

Pituitary Apoplexy Caused by Endocrine Stimulation Tests: A Case Report

Osamu Okuda, M.D., Hitoshi Umezawa, M.D., and Makoto Miyaoka, M.D.

Department of Neurosurgery, Fujisawa City Hospital, Fujisawa City, Kanagawa, Japan

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The case of a 60-year-old woman with a giant pituitary adenoma who suffered symptomatic pituitary apoplexy is reported. Hemorrhaging occurred during endocrine stimulation tests (triple bolus test) in and around the tumor. Both the level of consciousness and the hemiparesis improved after emergency decompression. Histologically the tumor was a chromophobe adenoma of the papillary type with diffuse hemorrhage. Subtotal removal of the tumor was successfully accomplished in a second operation. Routine anterior pituitary stimulation tests have the potential to develop pituitary apoplexy, and we advise that caution should be taken when such tests are planned. The possible mechanism resulting in bleeding is discussed.

KEY WORDS: Giant pituitary adenoma; Pituitary apoplexy; Stimulation tests; Triple bolus test

Pituitary apoplexy is a well-known clinical syndrome. Life-threatening bleeding that requires prompt surgical intervention, however, is not common. Pituitary apoplexy is thought to be caused by acute enlargement of a tumor due either to hemorrhage or hemorrhagic infarction within the tissue of a preexisting pituitary adenoma [6,7]. However, the cause of bleeding usually is obscure. The case of a 60-year-old woman with pituitary apoplexy related to stimulation tests resulted in marked deterioration of consciousness and severe hemiparesis. Hemorrhage was extensive and it was not only intratumoral but also in the peritumoral, subarachnoid, and intraventricular regions. The possible mechanism resulting in the bleeding is discussed.

Address reprint requests to: Makoto Miyaoka, M.D., Department of Neurosurgery, Fujisawa City Hospital, Fujisawa City, Kanagawa, Japan.

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Case Report

A 60-year-old woman with a 4-year history of syncope was referred to our hospital due to the presence of a large tumor in the midline frontal lobe, revealed by computed tomography (CT) scans. At this time, however, she was asymptomatic, and there was no impairment of vision. Physical examination revealed no focal abnormalities. Menopause had occurred at the age of 48.

Skull x-ray films demonstrated marked expansion of the sella and destruction of the sellar floor. A CT scan revealed a large lobulated iso-dense mass occupying the sella, sphenoid sinus, third ventricle, and the interhemispheric frontal region. The tumor was homogeneous and strongly enhanced by contrast medium (Figure 1). Cerebral angiography revealed bilateral elevation of the A1 segment of the anterior cerebral artery; however, neither staining of the tumor nor pathologic vessels were observed.

Stimulation tests using 100 μ g of luteinizing hormone-releasing hormone (LH-RH), 500 μ g of thyrotropin-releasing hormone (TRH), and 0.1 units/kg of regular insulin were performed in order to evaluate the preoperative hormonal condition. Ten minutes after the bolus injection, she complained of a headache and then of sweating and nausea. Immediate examination revealed her blood glucose level to be 76 mg/dL, not unusually low after the introduction of insulin, and her blood pressure was 120/80 mm Hg; an intravenous bolus injection of 20 mL of 20% glucose was quickly administered. Ninety minutes later, the patient suddenly became stuporous, left hemiparesis developed, and the test was immediately terminated. Emergency CT scans revealed severe pituitary bleeding not only within the tumor but also in the peritumoral, subarachnoid, and ventricular spaces, and the tumor markedly increased in volume (Figure 2).

Due to the extensive volume of tumor in the interhemispheric space, emergency decompression was performed by the interhemispheric approach. The tumor was soft and of reddish color due to diffuse hemorrhage. There also was peritumoral hemorrhage in the subarachnoid space. The tumor was suctioned easily with a

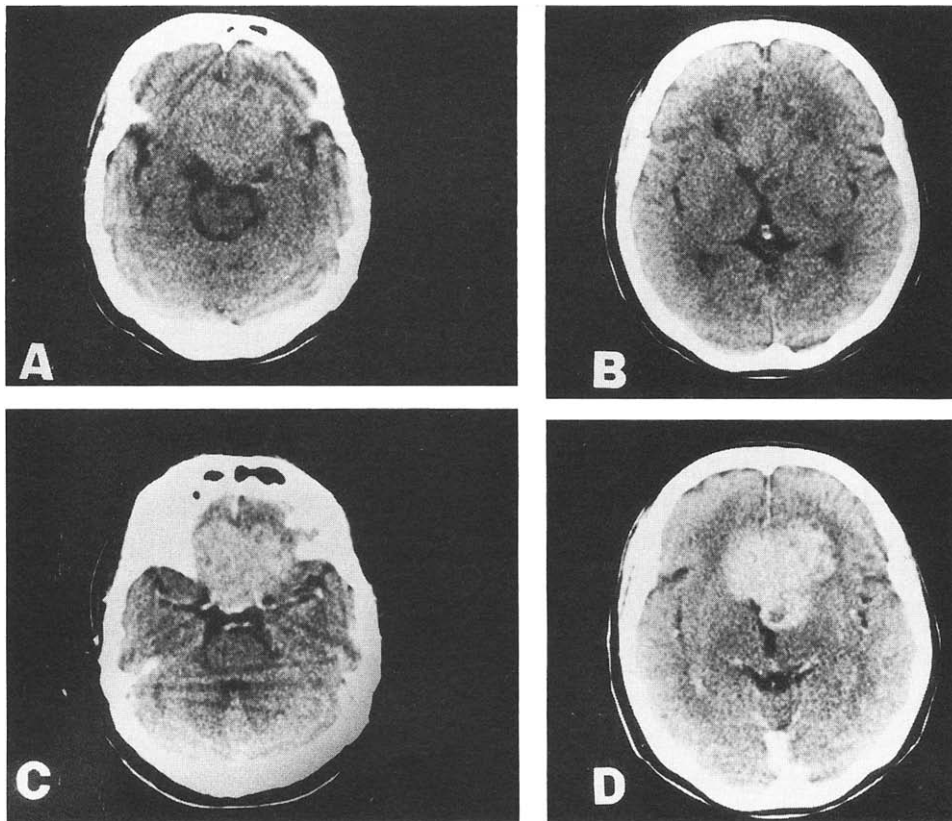


Figure 1. (A and B) A large lobulated iso-dense mass extends from the sella to the sphenoid sinus, third ventricle, frontal base, and interhemisphere. (B and C) It is homogeneously enhanced by contrast medium.

regular microsurgical suction tube, but partial removal was necessitated by tight adhesion to the adjacent swollen brain. The patient regained consciousness after the first operation but still was in a confused state, and there was improvement of the left hemiparesis. Results of the incomplete stimulation tests indicated panhypopituitarism.

In a second operation performed 17 days after the first, the residual tumor was removed successfully using a combination of interhemispherical and right pterional approaches. Pathologic examination of the surgical spec-

imens revealed a papillary-patterned chromophobe adenoma with diffuse hemorrhage; however, there was no indication of either necrosis or infarction (Figure 3).

At 1 week postoperative, the patient remained mildly confused but without hemiparesis. Follow-up CT scans revealed a small tumor remnant in the suprasellar region and hydrocephalus. Radiation therapy was applied to the remnant, and a ventriculoperitoneal shunt was inserted to treat the latter condition.

Discussion

Pituitary apoplexy normally causes a sudden enlargement of a preexisting pituitary adenoma. Many authors have presumed the apoplexy is the result of infarction or hemorrhagic infarction of the tumor, based on the unique anatomic vascular supply pattern of the hypophyseal-portal network [5].

In general, most cases of pituitary apoplexy occur spontaneously and the etiology is multifactorial, but the following precipitating factors have been documented: pregnancy, bleeding disorders, anticoagulant use, upper respiratory infections, nasal catarrh, mechanical respirators, head trauma, cerebral aneurysm, pituitary tumor radiation therapy, bromocriptine therapy, estrogen treatment, increased intracranial pressure, carotid angi-

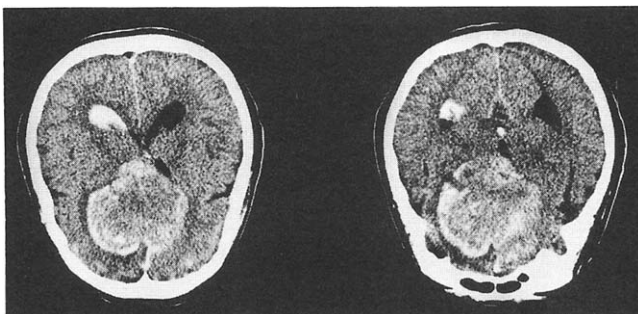


Figure 2. Plain CT scan showing the tumor enlargement with diffuse intratumoral hemorrhage that extends to the peritumoral, subarachnoid, and intraventricular spaces.

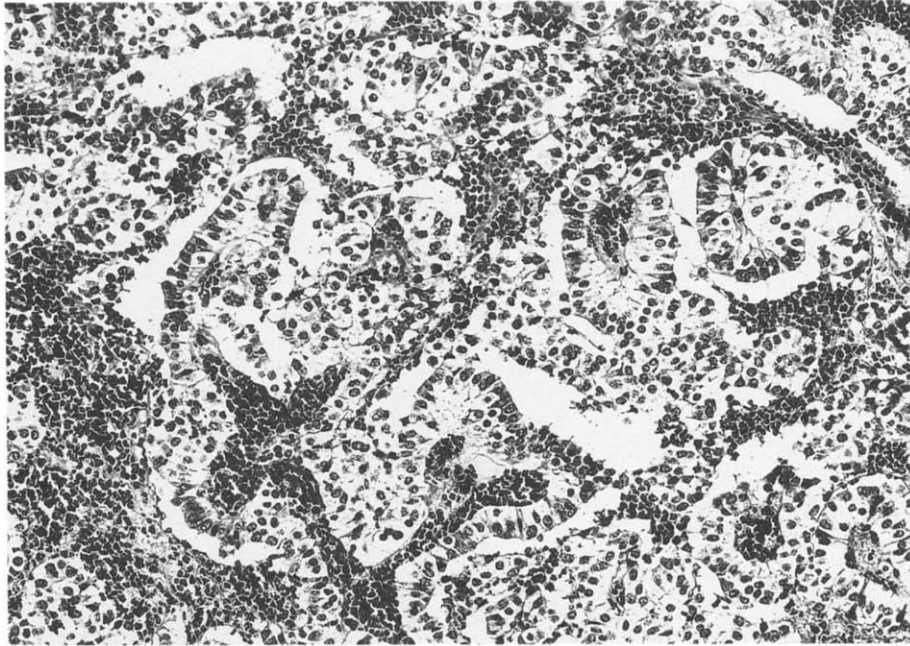


Figure 3. *Chromophobe adenoma of the papillary type with diffuse hemorrhage is observed (H & E \times 200).*

ography, lumbar puncture, myelography, and pneumoencephalography [1,6,7].

Endocrine stimulation tests would appear to be a rare cause of pituitary apoplexy. To date, there have been only three reports, including one abstract, in the English literature regarding pituitary apoplexy associated with such stimulation tests [2-4]. The first case was reported by Bernstein et al [2] in 1984. A 48-year-old man experienced a severe headache 5 minutes after a bolus injection. Twenty minutes later, he suddenly became stuporous and demonstrated left hemiparesis. CT scans revealed enlargement of an iso-density mass within the sella without any sign of hemorrhage. Cerebral angiography revealed occlusion of both internal carotid arteries at the cavernous portion. Emergency transsphenoidal decompression reversed his neurologic deterioration. Histologically, the tumor was a chromophobe adenoma recently subjected to total infarction. The second case, reported by Chapman et al [3] in 1985, involved a 39-year-old woman who displayed signs of hypoglycemia 30 minutes after a bolus injection and experienced a frontal headache 10 minutes later. The headache worsened thereafter, and impairment of vision and third nerve palsy developed on the third day. CT scans demonstrated a low-density area within the tumor that was a chromophobe adenoma with extensive infarction. Urgent surgical decompression via a craniotomy successfully restored neurologic function. The adenoma was of the prolactin-producing type. The third case was reported by Kimura et al [4] in 1989. A 14-year-old boy developed a severe headache, and 2

hours after the bolus injection developed vision impairment. He then gradually became restless. CT scans demonstrated a small high-density area in an intrasellar low-density mass. Transsphenoidal removal of the tumor corrected his neurologic deficits. He suffered from panhypopituitarism. The tumor was a chromophobe of the papillary type with fresh hemorrhaging and necrosis.

With respect to the manner in which the stimulation tests could cause pituitary apoplexy, Bernstein et al [2] postulated that TRH-induced vasospasm may precipitate pituitary gland infarction because hypoglycemia of their patient was not severe and was quickly reversed. Chapman et al [3] also presumed that TRH had an etiologic role in pituitary apoplexy, but the mechanism remained obscure.

It is known that TRH releases PRL and TSH directly into the pituitary gland, and that this reaction peaks 15 to 30 minutes after injection in normal subjects. Our case differed from the other reported cases in regard to the following: (1) the tumor was of extremely large volume; (2) hemorrhage within the tumor was diffuse and extensive; (3) hemorrhage extended to the peritumoral, subarachnoid, and ventricular spaces; (4) the tumor had a rich vasculature and neither necrosis nor infarction was observed. In addition, considering that apoplexy occurred within 10 minutes after the bolus injection, it was unlikely that infarction had occurred prior to the hemorrhage. Because hemorrhage was the result of diffuse vascular disruption in and around the tumor in our case, we assumed that the mechanism of pituitary apoplexy was induced by abrupt expansion of

the tumor due to increases in both blood flow and blood volume resulting from direct action of the TRH on both anterior pituitary lobe and the tumor.

In conclusion, we strongly recommend that the possibility of disastrous pituitary apoplexy be kept in mind when endocrine stimulation tests are planned for evaluation of the pituitary function of a large adenoma.

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