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Title	Pituitary Apoplexy Manifesting as Massive Intracerebral Hemorrhage : Case Report
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Citation	Neurologia medico-chirurgica, 52(8), 587-590 https://doi.org/10.2176/nmc.52.587
Issue Date	2012-08
Doc URL	https://hdl.handle.net/2115/70776
Rights(URL)	https://creativecommons.org/licenses/by-nc-nd/4.0/
Type	journal article
File Information	E21_52_3070.pdf



Pituitary Apoplexy Manifesting as Massive Intracerebral Hemorrhage

—Case Report—

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Abstract

A 68-year-old man presented with severe conscious disturbance caused by pituitary apoplexy resulting in massive intracerebral hemorrhage (ICH). He had been periodically followed up for asymptomatic pituitary adenoma at another hospital for 8 years. Neuroimaging examination revealed pituitary apoplexy and massive ICH located in the left frontal lobe, and the ICH was directly connected to the intratumoral hemorrhage. The diagnosis was massive ICH from pituitary apoplexy. The patient underwent emergent evacuation of hematoma and removal of the pituitary adenoma via bi-frontal craniotomy. Postoperatively, he continued to exhibit deep consciousness disturbance and died 1 month after the operation. Pituitary apoplexy is usually characterized by intra-tumoral hemorrhage. The treatment strategy for asymptomatic pituitary adenoma is still controversial. This case shows that we should always consider the risk of pituitary apoplexy manifesting as ICH which may cause a fatal outcome.

Key words: fatal pituitary apoplexy, pituitary adenoma, intracerebral hemorrhage, emergent surgery

Introduction

Pituitary apoplexy is a syndrome caused by an acute ischemic or hemorrhagic event in a pituitary adenoma.¹⁶⁻¹⁸⁾ Various precipitating events have been implicated in the pathogenesis of pituitary apoplexy such as head trauma, arterial hypertension, diabetes mellitus, pregnancy, estrogen or bromocriptine therapy, cardiac surgery, increased intracranial pressure, radiotherapy, dynamic pituitary function tests, or anticoagulation. However, the condition occurs spontaneously in the majority of patients with pituitary adenoma.^{16,20,24)} The incidence of pituitary apoplexy in patients with pituitary adenoma is 0.6–23%.^{2,3,8,9,13,16,24)} Pituitary apoplexy is characterized by sudden onset of headache, visual impairment, or ophthalmoplegia caused by acute enlargement of the tumor.^{3,6,11,26,27,30)} Intratumoral hemorrhage is the most common type of hemorrhage, but subarachnoid hemorrhage (SAH),^{16,17,19,27)} and intra-ventricular hemorrhage^{5,21,25)} may also result from pituitary apoplexy. Only one case of intracerebral hemorrhage (ICH) has been associated with pituitary apoplexy.¹⁰⁾

Here, we report a case of pituitary apoplexy with massive ICH which resulted in unfavorable outcome.

Case Report

A 68-year-old man first presented with hypertension and had been treated with medication therapy. He had no history of treatment for diabetes mellitus, head trauma, radiation therapy, dynamic pituitary function tests, or anticoagulation therapy. Non-functioning pituitary adenoma was diagnosed in May 2005 at another hospital. He had no disturbance of visual acuity and visual field at that time, so was treated conservatively with periodical follow up. During the follow-up period, he manifested no symptoms including disturbance of visual acuity and visual field. Magnetic resonance (MR) imaging revealed a tumor located in the intra- and supra-sellar region which considered to be stable pituitary adenoma (Fig. 1).

He suffered sudden consciousness disturbance after headache, nausea, and vomiting for a few days in April 2011. He was admitted to our hospital emergency room. On admission, he was comatose with anisocoria associated with right oculomotor nerve palsy. Hematological and biochemical profiles showed hyponatremia, and pituitary hormone status showed low levels of thyroid-stimulating hormone (TSH) (0.099 μ IU/ml, normal range 0.500–5.00), free triiodothyronine (1.72 pg/ml, range 2.30–4.30), and prolactin (PRL) (0.11 ng/ml, range 4.29–13.69). However, other pituitary hormones were within the normal ranges as follows: growth hormone (GH) 0.099 ng/ml, range <0.17; and adrenocorticotrophic hormone (ACTH)

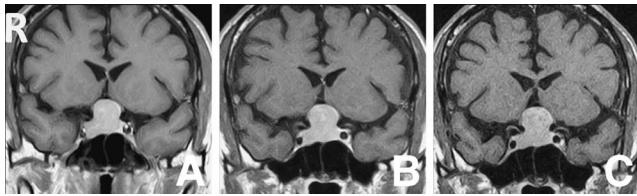


Fig. 1 Coronal T₁-weighted magnetic resonance images with gadolinium administration performed June 2005 (A), August 2008 (B), and February 2011 (C) showing no enlargement of the intra- and supra-sellar tumor which was considered to be pituitary adenoma.

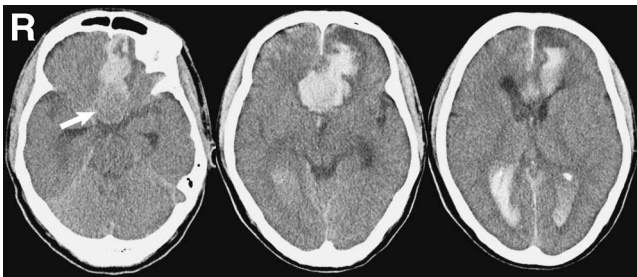


Fig. 2 Preoperative computed tomography scans showing massive intracerebral hemorrhage in the left frontal lobe and bilateral lateral ventricle hemorrhages, as well as the high density intra- and supra-sellar mass (arrow).

35.1 pg/ml, range 7.2–63.3.

Emergent computed tomography (CT) demonstrated a massive hematoma in the left frontal lobe and hematomas in the bilateral ventricles (Fig. 2), probably caused by intraventricular rupture of ICH. In addition, the intra- and supra-sellar high density mass was also observed. Three-dimensional CT angiography was performed to exclude vascular abnormalities, such as aneurysm or arteriovenous malformation. Only elevation of A1 segment in both anterior cerebral arteries was detected and no vascular abnormalities potentially causing the massive ICH were identified. MR imaging revealed a large well enhanced mass located in the intra- and supra-sellar region indicating pituitary adenoma surrounded by and connecting to the massive ICH (Fig. 3).

Under a diagnosis of ICH caused by pituitary apoplexy, emergent surgery on the day of admission was carried out via bifrontal craniotomy. Preoperatively, replacement of hydrocortisone was performed. The ICH located in the left frontal lobe was evacuated after the corticotomy. After the ICH was totally evacuated, we confirmed that the hematoma was connected to the left lateral ventricle. Next, tumor resection was performed through the anterior interhemispheric approach. The white aspirable tumor was located in the sella turcica and extended to the supra-sellar region. The bilateral optic nerves and chiasma were markedly stretched and displaced superiorly. The right oculomotor nerve was also compressed by the tumor laterally. During resection of the tumor, we confirmed that the intra-

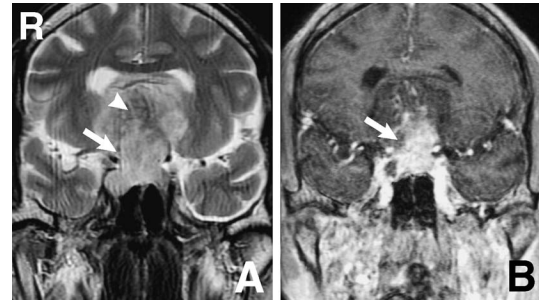


Fig. 3 A: Preoperative coronal T₂-weighted magnetic resonance (MR) image revealing a high intensity intra- and supra-sellar lesion representing pituitary apoplexy (arrow), and massive intracerebral hemorrhage in the frontal lobe (arrowhead). B: Coronal T₁-weighted MR image after gadolinium administration demonstrating the well enhanced intra- and supra-sellar mass which was considered to be pituitary adenoma, surrounded by massive intracerebral hemorrhage, as well as intra-tumoral hemorrhage appearing as a less enhanced area (arrow).

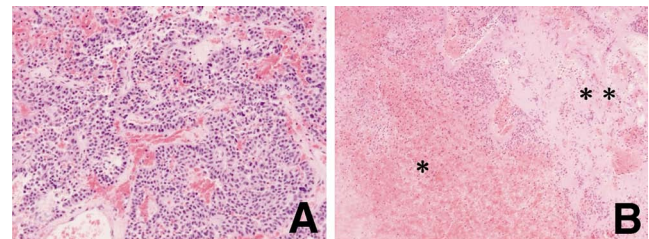


Fig. 4 A: Photomicrograph of the surgical specimen showing monomorphic proliferation of cells with uniform round nuclei and chromophobe cytoplasm, indicating typical pituitary adenoma, as well as intra-tumoral hemorrhage. Hematoxylin and eosin stain, original magnification $\times 100$. B: Photomicrograph of the surgical specimen showing hemorrhagic (*) and necrotic (**) components in the tumor. Hematoxylin and eosin stain, original magnification $\times 10$.

tumoral hemorrhage connected to the ICH located in the left frontal lobe. These operative findings indicated that the left frontal ICH was formed as a result of pituitary apoplexy. The tumor was semi-totally removed except for the intra-sellar lesion, because we considered that the intra-sellar lesion could be removed more easily by trans-sphenoidal surgery in the chronic stage. During the resection, the pituitary stalk was preserved. Finally the ICH and supra-sellar tumor were totally removed.

Histological examination of the surgical samples revealed hemorrhagic changes and necrotic changes (Fig. 4) which may have led to pituitary apoplexy. The histological diagnosis was pituitary apoplexy as a result of pituitary adenoma. Further immunohistological staining showed positive reaction for chromogranin, but not for prolactin, GH, ACTH, luteinizing hormone (LH), or follicle-stimulating hormone (FSH).

After the operation, he continued to exhibit deep consciousness disturbance. MR imaging revealed that mas-

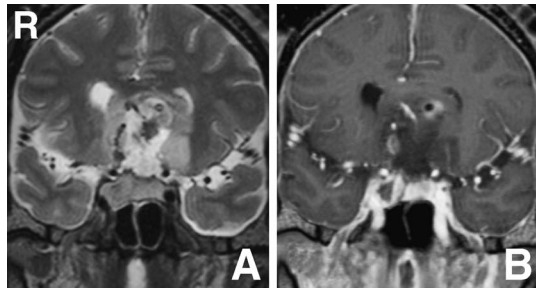


Fig. 5 Postoperative coronal T₂-weighted magnetic resonance (MR) image (A) and coronal T₁-weighted MR image after gadolinium administration (B) revealing removal of the tumor located in the supra-sellar region and the massive intracerebral hemorrhage.

sive ICH and the supra-sellar part of the pituitary adenoma had been totally removed (Fig. 5). Although we observed intraoperatively that the pituitary stalk and pituitary gland were preserved intact, he developed panhypopituitarism (PRL 1.02 ng/ml, GH 0.22 ng/ml, ACTH <2.0 pg/ml, LH <0.10 mIU/ml, FSH 0.30 mIU/ml, TSH <0.005 μ IU/ml). However, postoperative diabetes insipidus did not occur. Administration of hydrocortisone and thyroid hormone for replacement of hormonal therapy was performed. However, his general condition gradually worsened. He suffered severe aspiration pneumonia. Antibiotic medication was not effective. Unfortunately he died 1 month after the operation of progression of multiple organ failure.

Discussion

Pituitary apoplexy usually manifests as acute symptoms which may include headache, pituitary insufficiency, impaired consciousness, visual worsening and/or ophthalmoplegia.^{3,23} Acute tumor enlargement caused by intratumoral hemorrhage and compression of the surrounding tissues is important in causing these symptoms. The present case is unique because massive ICH resulting from pituitary apoplexy caused severe conscious disturbance.

Rare hemorrhagic patterns caused by pituitary apoplexy are known. SAH^{19,22,27} associated with pituitary apoplexy is a rare but well-known pattern of pituitary apoplexy. The anatomical proximity of the sellae turcica to the basal cistern may be the cause of this symptom. Extravasation of blood from a bleeding pituitary tumor may enter the subarachnoid space resulting in the clinical presentation of SAH.^{15–17,27} However, the present case manifested as massive ICH without SAH. Only one previous case report has involved ICH as the result of pituitary apoplexy.¹⁰ In our case, we observed that the tumor was partly embedded in the left frontal lobe. We speculate that necrotic and hemorrhagic changes occurred in this part of tumor leading to ICH. This entity may be difficult to distinguish from ruptured aneurysm of the anterior cerebral artery.¹⁰ However, we could diagnose this rare entity relatively easily in the present case, because we knew that the patient had been treated for non-functioning pituitary ade-

noma conservatively at another hospital.

Fatal pituitary apoplexy is known in only a few case reports.^{1,5,21,25,28} Hypothalamic compression caused by intratumoral hemorrhage and rapid enlargement of the tumor was considered to lead to unfavorable outcomes.^{1,28} Serious bleeding into the subarachnoid cistern and/or intraventricular space with unfavorable outcomes were also reported.^{5,21,25} Our patient also suffered a severe clinical course and finally died of massive ICH. Operative indications for asymptomatic non-functioning pituitary adenoma are still controversial, in spite of recent surgical developments for pituitary adenoma including endoscopic surgery.^{4,7,9,12,14,29} The present case shows that asymptomatic pituitary adenoma may occasionally cause pituitary apoplexy and may result in severe neurological deficit or even death.

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