Clinical Neurology and Neurosurgery 148 (2016) 142–146

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Ischemic pituitary adenoma apoplexy—Clinical appearance and prognosis after surgical intervention

Yoshikazu Ogawa[a,*], Kuniyasu Niizuma[b], Shunji Mugikura[c], Teiji Tominaga[b]

[a] Department of Neurosurgery, Kohnan Hospital, Sendai, Miyagi, Japan
[b] Department of Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan, Japan
[c] Department of Diagnostic Radiology, Tohoku University Graduate School of Medicine, Sendai. Miyagi, Japan

ARTICLE INFO

Article history:
Received 6 May 2016
Received in revised form 4 July 2016
Accepted 6 July 2016
Available online 7 July 2016

Keywords:
Infarction
Ischemic
Pituitary apoplexy
Prognosis
Progression
Transsphenoidal approach

ABSTRACT

Background: Several retrospective investigations have recommended more passive surgical indications for intratumoral hemorrhage of pituitary adenomas due to probable spontaneous resolution. However, no definitive analyses have compared pituitary adenomas with hemorrhagic apoplexy and intratumoral hemorrhage without evident apoplectic symptoms or pituitary adenoma infarction.
Methods: This study retrospectively identified 43 patients with symptomatic pituitary apoplexy among 1067 patients with pituitary adenomas initially treated by surgery at a single institute between April 2005 and May 2015, with 27 cases of hemorrhagic (2.53%) and 16 cases of ischemic apoplexy (1.50%). The inclusion criteria involved evident and sudden onset of symptoms and simultaneous histological confirmation as hemorrhagic or ischemic pituitary apoplexy. Diagnostic differentiation with magnetic resonance (MR) imaging was performed to examine the agreement between MR imaging and histological findings, and the clinical appearance and mid-term prognosis were compared for ischemic pituitary apoplexy and hemorrhagic apoplexy.
Results: Diagnostic matching with MR imaging could be performed in 41 of 43 patients (25 with hemorrhagic and 16 with ischemic apoplexy). Agreement with the histological finding was found in 32 of 41 patients overall (78%), 23 of 25 patients with hemorrhagic apoplexy (92%), and 9 of 16 patients with ischemic apoplexy (56%). The main reason for diagnostic discrepancy was thought to be the difficulty in identifying ischemic lesion. All patients in the ischemic group suffered progression of symptoms from initial onset including various cranial nerve palsies, aseptic meningitis, and decreased level of consciousness, whereas the hemorrhagic group suffered progression in 4 of 27 patients. Ischemic group showed a statistically stronger tendency to disease progression than the hemorrhagic group ($P < 0.001$). Endocrinological examinations showed 4 patients required no hormone supplement therapies but the other 11 patients had persistent hypopituitarism and required hormone supplementation in the ischemic group, whereas 2 of 25 patients required hormone supplementation in the hemorrhagic group. Endocrinological recovery showed a significant difference between the ischemic group and hemorrhagic group ($P < 0.01$).
Conclusions: Ischemic pituitary adenoma apoplexy has a more severe clinical course than hemorrhagic apoplexy. Development of preoperative diagnostic technology to differentiate ischemic from hemorrhagic apoplexy is required to improve the low rate of agreement between the histological and MR imaging findings in patients with ischemic apoplexy.

1. Introduction

Improved detection with high-resolution magnetic resonance (MR) imaging has increased the reported incidence of intratumoral hemorrhage in pituitary adenomas [1–7], and 2% to 6% of pituitary adenomas are now thought to reveal typical classical pituitary apoplexy [1,4,6,8–20]. Several retrospective investigations recommend establishment of more passive surgical indications due to the probability of spontaneous resolution [12,18,21–23]. However, no definitive analyses have compared pituitary adenomas with hemorrhagic apoplexy and intratumoral hemorrhage without evident apoplectic symptoms or pituitary adenoma infarction [24], so the clinical appearance and categories of prognoses remain unclear.

* Corresponding author at: Department of Neurosurgery, Kohnan Hospital, 4–20–1 Nagamachiminami, Taihaku–ku, Sendai, Miyagi 982–8523, Japan.
E-mail address: yogawa@kohnan-sendai.or.jp (Y. Ogawa).

http://dx.doi.org/10.1016/j.clineuro.2016.07.013
0303-8467/

This study describes the clinical appearance and mid-term prognosis for ischemic pituitary apoplexy histologically confirmed after successful treatment by transsphenoidal surgery.

2. Materials and methods

This study retrospectively identified 43 patients with symptomatic pituitary apoplexy among 1067 patients with pituitary adenomas initially treated by surgery at the Department of Neurosurgery, Kohnan Hospital between April 2005 and May 2015, with 27 cases of hemorrhagic (2.53%) (Fig. 1 left) and 16 cases of ischemic apoplexy (1.50%) (Fig. 1 right). The inclusion criteria of this study were evident and sudden onset of symptoms like retroorbital pain, and simultaneous histological confirmation as hemorrhagic or ischemic pituitary apoplexy.

All patients underwent coronal and sagittal T1-weighted, with and without contrast medium, and T2-weighted MR imaging (1.5 T system; Magnetom, Siemens AG, Erlangen, Germany and Signa Horizon, General Electric, Milwaukee, WI; 3.0 T system) preoperatively and 6 months postoperatively. To examine the consistency of MR imaging with histological findings, two radiologists (KN and MS) unaware of the clinical information undertook retrospective diagnostic differentiation. Visual acuity and visual field were also evaluated using the Humphrey field analyzer preoperatively, and 11 days and 6 months after the operation. All cranial nerve functions such as eye movement, size and shape of pupils, and the presence of ptosis were also evaluated by the confrontation method preoperatively, and 11 days and 6 months after the operation. The morning serum concentrations of luteinizing hormone, follicle-stimulating hormone, thyroid-stimulating hormone, free T3, free T4, growth hormone (GH), insulin-like growth factor-1, prolactin (PRL), adrenocorticotropic hormone, and cortisol were measured in addition to urinary free cortisol, preoperatively, and 11 days and 6 months after the operation. If preoperative hyposecretion was suspected, supplementation of glucocorticoid and levothyroxine were introduced. Stimulation tests were performed postoperatively to avoid possible induction of iatrogenic pituitary apoplexy.

The surgical specimens were immediately fixed for histological and immunohistochemical examinations with 10% buffered formalin, embedded in paraffin, and serial sections were cut to 3-μm thickness. Hematoxylin and eosin, and periodic acid-Schiff staining were performed in all cases. The avidin-biotin-peroxidase complex method was applied for immunohistochemical staining using the pituitary hormone antibodies. Extremely extensive coagulation necrosis with spotty hemorrhage was diagnosed as infarction. Senior pathologist (HI) made and established diagnoses for this investigation (addressed courtesy in acknowledgement).

The clinical appearance and mid-term prognosis of ischemic and hemorrhagic pituitary apoplexy were examined and compared. Statistical comparisons used Mini Statmate software (ATMS Co., Ltd., Tokyo, Japan), and P values of less than 0.05 were regarded as significant. Overall study design was approved by the Ethical Committee of Kohnan Hospital 2015.

3. Results

For patients with ischemic pituitary apoplexy, all tumors were macroadenomas with expansion to the suprasellar cistern, with maximum tumor diameters from 15 to 36 mm (mean 23.6 mm). The initial symptoms were sudden whole cranial headaches with repeated vomiting in 9 patients, and severe but more focal retro-orbital pains in 5 patients. Two patients suffered moderate headaches, but were able to eat and work. All patients suffered progression of symptoms from initial onset including cranial nerve palsies (decreased visual acuity, diplopia, ptosis), aseptic meningitis, and decreased consciousness levels. The intervals from initial onset and progression varied from several hours to 12 days (mean 3.5 days). After transsphenoidal microsurgical and/or endoscopical surgeries all patients were released from the intensive care unit within a few days with complete remission of neurological deficits in 6 patients, but persistent cranial nerve palsies in 10 patients. Six months after the operation, 12 patients were free from neurological deficits, 3 patients had unilateral incomplete oculomotor nerve palsies, and one patient died of leukemia. Histopathology of the tumors included 9 cases of non-functioning adenomas and 7 cases of functioning adenomas (3 thyrotroph cell adenomas, 3 GH and PRL cell adenomas, 1 prolactinoma), indicating no evident histological predominance. Extremely extensive coagulation necrosis was seen in the majority of the patients with frequent involvement of the normal pituitary gland.

For patients with hemorrhagic pituitary apoplexy, all tumors except 2 were macroadenomas with maximum tumor diameters from 5 to 45 mm (mean 22.5 mm). The initial symptoms were similar to those in the ischemic pituitary apoplexy group. Four of the 27 patients suffered disease progression, including oculomotor nerve palsy, decreased visual acuity, secondary amenorrhea, and rebleeding from the tumor in one each. The ischemic group showed a statistically stronger tendency to disease progression than the hemorrhagic group (Mann-Whitney's U test, $P < 0.001$). After the surgeries all patients were released from the intensive care within a few days with complete remission of neurological deficits in 24 patients but persistent incomplete cranial nerve palsies in 3 patients. Six months after the operation, 26 patients were free from neurological deficits and cranial nerve palsies were resolved in all the affected patients, but one patient suffered prolonged

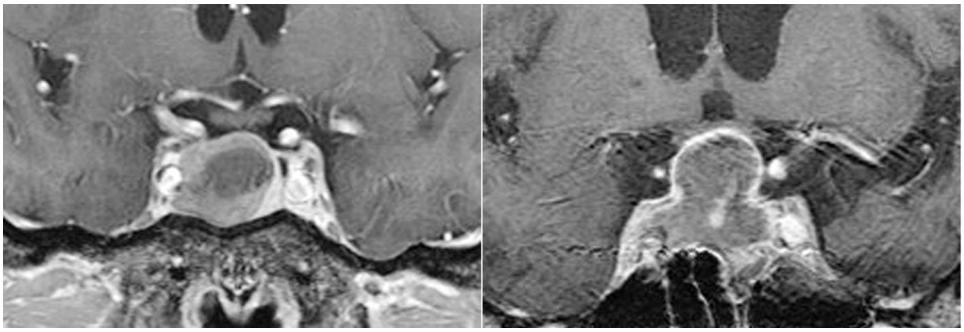

Fig. 1. Coronal MR image of a patient with ischemic pituitary apoplexy showing a tumor in the sella turcica with homogeneous signal intensity, which had compressed the optic chiasm upwards (right). Coronal MR image of a patient with hemorrhagic pituitary apoplexy showing a tumor in the sellar turcica with homogeneous signal intensity (left).