Evaluation of Fine Feeding System and Angioarchitecture of Giant Pituitary Adenoma—Implications for Establishment of Surgical Strategy

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■ BACKGROUND: **Giant pituitary adenomas carry higher surgical risks despite recent advances in microsurgical and/or endoscopic surgery, and postoperative acute catastrophic changes without major vessel disturbance are still extremely difficult to predict, may manifest as postoperative pituitary apoplexy, and are associated with poor outcomes.**

■ METHODS: **Eight males and 4 females aged 31–72 years (mean 50.7 years) with giant pituitary adenomas underwent preoperative investigation of fine angioarchitecture using C-arm cone-beam computed tomography with a flat-panel detector. Angiographical findings were used to decide the surgical routes and compared with clinical outcome.**

■ RESULTS: **Feeding arteries were verified in 10 of 12 patients, whereas no feeding arteries were evident in 2 patients. The patients were divided into the faint tumor staining group and the significant staining group, which was reconfirmed by region of interest analysis. The former group had faint supply from the ipsilateral superior hypophyseal arteries and meningohypophyseal trunk, and the latter group had significant supply from the meningohypophyseal and inferolateral trunks, which passed centrifugally from the inferoposterior pole of the tumor. All patients were treated through the extended transsphenoidal approach. Intraoperative bleeding was significantly greater in the latter group ($P = 0.013$). All patients had improvement of neurologic deficit and were released from the intensive care unit within a few days.**

■ CONCLUSIONS: **Major blood supply of giant pituitary adenomas originates from branches of the infraclinoidal portion of the internal carotid artery, different from the normal anterior pituitary gland. Surgical route should depend on not only tumor shape and extension but also feeding systems.**

INTRODUCTION

Pituitary adenomas are usually indolent with a slowly progressive course resulting in compression of the surrounding normal structures and generally can be controlled with orthodox surgical removal and adjuvant multimodal treatments.[1] Surgical risks are increased by cavernous sinus invasion, encasement of major intracranial vessels, and extensive destruction of skull base, which are all known to occur with giant pituitary adenomas.[1-3] Modern imaging studies can identify these adverse factors before surgery, but postoperative acute catastrophic changes without major vessel disturbance remain extremely difficult to predict. Such acute changes are reported in 1%–3% of cases of pituitary surgery; occur as vasospasm,[4-13] cerebral infarction, diffuse subarachnoid hemorrhage, and postoperative pituitary apoplexy[2,14-17]; and are associated with poor outcome irrespective of early and best management. Retrospective analysis of a single-center experience found acute changes after 13 of 177 giant pituitary adenoma surgeries, resulting in 12 deaths.[2] Another review found 19 cases of postoperative vasospasm, which resulted in 5 deaths.[14] The probable mechanisms of these changes include intratumoral primary hemorrhage, acute ischemia and resultant necrosis in the secondary hemorrhagic tissues, and edema and raised intratumoral pressure resulting in continuous hemorrhage. However, these mechanisms are not associated with injuries to the major intracranial vessels or perforators passing through the subarachnoid spaces but rather with injuries to the intratumoral feeders and/or drainers and the resultant drastic changes in the hemodynamics of the tumor.

Key words
- Angioarchitecture
- Feeding artery
- Giant pituitary adenoma
- Inferior hypophyseal artery
- Meningohypophyseal trunk

Abbreviations and Acronyms
CT: Computed tomography
DSA: Digital subtraction angiography
MR: Magnetic resonance

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Citation: World Neurosurg. (2016) 85:244-251.
http://dx.doi.org/10.1016/j.wneu.2015.09.087

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

The present study investigated the precise angioarchitectures, particularly the feeding system, of giant pituitary adenomas subsequently treated by surgery.

MATERIALS AND METHODS

This study prospectively identified 8 males and 4 females aged 31–72 years (mean 50.7 years) with maximum tumor diameter >40 mm among 392 patients with pituitary adenomas initially treated by surgery with histologic confirmation at the Department of Neurosurgery, Kohnan Hospital between November 2011 and December 2014. The tumors manifested as obstructive hydrocephalus, packing of the cavernous sinus, and extensive destruction of the skull base including the middle cranial fossa. All patients were investigated with axial, coronal, and sagittal T1-weighted, with and without contrast medium, and T2-weighted magnetic resonance (MR) imaging (Signa Horizon, General Electric, Milwaukee, Wisconsin, USA; 3.0 Tesla system) and bone image computed tomography (CT) (Discovery CT 750 HD, General Electric) preoperatively (Table 1). After the introduction of general anesthesia on the operation day, the angioarchitecture of the tumors was evaluated with digital subtraction angiography (DSA) using C-arm cone-beam CT with a flat-panel detector (GE Healthcare, Buc, France) and 50%-diluted contrast medium. The three-dimensional volume-rendered images and CT-like reconstructions in the sagittal, coronal, and axial planes were developed with an Advantage Workstation 4.6 (GE Healthcare).

Tumor Stain Measurement

To investigate the impact of angiographic tumor stain on the surgical procedure, region of interest (ROI) analysis was performed.[18] Briefly, conventional digital-subtracted angiographic image sequence data were processed with ImageJ (National Institutes of Health, Bethesda, Maryland, USA) to measure optical density as the contrast medium passes through the tumor. ROI of 3.0 mm^2 were drawn on the intrasellar area in the lateral view obtained by the internal carotid artery injection (Figure 1, right). The location of ROI was corresponded to the tumor image on sagittal image of MR imaging. Time-density curve of each ROI was given as the mean of the optical density for all the pixels in the ROI (see Figure 1, left). As pituitary tumor stain is regarded as contrast retention at the late phase of angiogram, we measured differences of the optical density between the beginning of a run and a plateau of the late phase in the time-density curve. If the tumor stain was revealed on the carotid angiogram bilaterally, the greater difference was recorded. All ROIs were drawn by a radiologic technician unaware of the patient's clinical condition and surgical results, and the results were compared with conventional evaluation.

Immediately after evaluation of tumor staining with contrast medium by the neuroendovascular surgeon (K.S.), the tumors were maximally removed according to the angiographic information (Y.O.). Basic surgical strategy was planned as initial removal and coagulation of the tumor from the side of the main feeding systems and gradually to the opposite side. The surgical policy was explained preoperatively to the patients, and written informed consents were obtained. Overall study design was approved by the Ethical Committee of Kohnan Hospital in 2015.

RESULTS

Feeding arteries and tumor staining were verified in 10 of 12 patients, whereas no feeding arteries or tumor staining were evident in 2 patients. The patients were divided into the no or very faint tumor staining group and the moderate to significant tumor staining group by conventional evaluation, which was reconfirmed by ROI analysis. In the no or very faint tumor staining group, the feeding arteries were the ipsilateral superior hypophyseal arteries and meningohypophyseal trunk, which passed centripetally from the surface of the tumor. Optical density difference varied from

Table 1. Clinical Characteristics of Patients

Case No.	Age (years), Sex	Pathology	Size (mm)	Remarks
1	31, M	Atypical adenoma	41 × 32 × 35	Cavernous invasion multilobular
2	62, M	Plurihormonal adenoma	45 × 22 × 34	Obstructive hydrocephalus
3	44, M	Plurihormonal adenoma	40 × 35 × 32	Destruction of clivus
4	64, M	Plurihormonal adenoma	40 × 35 × 25	Cavernous invasion multilobular
5	46, F	Null cell adenoma	53 × 42 × 41	Obstructive hydrocephalus
6	69, F	Gonadotroph cell adenoma	41 × 37 × 36	Cavernous invasion multilobular
7	47, M	Gonadotroph cell adenoma	54 × 42 × 31	Bilateral cavernous invasion
8	31, M	Atypical adenoma	54 × 47 × 49	Extended to right middle cranial fossa
9	56, M	Atypical adenoma	35 × 46 × 33	Cavernous invasion multilobular
10	38, F	Plurihormonal adenoma	40 × 28 × 25	Cavernous invasion, fibrous tumor
11	72, M	Plurihormonal adenoma	40 × 28 × 28	Obstructive hydrocephalus
12	48, F	Null cell adenoma	82 × 53 × 38	Extensive destruction of skull base

M, male; F, female.