymal cell			
		Breast	Lung			Breast	Melanoma	Lung					
Organ													
Marker	CAM5.2 AE1/AE3 CK7 CK20 SP CgA CD56 PLAP c-Kit HCG GFAP Olig2 CD20 CD3 MUM-1 HER2 ER PgR S-100 HMB45 TTF-1 SMA Desmin F-VIII CD31 CD34	No	No	No	No	No	No	No	No	No	No	No	No
Reactivity	No	No	No	No	No	No	No	No	No	No	No	No	No

CAM5.2: Cytokeratin CAM5.2, AE1/AE3: Cytokeratin AE1/AE3, CK7: Cytokeratin 7, CK20: Cytokeratin 20, SP: Synaptophysin, HCG: Human chorionic gonadotropin, GFAP: Glial fibrillary acidic protein, MUM-1: Multiple myeloma oncogene 1, HER2: Human epidermal growth factor receptor type 2, ER: Estrogen receptor, PgR: Progesterone receptor, HMB45: Human melanin black 45, TTF-1: Thyroid transcription factor-1, SMA: Smooth muscle actin, F-VIII: Factor-VIII

intracerebral hemorrhage secondary to pituitary apoplexy is rare, and almost all patients have been shown to harbor underlying pituitary adenomas.^[8,12,14] Only one case of tumor-induced SAH irrelevant to pituitary adenoma has been reported in the literature, which was secondary to metastasis to the pituitary gland.^[14]

The present case is unique in the respect that SAH was caused by an undifferentiated sarcoma and not by a pituitary adenoma. Sarcomas in the sellar region in the absence of a history of radiation exposure are very rare, with <10 cases reported in the literature excluding hemangiopericytoma.^[1,2,6,7,11] The great majority of patients with sellar sarcomas presented with disturbances in ocular movement or visual field.^[1,2,6,7,11] In this context, ours may be the first sarcoma case that developed SAH. The rapid clinical deterioration due to diffuse SAH and the propensity for active bleeding during surgery may be explained by the histopathological finding of the tumor, for instance, aggressive vascular invasion. Lack of enlargement of the sella turcica also indicated that the tumor may have proliferated rapidly without destruction of the bony structure. Due to profuse bleeding from the tumor and limited intraoperative visibility due to SAH-induced brain swelling, we could not make an adequate observation regarding the integrity of the diaphragma sellae and its interface with the tumor.

Specifying the histological origin of the tumor was difficult due to lack of immunoreactivity to tumor markers barring vimentin and p53 [Table 1], and we could only conclude that the tumor was most likely an undifferentiated sarcoma. Alpert *et al.*,^[1] Manoranjan *et al.*,^[7] and Sareen *et al.*^[11] recently reported cases of undifferentiated sellar sarcomas, for which few tumor markers were positive, and it can be speculated that sarcomas in the sellar region may have a tendency for undifferentiated proliferation. At the same time, however, we need to be cautious with respect to jumping to such speculation because of very limited number of cases in the literature. Due to the lack of an autopsy, it could not be definitely concluded whether the sarcoma originated from the sellar region or was metastatic. Although the characteristic CT finding, for instance, the presence of a central low density within high density [Figure 1a], and clinical symptoms (monocular blindness) suggested the presence of a sellar tumor, we were convinced preoperatively that the tumor was a pituitary adenoma. Making an accurate preoperative diagnosis of a sarcoma

may have been difficult due to its rarity, and the fatal outcomes may not have been unavoidable, considering the severe brain damage inflicted by the diffuse SAH and subsequent vasospasm-induced infarction. Nevertheless, this case was informative in the respect that the presence of tumors other than pituitary adenomas has to be ruled out in patients presenting with pituitary apoplexy.

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Conflicts of interest

There are no conflicts of interest.

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