Int J Clin Exp Med 2015;8(5):7477-7486
www.ijcem.com /ISSN:1940-5901/IJCEM0007205

Original Article

Clinical analysis of infarction in pituitary adenoma

Deyong Xiao[1,3], Shousen Wang[1,2], Yinxing Huang[2], Lin Zhao[2], Liangfeng Wei[2], Chenyu Ding[2]

[1]Department of Neurosurgery, Fuzong Clinical College, Fujian Medical University, Fuzhou 350025, P.R. China; [2]Department of Neurosurgery, Fuzhou General Hospital, Fuzhou 350025, P.R. China; [3]Department of Neurosurgery, No. 2 Hospital of Xiamen, Xiamen 361026, P.R. China

Received February 19, 2015; Accepted April 20, 2015; Epub May 15, 2015; Published May 30, 2015

Abstract: Objectives: This study is to summarize the clinical manifestations, imaging findings, treatment and prognosis of pituitary apoplexy caused by ischemic infarction. Methods: From January 2010 to March 2014, 412 patients with pituitary adenoma were admitted in the Department of Neurosurgery at Fuzhou General Hospital, with 9 cases being diagnosed with ischemic infarction stroke. Imaging examinations were performed, including computed tomography and magnetic resonance imaging. Pituitary adenomas were evaluated according to suprasellar, infrasellar, parasellar, anterior and posterior classification. Hematoxylin and eosin staining and immunohistochemical staining were used for identifying pituitary adenoma. Results: Tumor height was 1.3-3.3 cm, with an average of 2.27 cm. Eight patients had typical clinical stroke symptoms. Preoperatively, high blood growth hormone concentration was presented in 6 cases, full hypopituitarism in 2 cases, dysfunction of corticosteroids and gonads in 4 cases, and single gonadal dysfunction in 2 cases. Ring enhancement was presented in 8 cases on constructed computed tomography or magnetic resonance images, and sellar settlement in 7 cases. Eight patients were conducted with transsphenoidal resection, and secondary transsphenoidal after craniotomy in 1 case. During surgery, poor tumor blood supply was found in 7 cases, cheese-like or tofu-like necrotic tissues in 5 cases, and few dark blood clots in 2 cases. Conclusions: Pituitary ischemic infarction stroke is clinically rare, but can be correctly diagnosed before surgery by imaging examinations. The pathological characteristics of the tumor are necrosis and fibrosis, which are easy for resection. Therefore, pituitary adenoma usually has good prognosis.

Keywords: Pituitary adenomas, apoplexy, ischemia, infarction

Introduction

Pituitary apoplexy is a clinical syndrome caused by adenoma hemorrhage or ischemic infarction. Clinically, pituitary apoplexy can be classified into typical stroke and subclinical stroke. Common clinical manifestations of pituitary apoplexy include acute headache, nausea, visual dysfunctions, and cranial nerve palsy and consciousness difficulty [1-3]. Subclinical stroke has untypical manifestations such as slow onsets of progressive vision loss and endocrine changes. Histopathological investigations suggest that the mechanisms of pituitary apoplexy include hemorrhagic infarction, ischemic infarction and mixed infarction of hemorrhage and infarction [4-7]. Pituitary apoplexy with ischemic infarction is rare in clinical practice [8-10], and is only described in several case reports [10-13]. In this study, we analyze the clinical data of 9 patients with ischemic infarction stroke.

Materials and methods

Patients

From January 2010 to March 2014, 412 patients with pituitary adenoma were admitted in the Department of Neurosurgery at Fuzhou General Hospital, with 9 cases being diagnosed with ischemic infarction stroke by operational and postoperational pathological examinations. The inclusion criteria were: i) patients with pituitary adenoma surgery at our Department from January 2010 and March 2014; ii) patients with pituitary apoplexy confirmed by operational and postoperational pathological examinations, mainly or only exhibiting ischemic infarction; iii) patients with complete clinical data. Exclusion criteria were: i) patients only or mainly with hemorrhagic pituitary apoplexy; ii) patients with second time surgery.

Among the 9 included cases, 8 had typical clinical stroke manifestations, 1 case had untypical

symptoms. Among the 8 cases with typical pituitary apoplexy, 3 had acute onset (< 3 days), and 5 had subacute onset (3 days-2 weeks). In addition, all 8 patients had headache, 3 patients had nausea and vomiting, 5 had visual loss, 5 had visual field defects, 2 had ophthalmoplegia, 1 had fever, 1 had fatigue, and 1 had consciousness disorders. Furthermore, 1 patient had a history of menstrual disorders, 3 patients had acral growth, 4 had a history of hypertension, 1 had cerebral hemorrhage surgery and left vertebral artery stenting, 1 had severe sleep apnea syndrome, and 1 had cervical flexion deformity. Before surgery, all patients received routine examinations of hormones including prolactin (PRL), growth hormone (GH), thyrotropin (TSH), follicle stimulating hormone (FSH), luteinizing hormone (LH), adrenocorticotropic hormone (ACTH), 3,5,3'-triiodothyronine (T3), and thyroxine (T4). Among the 9 patients, 1 had normal levels of hormones, 6 had high levels of blood GH, 2 had panhypopituitarism, 4 had dysfunctions in both glucocorticoid axis and gonadal axis, and 2 had dysfunction in gonadal axis only (**Table 1**).

Imaging examinations

All patients received imaging examinations on the day of or one day after admission into the hospital, including 7 patients with unenhanced pituitary magnetic resonance imaging (MRI) and enhanced three-dimensional sequence scanning (Siemens 3.0T, Berlin, Germany) and 2 patients with computed tomography (CT). Axial, coronal and sagittal three-dimensional thin layer scanning was used for CT. The parameters for MRI were as follows: T1-weighted imaging (T1WI) turbo spin echo (TSE) sequences TR of 400-600 ms and TE of l5-30 ms; T2-weighted imaging (T2WI) TSE sequences TR of 3000-4000 ms and TE of 80-150 ms; matrix 384×256; collection for 2-3 times; axial layer thickness 5 mm and layer distance 6-7.5 mm; coronal and sagittal layer thickness 2.5-3 mm and layer distance 2.75-3 mm. Contrast agent was gadopentetate dimeglumine injection (0.2 mmol/kg body weight). Two patients underwent CT angiography (CTA) before surgery to exclude the possibility of intracranial aneurysm.

Pituitary adenomas were evaluated according to suprasellar, infrasellar, parasellar, anterior and posterior (SIPAP) classification [14]. Suprasellar classification included grades 0-4; infrasellar classification included grades 0-2; parasellar classification included left and right sides, with 0-4 grades according to Knosp-Steiner classification [15]; anterior classification included grades 0-1; posterior classification included grades 0-1.

Treatment and follow-ups

One case (No. 6 in **Table 1**) had aggravated condition (prefrontal cerebral hemorrhage) after admission to hospital, and received craniotomy followed by transsphenoidal hypophysectomy. The other 8 cases received mononostril-transsphenoidal hypophysectomy. All 9 cases had complete resection of pituitary adenoma, without operational cerebrospinal fluid leakage. After surgery, conventional infection prevention, fluid infusion, and hormone replacement were performed. Follow-ups were carried out on all 9 patients for 4 months to 3 years.

Hematoxylin and eosin (HE) staining and immunohistochemical staining

Surgical resection specimens of pituitary adenoma tissues were fixed by formaldehyde and embedded by paraffin wax for slicing. For conventional smear preparations, conventional smear glass slides were fixed with 95% ethanol for at least 15 minutes, and then treated with water for 1 minute, hematoxylin for 10 minutes, running water for 15 minutes, eosin for 30 seconds, 95% ethanol for 1 minute, and 100% ethanol for 2 minutes. Stained slides were cover-slipped with Permount. Finally, the entire HE-stained cells were examined under a bright light microscope using 100-400× magnification.

For immunohistochemical staining, paraffin sections were cut and mounted on glass slides, and 5 μm sections from formalin-fixed and paraffin-embedded specimens were deparaffinized using xylene and rehydrated in graded ethanol. Samples were then preincubated with 3% H_2O_2 to eliminate endogenous peroxidase activity. Antigen retrieval was achieved by heating the sections for 2 min at 100°C in citric acid buffer (0.01 mol/L, pH 6.0). Primary antibody (Beijing Zhongshan Goldbridge Biological Technology Co., Ltd., Beijing, China) was added and incubated for 2 h at room temperature. The sections were incubated with biotin-labeled secondary antibodies. Horseradish peroxidase-labeled streptavidin was added and incubated for 30 min at 37°C. Immunoreactivity was visualized using chromogen, 3,3'diamino-benzidine

Table 1. The clinical manifestations and serum hormone level changes in 9 cases of pituitary ischemic stroke

Case No.	Age	Sex	History of main diseases	Complications	Before surgery	One week after surgery
1	60	Female	Headache and dizziness; blurred vision of both eyes; aggravation for 1 week	None	GH↑, cortisol↓, estradiol↓	GH normal, cortisol↓, T3↓, FT3↓, estradiol↓
2	68	Male	Headache for 2 days; vomiting for 1 day; sudden left ptosis in hospital; fixed eyeball	Hypertension; cerebral hemorrhage surgery; left vertebral artery stenting; long-term oral intake of ASP and Plavix	GH↑, T4↑, testosterone↓	GH↑, cortisol↓, estradiol↓, testosterone↓
3	60	Female	Lips and tongue thickening; acral enlargement for 1 year; severe snoring for 1 month	Hypertension, severe sleep apnea syndrome	GH↑, estradiol↓	None
4	39	Female	Menstrual disorders for 2 years; acute headache for 2 days	None	Normal	Cortisol↓, T3↓, T4↓, FT3↓, testosterone↓
5	55	Male	Progressive limb acromegaly for 9 years; headache for 1 week	Cervical flexion deformity	GH↑, cortisol↓, testosterone↓	Cortisol↓, testosterone↓
6	48	Male	Sudden headache and blurred vision for 10 days; aggravation with vomiting for 1 day	Hypertension	GH↑, cortisol↓, testosterone↓	Cortisol↓, testosterone↓
7	52	Male	Fever and cough for 15 days; headache for 3 days	Hepatitis B	GH↑, cortisol↓, estradiol↓	GH normal, cortisol↓, estradiol↓, testosterone↓
8	46	Male	Acute headache and right ptosis for 8 days	Hypertension for 2 years	T3↓, FT3 ↓, cortisol and ACTH↓, FSH and LH↓, testosterone↓	Cortisol↓, T3, FT3↓, gonadotropin and testosterone↓
9	50	Male	Acute headache, blurred vision and fatigue for 1 week	None	T3↓, TSH↓, PRL↓, LH↓, testosterone↓	Cortisol↓, T3↓, FT3↓, FT4↓, LH↓, testosterone↓

Note: GH, growth hormone; T3, triiodothyronine; FT3, unbound triiodothyronine; T4, thyroxine; FT4, unbound thyroxine; LH, luteinizing hormone; ACTH, adrenocorticotropic hormone; FSH, follicle stimulating hormone; TSH, thyrotropin; PRL, prolactin. ↑, indicates levels higher than normal ranges; ↓ indicates levels lower than normal ranges. The normal ranges are: GH, < 10 ng/mL; T3, 0.92-2.79 ng/mL; FT3, 3.5-6.5 pmol/L; T4, 58.1-140.6 ng/mL; FT4, 11.5-22.7 pmol/L; TSH, 0.35-5.5 μIU/mL; LH, 1.9-12.5 mIU/mL at follicular phase and 0.5-16.9 mIU/mL at luteal phase; ACTH, 4.7-48.8 pg/mL; FSH, 9.7-208 mIU/mL during pregnancy, 2.5-10.2 mIU/mL at follicular phase, and 1.5-9.1 mIU/mL at luteal phase; PRL, 2.8-29.2 ng/mL without pregnancy, 1.8-20.3 ng/mL in menopause, and 3.4-33.4 ng/mL in ovulation.

Table 2. Imaging examinations of 9 cases of pituitary ischemic stroke

Case No.	Before surgery			During surgery					Pathological reports	
	Tumor diameter (cm)	SIPAP classification	MRI signal characteristics	Tumor color	Texture	Blood supply	Boundary	Other	IHC	Histopathology
1	2.7	310000	T1, mixed heights; T2, mixed heights; uneven ring enhancement; infrasellar subsidence	Grey and yellow	Soft	Usual	Clear	Old blood in tumor; orange remnant pituitary tissues around tumor	GH	Large coagulated and necrotic tissues
2	1.3	110200	T1, mixed heights; T2, strong signals; uneven enhancement; invasion in left sellar base and cavernous sinus	Yellow-brown; large tofu-like necrotic tissues	Tough	Poor	Not clear	Infrasellar subsidence; incomplete bone	GH	Large coagulated and necrotic tissues with adenoid structure
3	1.4	100100	T1, week signals; T2, strong signals; uneven enhancement	Grey	Very soft	Poor	Clear		GH+FSH	Large coagulated and necrotic tissues
4	3.1	211100	T1, even signals; T2, strong signals; suprasellar part had 2 small cysts with liquid surface; uneven ring enhancement	Grey; cheese-like	Very soft	Poor	Not clear	Dark red blood clot in tumor	No function	Large coagulated and necrotic tissues
5	2.1	211100	CT: high-density tumor, 2.0×1.8 cm, slight ring enhancement, infrasellar subsidence	Yellowish	Tough	Poor	Clear		GH	Large coagulated and necrotic tissues
6	2.5	224410	CT: high-density tumor, 2.5×2.4 cm, invasion in sphenoid sinus, infrasellar subsidence	Dark red (craniotomy)	Soft and tough	Abundant	Not clear	Invasiveness; craniotomy followed by transsphenoidal surgery	GH	Necrosis with hemorrhage; invasion
7	1.6	210100	T1, uneven strong signals; T2, mixed signals; uneven enhancement; slight infrasellar subsidence	Yellow	Stiff	Poor	Unclear; adhesive		GH+FSH	Coagulated necrosis surrounded by granulation tissues
8	3.3	313300	T1, low signals; T2, high signals; uneven enhancement	Grey-yellow; cheese-like necrotic tissues	Tough	Poor	Not clear; adhesive	Sellar bone destruction	No function	Necrosis with hemorrhage
9	2.3	300000	T1 and Flair, mainly high signals; T2, mainly low signals; uneven ring enhancement	Grey-yellow; cheese-like necrotic tissues	Soft	Poor	Clear	Sphenoid sinus mucosa significantly thickened; pale diaphragm of saddle	PRL	Large coagulated and necrotic tissues

Note: IHC, immunohistochemistry; CT, computed tomography; GH, growth hormone; FSH, follicle stimulating hormone; PRL, prolactin.

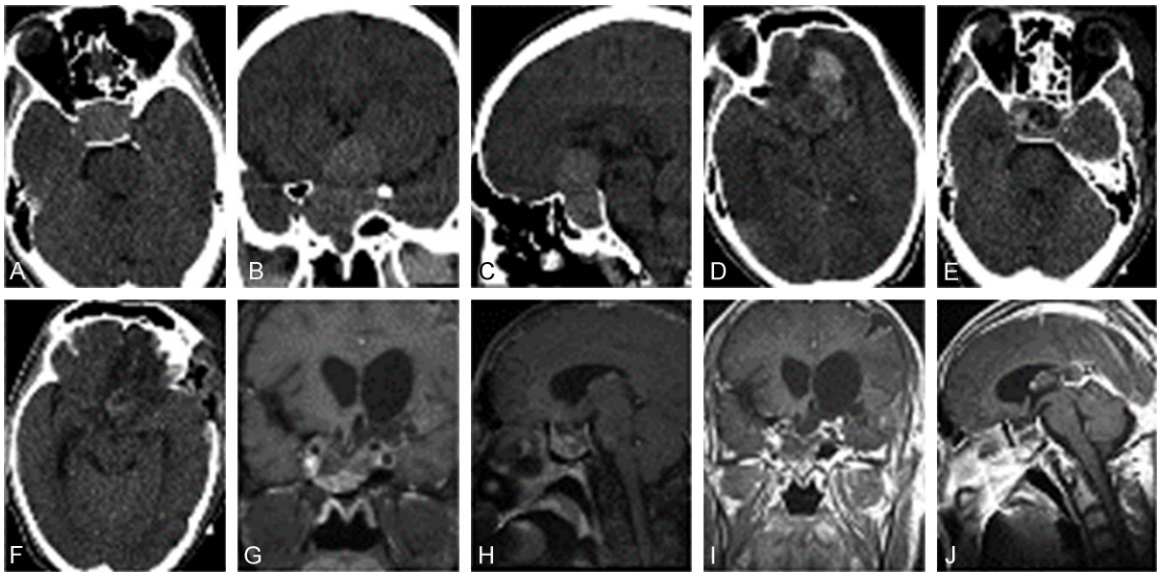

Figure 1. Imaging manifestations of case No. 6. (A) Axial (B) coronal and (C) sagittal computed tomography (CT) non-contrast enhanced scanning before admission to hospital. (D) Axial CT on the patient with aggravated condition on the second day after admission. (E and F) CT on the second day after craniotomy. (G) Coronal and (H) sagittal enhanced MRI scans before secondary transsphenoidal surgery. (I) Coronal and (J) sagittal enhanced MRI scans four months after transsphenoidal surgery. MRI, magnetic resonance imaging.

and terminated with distilled water. The sections were then counterstained with hematoxylin, differentiated with hydrochloric acid ethanol, dehydrated with gradient alcohol and xylene, and mounted onto coverslips. Examination was performed using optical microscopy. Negative controls were treated identically but with the primary antibody being omitted. Immunoreactivity was evaluated independently by three researchers.

The examinations of HE and immunohistochemical staining were performed according to World Health Organization classification in 2004 [16] to classify hormone type of pituitary adenoma.

Results

The typical imaging manifestations of pituitary apoplexy caused by ischemic infarction are uneven ring enhancement around tumor, unenhanced region inside tumors, and infrasellar subsidence

To investigate the characteristics of pituitary adenoma, imaging examinations were performed. The data showed that the maximum height of pituitary adenoma were 1.3-3.3 cm, with an average of 2.27 cm (**Table 2**). CT results on the two patients without MRI examination before surgery showed high-density tumor mass in sellar and suprasellar areas with clear boundaries, having sizes of 2.5×2.4 cm and 2.0×1.8 cm, respectively. In addition, sella turcica was enlarged and infrasella subsided. One of the two patients showed slightly ring enhancement around tumor, and the other had invasion into sphenoid sinus and bilateral cavernous sinus. CT scanning on the latter patient showed pituitary apoplexy followed by left frontal cerebral hemorrhage. This patient received craniotomy followed by transsphenoidal hypophysectomy (**Figure 1**). Preoperational MRI data of the other seven patients showed that signals of pituitary adenoma were not even: for T1WI, four cases had mixed signals with short T1 being dominant, one case had equal T1 signal, and two cases had long T1 signals; for T2WI, six cases had mixed signals with long T2 being dominant, and one case had mixed signals with short T2 being dominant; one case (No. 4) had two small liquid surfaces in T2WI, with signals above/below liquid surface being low/equal signals. Enhanced MRI showed that the seven cases had uneven ring enhancement around tumor, with unenhanced area being inside the tumor (**Figures 2** and **3**). Two cases had slight uneven enhancement. Postoperational dynamic imaging examinations showed that the tumor was completely resected. MRI examination four months after surgery showed

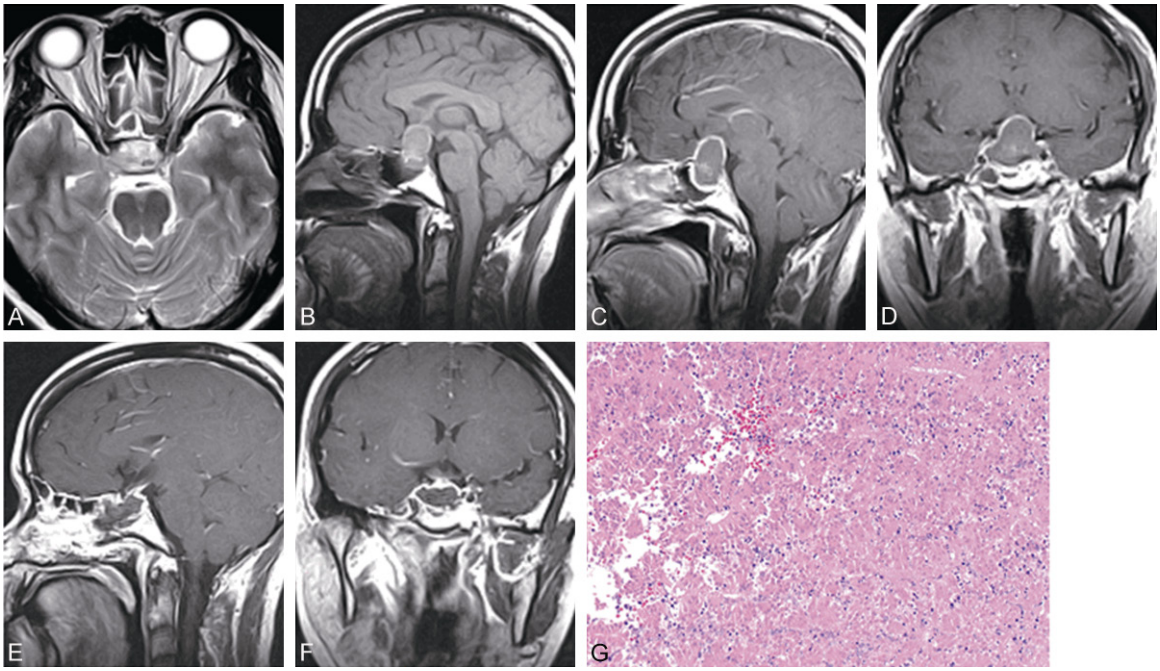

Figure 2. Imaging and histopathological manifestations of case No. 4. (A) Axial T2WI, (B) sagittal T1WI, (C) sagittal T1+, and (D) coronal T1+ MRI before surgery. (E) Coronal T1+ and (F) sagittal T1+ MRI after surgery. MRI, magnetic resonance imaging. (G) Hematoxylin and eosin staining of tumor tissues (×100). Inflammatory cells are stained blue.

no obvious residue or recurrence of pituitary adenoma. The typical imaging manifestations of pituitary apoplexy caused by ischemic infarction are uneven ring enhancement around tumor, unenhanced region inside tumors, and infrasellar subsidence.

Cheese-like ischemic necrosis during surgery is the main characteristics of pituitary apoplexy caused by ischemic infarction

Case 6, bearing GH pituitary adenoma with, underwent two surgeries due to acute ischemic infarction that occurred before cerebral hemorrhage. During the first surgery, the tumor was dark red and tough in texture, with abundant blood supply and blurred boundary. Large areas of necrotic tissues and hemorrhage existed in the tumor, and invasion occurred in sphenoid sinus and cavernous sinus. Among the other 8 patients, 6 showed grey-yellow tumor mass, and 2 had grey tumor mass; 5 cases had cheese-like or tofu-like necrosis; 7 had poor blood supply in tumor mass, and 1 had usual blood supply; 4 cases had soft to very soft tumors, and 4 had tough to stiff tumors; 4 cases had clear boundary, while 4 had unclear boundary; 2 cases had obvious adhesion around tumor, while 6 had no obvious adhesion; 2 cases had dark red blood clots (case 4) or a little old blood (case 1) within tumor mass; 6 cases had thinner or incomplete sellar bone. Tumors were completely resected under the microscope, without cerebrospinal fluid leakage (**Table 2**). These data suggest that cheese-like ischemic necrosis during surgery is the main characteristics of pituitary apoplexy caused by ischemic infarction.

Large areas of coagulation necrosis are the main pathological outcomes of pituitary apoplexy caused by ischemic infarction

HE staining showed that 7 cases had large areas of coagulation necrosis, which showed large areas of red cell-free structures under the microscope. Chrysanthemum-like contour structure was partially observed, but cells were broken, with karyopyknosis, nuclear fragmentation, and inflammatory cell infiltration being observed in necrotic areas (**Figure 2**). The other 2 cases showed necrosis and hemorrhagic changes, with hemosiderin and macrophages being observed. Immunohistochemical staining results showed that 4 cases were GH pituitary adenoma, 2 cases were GH and FSH pituitary

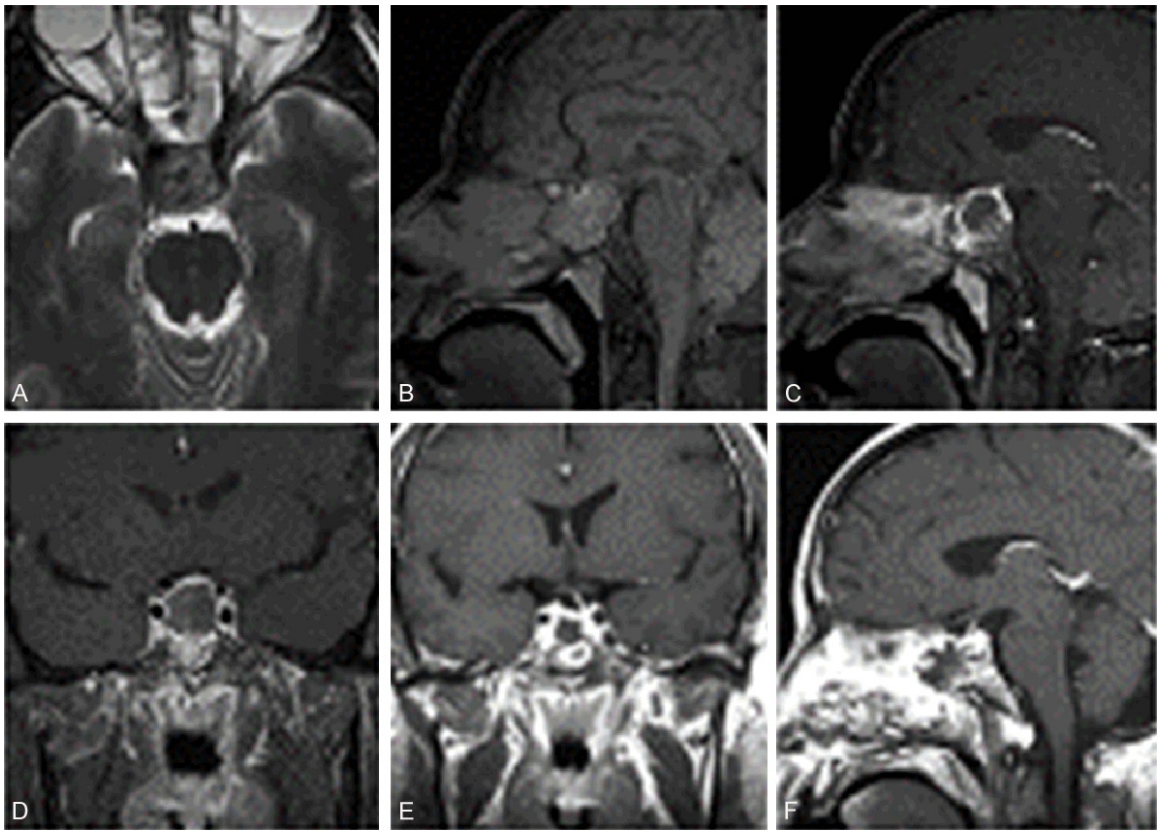

Figure 3. Imaging manifestations of case No. 8. (A) Axial T2WI, (B) sagittal T1WI, (C) sagittal T1+, and (D) coronal T1+ MRI before surgery. T1WI mainly shows high signals; T2WI mainly shows low signals. (E) Coronal T1+ and (F) sagittal T1+ MRI four months after surgery. MRI, magnetic resonance imaging.

adenoma, 1 case was PRL adenoma, and 2 cases were null cell adenoma (**Table 2**). These results indicate that large areas of coagulation necrosis are the main pathological outcomes of pituitary apoplexy caused by ischemic infarction.

Early transsphenoidal resection of tumors leads to few complications and good prognosis for the treatment of pituitary apoplexy caused by ischemic infarction

All patients had good recovery after surgery, with clinical symptoms being ameliorated. For example, headache and decreased vision were improved. Among these patients, 2 cases of oculomotor paralysis had fully recovered 4 months after surgery. Two cases had transient diabetes insipidus after surgery, but were recovered by treatment with pituitrin. Dynamic blood hormone examinations showed that high GH blood concentration before surgery was lowered or returned to normal. Nearly all patients had cortisol dysfunction one week after surgery, and 4 patients had thyroid hypofunction. Hormone replacement therapy was used on all patients but one patient, who was treated with low dose of prednisone for 1 year. Four to six months after treatment, blood cortisol and thyroid hormone levels returned to normal. Follow-ups for 4 months to 3 years showed no tumor recurrence. These data suggest that early transsphenoidal resection of tumors leads to few complications and good prognosis for the treatment of pituitary apoplexy caused by ischemic infarction.

Discussion

In this study, we investigated the clinical data of 9 patients with pituitary ischemic infarction stroke and summarized the following characteristics. i) Patients were in middle age, with a male and female ratio of 2:1. This concurs with previous report that pituitary apoplexy patients are usually between 50 and 60 years old, with the number of men being larger than that of women [3]. ii) The clinical manifestations of

pituitary ischemic infarction stroke are mostly typical and acute or subacute, with only one untypical patient who had slight headache when admission into hospital. iii) Factors responsible for cerebral ischemia and hypoxia might facilitate or aggravate pituitary ischemic stroke. In this study, vertebral artery stenosis, cervical abnormalities, and severe sleep apnea syndrome were found. More than half of the patients had history of hypertension, which might lead to vascular sclerosis that was responsible for ischemic stroke. iv) Enhanced scanning showed uneven ring enhancement around tumor, unenhanced region inside tumors, infrasellar subsidence or downward tumor invasion. When tumor ischemic infarction and hemorrhage occur, cysts and fluid levels are observed (Cases 1 and 4). V) During operation, the color of tumors was usually grey-yellow, with poor blood supply. Large areas of necrotic cheese-like tissues were usually observed, and secondary hemorrhage usually occurs in soft tumors. Vi) The pathological manifestations were usually large areas of coagulated necrosis. Immunohistochemistry showed that ischemic stroke mostly occurs in GH type pituitary adenoma, and only a few occur in nonfunctional macroadenomas or PRL type adenomas. Vii) Postoperational prognosis was generally good, with symptoms being ameliorated. Short-term urine increase and hypopituitarism were observed, but no permanent diabetes insipidus was observed.

Before surgery, 4 cases had mixed signals of MRI-T1WI, with short T1 being dominant; 6 cases had T2WI, with long T2 being dominant. These phenomena are usually considered as hemorrhagic or thrombus signs. Although 2 cases had dark red blood clots and old hemorrhage during operation, tumor tissues in other cases had no blood supply during operation and exhibited grey-yellow cheese-like necrosis, with no obvious intratumoral hemorrhage. This suggests that infarction exists in pituitary apoplexy and might be a key mechanism. However, infarction and hemorrhage usually coexist. Other imaging characteristics were uneven ring enhancement around tumor, unenhanced region inside tumor, and infrasellar subsidence. Combined with what was observed during operations, we consider central unenhanced region to be infracted tumor tissues or blood clots, while surrounding ring enhancement indicates normal pituitary and active tumor tissues. Zada G et al. reported that GH type pituitary adenoma tends to grow towards infrasella, while nonfunctional adenoma tends to grow towards suprasella [17]. This explains why most cases in the present study had infrasellar subsidence, and infrasellar bone damage. Immunohistochemistry shows that GH type pituitary adenoma has obvious occurrence tendency, which concurs with previous reports that demonstrate GH type adenoma is predominant [10-13, 18].

The exact pathological mechanism of pituitary apoplexy is not clear by now. Most literatures fail to define simple infarction stroke and hemorrhagic stroke. There is no clear explanation about which one of hemorrhage and infarction precedes the other. Chacko et al. suggest that pituitary ischemic necrosis is only a stage in hematoma absorption process after adenoma hemorrhagic infarction [6]. By contrast, Wang et al. indicate that hemorrhage occurs after pituitary ischemic infarction, and stroke includes early stage of hemorrhagic infarction and late stage of necrosis [17]. Tumor infarction and secondary hemorrhage coexist in the early stage, in which hemorrhage is observed by MRI; in late stage after hematoma absorption, cystic necrosis is observed in MRI (long T1 and T2 signals) [17]. In the present study, 2 cases showed dark red small blood clots or a little old hemorrhage in the large areas of cheese-like or tofu-like necrotic tissues. One of the two cases showed two small liquid surfaces above the saddle of the tumor, which is consistent with the fact that a little bleeding follows infarction. In addition, patient No. 6 was admitted into our hospital due to sudden headache with blurred vision for 10 days, followed by aggravation with vomiting for 1 day. Initial CT on this patient showed sellar tumor but no visual intratumoral hemorrhage. After aggravation, secondary CT showed pituitary apoplexy and subsequent cerebral hemorrhage. These indicated that hemorrhage can occur after pituitary ischemic infarction, being consistent with the findings by Wang et al. [12]. By contrast, other cases presented simple infarction stroke, without obvious intratumoral hemorrhage, suggesting that there is simple infarction factor in pituitary apoplexy, and that infarction might be a key mechanism for pituitary apoplexy.

A literature shows that pituitary adenoma hemorrhage rate is about 20-30%, being 5.4 times

of other cerebral tumors [7]. The necrosis and cystic change rate is about 5-18%, explaining why Pituitary apoplexy is mainly hemorrhagic and simple infarction stroke is rare.

Currently, it is not clear about the mechanism by which pituitary adenoma quickly becomes ischemic and necrotic, instead of developing extensive hemorrhage. The main mechanisms of pituitary ischemic infarction might be: i) fast growth of tumor, leading to insufficient blood supply and finally ischemic necrosis; ii) unique blood supply of hypophyseal portal system; iii) pituitary artery was pressed at saddle compartment hole when expanding to saddle, leading to restricted blood supply, necrosis and bleeding; iv) tumor angiopathy leads to infarction or hemorrhage. Of note, these factors might act in combination instead of being alone.

Regarding the treatment of pituitary acute stroke, most researchers suggest early surgery in order to eliminate placeholder and ease the pressure on pituitary tissues and cranial nerves. Visual impairment and consciousness decrease are clear indicators for surgical decompression. Transsphenoidal surgery is the most commonly used method, with advantages of minimal invasiveness, few complications, efficaciousness, and low rate of hypopituitarism [19]. All patients in the present study underwent early surgery, with solid effects. After surgery, the situation of them was ameliorated, without obvious complications. After pituitary ischemic infarction, some pituitary tissues underwent necrosis, leading to delayed pituitary dysfunction after surgery. Therefore, pituitary tissues that already changed colors or nature should be carefully protected during surgery. In addition, pituitary function should also be monitored closely after surgery in case of need of hormone replacement therapy.

To summarize, pituitary ischemic infarction stroke is clinically rare, but can be correctly diagnosed before surgery by imaging examinations. The pathological characteristics of the tumor are necrosis and fibrosis, which are easy for resection. Therefore, pituitary adenoma usually has good prognosis. Although ischemic infarction and hemorrhagic stroke have clinical differences, they are not extensively studied and need further case researches and experimental investigations.

Acknowledgements

This work was supported by the Medical Science Innovation Research Fund of Nanjing Military Region, China (No. 11Z034).

Disclosure of conflict of interest

None.

Address correspondence to: Shousen Wang, Department of Neurosurgery, Fuzhou General Hospital, Fuzong Clinical College, Fujian Medical University, No. 156 North West-Second-Ring Road, Fuzhou 350025, Fujian Province, P.R. China. Tel: 86-13950-482966; Fax: 86-591-87640785; E-mail: xiaody76@163.com

References

[1] Kleinschmidt-DeMasters BK and Lillehei KO. Pathological correlates of pituitary adenomas presenting with apoplexy. Hum Pathol 1998; 29: 1255-1265.

[2] Ma JK, Xing B and Wang RZ. Treatment of pituitary apoplexy with oculomotor paralysis. Chinese Journal of Neurosurgical Disease Research 2014; 13: 105-109.

[3] Verrees M, Arafah BM and Selman WR. Pituitary tumor apoplexy: characteristics, treatment, and outcomes. Neurosurg Focus 2004; 16: E6.

[4] Mou C, Han T, Zhao H, Wang S and Qu Y. Clinical features and immunohistochemical changes of pituitary apoplexy. J Clin Neurosci 2009; 16: 64-68.

[5] Murad-Kejbou S and Eggenberger E. Pituitary apoplexy: evaluation, management, and prognosis. Curr Opin Ophthalmol 2009; 20: 456-461.

[6] Chacko AG, Chacko G, Seshadri MS and Chandy MJ. Hemorrhagic necrosis of pituitary adenomas. Neurol India 2002; 50: 490-493.

[7] Semple PL, Jane JA, Lopes MB and Laws ER. Pituitary apoplexy: correlation between magnetic resonance imaging and histopathological results. J Neurosurg 2008; 108: 909-915.

[8] Ren M, Zhang HW and Zhang MS. Pituitary tumor coagulation necrosis: 7 cases report and literature review. J Neurosurg 2014; 30: 114.

[9] Kim JP, Park BJ, Kim SB and Lim YJ. Pituitary Apoplexy due to Pituitary Adenoma Infarction. J Korean Neurosurg Soc 2008; 43: 246-249.

[10] Nishioka H, Haraoka J and Miki T. Spontaneous remission of functioning pituitary adenomas without hypopituitarism following infarctive apoplexy: two case reports. Endocr J 2005; 52: 117-123.

[11] Imaki T, Yamada S, Harada S, Tsuchiya M, Sano T and Demura H. Amelioration of acromegaly after pituitary infarction due to gastrointestinal hemorrhage from gastric ulcer. Endocr J 1999; 46: 147-151.
[12] Wang HF, Huang CC, Chen YF, Ho DM and Lin HD. Pituitary apoplexy after thyrotropin-releasing hormone stimulation test in a patient with pituitary macroadenoma. J Chin Med Assoc 2007; 70: 392-395.
[13] Cinar N, Metin Y, Dagdelen S, Ziyal MI, Soylemezoglu F and Erbas T. Spontaneous remission of acromegaly after infarctive apoplexy with a possible relation to MRI and diabetes mellitus. Neuro Endocrinol Lett 2013; 34: 339-342.
[14] Edal AL, Skjodt K and Nepper-Rasmussen HJ. SIPAP--a new MR classification for pituitary adenomas. Suprasellar, infrasellar, parasellar, anterior and posterior. Acta Radiol 1997; 38: 30-36.
[15] Knosp E, Steiner E, Kitz K and Matula C. Pituitary adenomas with invasion of the cavernous sinus space: a magnetic resonance imaging classification compared with surgical findings. Neurosurgery 1993; 33: 610-617; discussion 617-618.
[16] DeLellis RA, Lloyd RV, Heitz PU and Eng C. Pathology and generetics of tumors of endocrine organs: World health organization classification of tumors. Lyon: IARC Press; 2004.
[17] Zada G, Lin N and Laws ER Jr. Patterns of extrasellar extension in growth hormone-secreting and nonfunctional pituitary macroadenomas. Neurosurg Focus 2010; 29: E4.
[18] Lee DH, Chung MY, Chung DJ, Kim JM, Lee TH, Nam JH and Park CS. Apoplexy of pituitary macroadenoma after combined test of anterior pituitary function. Endocr J 2000; 47: 329-333.
[19] Dubuisson AS, Beckers A and Stevenaert A. Classical pituitary tumour apoplexy: clinical features, management and outcomes in a series of 24 patients. Clin Neurol Neurosurg 2007; 109: 63-70.