

Clinical Article

Pituitary Hemorrhage : Classification and Related Factors

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Objective : Clinical features of pituitary hemorrhage vary from asymptomatic to catastrophic. The purpose of this study was to evaluate the factors related to severity of hemorrhage of pituitary adenoma.

Methods : Pituitary hemorrhage was noted in 32 of 88 patients who underwent operations between January 2000 and December 2007. Clinical status was classified into group I (no hemorrhage symptoms), II (mild to moderate symptoms without neurological deficit), and III (with neurological deficit), and was compared to radiological, pathological, and operative findings. All patients were operated by transsphenoidal approach, and hemorrhage-related symptoms were relieved.

Results : Groups I, II, and III comprised 15, 10 and 7 patients, respectively. In group I, hemorrhage volume was under 1 mL in 11 (73.3%), but, it was above 1 mL in 7 (70%) of group II and in all cases of group III. Hemorrhage stage based on MRI findings was chronic or subacute in 11 (73.3%) of group I, acute in 6 (60%) of group II, and acute or hyperacute in 6 (85.7%) of group III. Pathological examination revealed chronic-stage hematomas in 5 (50%) group II patients. Functioning adenomas were found in 5 (33.3%) group I patients but none in group II or III patients. Silent adenomas were found in 4 (26.7%), 8 (80%), and 3 (42.9%) in groups I, II, and III, respectively.

Conclusion : Clinical features of pituitary hemorrhage may differ with the radiological and immunohistopathological findings. Persistent symptoms are related to the chronic stage of hematoma requiring surgery for symptom relief. Neurological deficits are caused by large amount of acute hemorrhage requiring emergency operation. Silent adenoma is related to the severity of pituitary hemorrhage.

KEY WORDS : Pituitary adenoma · Hemorrhage.

INTRODUCTION

Pituitary apoplexy is an acute clinical syndrome characterized by sudden onset of headache, vomiting, visual disturbance, ophthalmoplegia, and altered consciousness. Pituitary apoplexy is usually the result of hemorrhage or hemorrhagic infarction associated with a pituitary adenoma. The hemorrhagic episode is usually obvious in clinical setting, but often presents mild symptoms similar to non-specific headache. With the development of radiological techniques, small in-tumor hemorrhages lacking any symptoms or signs of hemorrhage can be easily detected.

The incidence of clinical pituitary apoplexy is reportedly 0.6 - 9.1% in several large series of surgically treated patients

with pituitary adenomas^{13,19,24}. However, the incidence of asymptomatic intratumoral hemorrhage or subclinical apoplexy is 14 - 22%^{12,16,19,23}.

Functioning adenomas are more likely to be diagnosed on presentation of small-size tumors rather than non-functioning tumors. Cases of non-functioning pituitary adenoma with immunological reactivity to the pituitary hormones (i.e., silent adenoma) are known to have a tendency to bleed, recur, and be invasive compared to null-cell adenoma cases²⁰.

The pathogenesis and predisposing factors of pituitary hemorrhage are not yet clear. The purposes of this study were to classify the clinical status of pituitary hemorrhage including pituitary apoplexy by comparing the clinical status to radiological, histopathological, and operative findings, and analyzing the factors related to hemorrhage severity, thus suggesting its pathogenesis and facilitating an optimal treatment plan.

MATERIALS AND METHODS

Between January 2000 and December 2007, 88 patients

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with pituitary adenomas were operated through transsphenoidal and transcranial approach by one neurosurgeon. Upon radiological examination, 32 (36%) of these 88 patients were diagnosed with pituitary tumor bleeding. Of 32 patients, pure infarction of the pituitary adenoma or the adjacent tissue of the pituitary gland was not found on radiologic and pathologic examination. The definition of "pituitary apoplexy" used for patients in the study was based on pertinent medical history, clinical symptoms, appropriate findings on CT or MRI, and histopathological confirmations of hemorrhage. Patients diagnosed with non-hemorrhagic pituitary adenoma comprised the control group.

Clinical status at presentation was assessed and classified into three groups. Group I comprised patients who had no symptoms or signs related to hemorrhage, despite the discovery of hemorrhage or infarction via imaging or histopathological studies. Group II comprised patients who had abrupt onset episodes of mild to moderate headache without neurological deficit. Headache was not relieved with medicine and persisted until surgery. Patients with sudden, severe headache with neurological deficit such as ophthalmoplegia, visual loss, or visual field defect as well as decreased mentation, ptosis, and nausea and vomiting were defined as being in group III. Symptoms that were not associated with hemorrhage, such as hormonal symptoms and progressive mass effect, were not considered in clinical group classification.

Detailed neurological examinations were performed and neuroendocrinological symptoms and signs were evaluated. Possible predisposing events with relation to hemorrhage including hypertension, diabetes mellitus (DM), head trauma, and history of drug use were investigated. Baseline hormones were studied by measuring serum levels.

Brain magnetic resonance images (MRI)-including T1-weighted images (T1-WI), T2-weighted images (T2-WI) and enhanced images after administration of gadolinium-diethylenetriamine penta-acetic acid (Gd-DTPA)-were obtained in a serial thin-slice dynamic scan. Tumor size and hemorrhage volume were measured and age was estimated. Chronological classification of hematomas by MRI signal is well established. Low signal intensity in T2-WI and iso- or high signal intensity in T1-WI suggests the acute stage, while high signal intensity in both T2-WI and T1-WI in the hematoma denote the subacute stage. High signal intensity in T2-WI and high or low signal intensity in T1-WI suggest the chronic stage.

All patients underwent operation using the transsphenoidal approach. Although operations were performed primarily for tumor removal, the timing of the surgery for the group II and III was determined by the hemorrhage-related

symptoms. In group II, surgery was performed as early as possible for the intractable headache, and it was performed urgently in group III. In addition to tumor removal, liquefied hemorrhage was suctioned out, and a surgical specimen, including hematoma and surrounding fibrous tissue that was suspected of organizing hemorrhage, was obtained and sent for histopathological evaluation, whenever possible.

Surgical specimens were examined by immunohistochemical staining in addition to hematoxylin and eosin staining (H & E). Immunostaining was performed using the avidin-biotin-peroxidase complex technique and detected using a DACO EnVision Kit (Dako, Denmark). Specimens were examined not only for functioning adenoma, but also for non-functioning adenoma. Clinically and endocrinologically, non-functioning adenomas that stained positive staining for pituitary hormone following immunological examinations were defined as denoting silent adenoma.

Postoperatively, patients were managed with attention to clinical symptoms and signs of hemorrhage in addition to usual care of pituitary adenoma. Endocrinological evaluations as well as follow-up MRIs were performed. The follow-up period ranged from 6 months to 7 years (mean, 1.75 years). Tumor specimens were examined by immunohistochemical studies, and non-tumorous tissues were examined carefully. For each group, clinical status was evaluated and radiological, operative, and pathological findings were assessed.

Statistical significances of the results were determined based on the t-test, chi-square test, and Fisher exact test using a statistical analysis program (SPSS Version 12.0 for Windows, SPSS Inc., Chicago, IL, USA). Results were considered statistically significant if the two-tailed probability value was under 0.05.

RESULTS

Clinical features

Of the 32 patients, 15 (46.9%) were in group I, 10 (31.2%) were in group II, and seven (21.9%) in group III. There were 17 females (53%) and 15 males (47%). In group I, there were 10 females (66.7%) and five males (33.3%); in group II, there were six females (60%) and four males (40%). In group III, six of the seven subjects (85.7%) were male. The mean age at the time of diagnosis was 46.4 years (range, 17 - 70 years). Neither age nor gender showed a statistically significant relationship with clinical classification ($p = 0.540$ for age, $p = 0.063$ for gender) (Table 1).

Hypertension was the most common coexisting medical illness factor (8 patients, 25%). Prior to their apoplectic episodes, these patients had been diagnosed with hyper-

Table 1. Age and gender

Age (average age = 46.4)	Group I (n = 15)		Group II (n = 10)		Group III (n = 7)	
	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)
Under 46.4	3 (20)	5 (33.3)	2 (20)	3 (30)	2 (28.6)	0
Above 46.4	2 (13.3)	5 (33.3)	2 (20)	3 (30)	4 (57.1)	1 (14.3)
M / F ratio	5 (33.3)	10 (66.7)	4 (40)	6 (60)	6 (85.7)	1 (14.3)

M: male, F: female ($p = 0.540$ for age, $p = 0.063$ for gender)

Table 2. Coexisting medical illness

Coexisting illness	Group I (n = 15) (%)	Group II (n = 10) (%)	Group III (n = 7) (%)	Total (n = 32) (%)	Control (n = 56) (%)
Hypertension	3 (25)	3 (20)	2 (28.6)	8 (25)	16 (28.6)
Diabetes mellitus	1 (3.1)	2 (10)	1 (14.3)	4 (12.5)	12 (21.4)
History of head trauma	2 (6.3)	1 (10)	0	3 (9.4)	1 (1.8)
Aspirin therapy	0	1 (10)	1 (14.3)	2 (6.3)	5 (8.9)
Oral contraceptives	2 (3.1)	0	0	2 (6.3)	1 (1.8)
Tsutsugamushi fever	1 (3.1)	0	0	1 (3.1)	0
Cerebral infarction	1 (3.1)	0	0	1 (3.1)	0

Table 3. Symptoms and signs in clinical groups

Symptoms and signs	Group I (n = 15)	Group II (n = 10)	Group III (n = 7)
Headache	6	10	7
Chronic & mild	6	0	0
Acute & moderate	0	10	0
Acute & severe	0	0	7
Visual field defect	4	2	5
Progressive	4	2	0
Abrupt	0	0	5
Decreased visual acuity	4	4	0
Amenorrhea / Galactorrhea	3	0	0
Acromegalic feature	1	0	0
Nausea	0	4	7
Cranial nerve palsy	0	0	5
Dizziness	0	2	4
Decreased mentality	0	0	2
Blindness	0	0	1
General weakness	0	0	1

tension and had been prescribed anti-hypertensive medication. Four patients had DM (12.5%), and three patients had a head trauma history as a result of traffic accidents within the previous three weeks. Two patients (6.3%) had been administered aspirin, and two patients were taking oral contraceptives. One patient had a history of infectious disease (tsutsugamushi fever) in the previous 2 weeks and another patient had a cerebral infarction before the apoplectic event. Most of these coexisting medical illness were distributed in all groups. However, use of oral contraceptives, history of infectious disease, and cerebral infarction were found in group I only (Table 2).

In group I (15 patients), the presenting symptoms were relatively chronic, slow, and progressive; the subjects therein mainly presented features of pituitary adenoma, such as endocrinal dysfunction or mass effect. Six patients (40%)

presented chronic headache that seemed unrelated to the hemorrhage. A progressive visual field defect was detected in four patients (26.6%), while three patients (20%) complained of amenorrhea and galactorrhea. One patient (6.6%) had an acromegalic feature. Additionally, pituitary hemorrhage was detected incidentally through regular health screening in four patients (26.6%) (Table 3).

In group II (10 patients), classical clinical features of pituitary adenoma—such as visual symptoms and endocrinal features—were similar to those of group I. However, there were differences in the headache in terms of onset, nature, and clinical course. All patient remembered the initial episode of headaches, with accompanying symptoms such as nausea and dizziness in four of 10 (40%) patients. Headache was not relieved by medication, but improved after surgery (Table 3).

All patients from group III (7 patients) presented with sudden severe headache, coupled with nausea and vomiting. Other presenting symptoms included abrupt onset of visual field defect in 5 patients (71.4%), ocular palsy in 5 patients (71.4%), ptosis in the 2 (28.6%), decreased mentation in the 2 (28.6%) and complete blindness in 1 (14.3%) (Table 3).

Endocrinological findings

Of the 32 patients, 27 had non-functioning adenoma, and four had prolactinoma, and one had GH-secreting adenoma. Group I included 11 cases of non-functioning adenomas, four cases of prolactinomas, and one case of GH-secreting adenoma. All patients in groups II and III had non-functioning adenomas.

Hypopituitarism was noted in the initial endocrinological study in seven (21.9%) patients. Of these, one belonged to group I (6.6%), three were from group II (30%), and three were from group III (42.9%). Additionally, a thyroid-stimulating hormone deficiency was noted in five (71.4%) patients, adrenocorticotrophic hormone (ACTH) deficiency in two (28.5%), and gonadotropin deficiency in two (28.5%) (Table 4). Moreover, three patients had diabetes

Table 4. Hormone secretion characteristics

Hormone status	No. of patients (%)		
	Group I	Group II	Group III
Hypofunction of pituitary	1 (6.6)	3 (30)	3 (42.9)
TSH	1	1	3
ACTH	0	0	2
Gonadotropin	0	2	0
Hyperfunction of pituitary	5 (33.3)	0	0
PRL	4	0	0
GH	1	0	0

TSH : thyroid stimulating hormone, ACTH : adrenocorticotrophic hormone, PRL : prolactin, GH : growth hormone

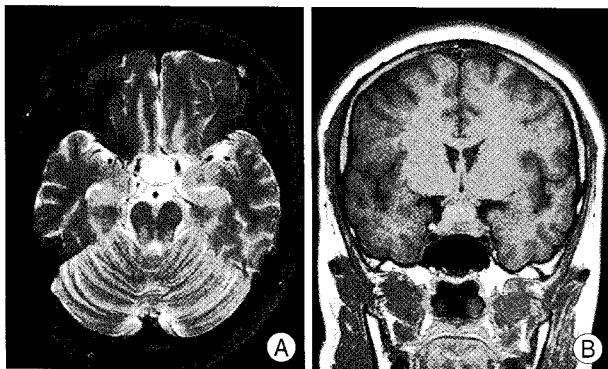


Fig. 1. Magnetic resonance image scans of a patient categorized as group II showing a pituitary adenoma with high signal intensity in the T2 weighted image (A) and T1-weighted image (B) indicating subacute hemorrhage.

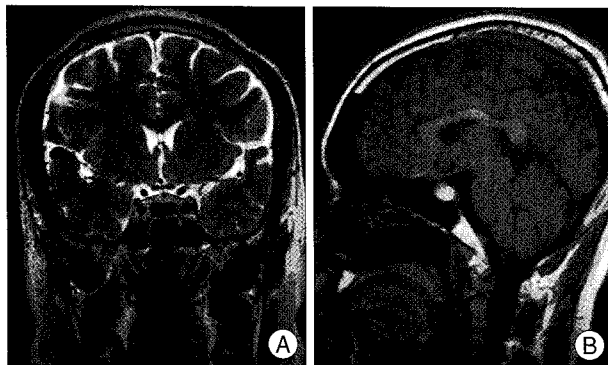


Fig. 2. Magnetic resonance image scans of a patient categorized as group III showing pituitary mass with low signal intensity in the T2-weighted image (A) and high signal intensity in the T1 weighted images (B) indicating acute hemorrhage.

insipidus (DI) at diagnosis, and hypernatremia was noted in one patient.

Radiological findings

MRI showed four cases of microadenoma, and 28 cases of macroadenoma. Hematoma size was under 1 mL in 11 of the 15 (73.3%) patients in group I, but above 1 mL in seven of the 10 (70%) patients in group II and in all patients in group III. Hemorrhage volume had a statistically significant relationship with clinical status ($p = 0.003$).

In group I, hemorrhage was in the acute stage in four of

the 15 (26.7%) patients, the subacute stage in three (20%) and in the chronic stage in eight (53.3%) patients. In group II, it was the acute stage in six of the 10 (60%) and in the subacute stage in the other four patients (40%) (Fig. 1). Six patients (85.7%) in group III were in the acute stage (Fig. 2) and one patient in group III was in the subacute stage.

Hemorrhage age showed a statistically significant relationship with clinical status ($p = 0.007$) (Table 5).

Operative findings

In group I, hematomas were confined to the adenoma and were suctioned out after adenoma removal. Every effort was made to obtain any abnormal tissue around the hematoma for the detection of hematoma organization or fibrosis. In group II, hematomas were found to be chronic in the five patients, and clot-forming in the three and a cystic component was noted in the two patients.

In group III, hematomas were gushed out at the time of dura opening. After hematoma removal, tumorous tissue was identified in the three patients, of which specimens were obtained for tissue diagnosis. In the remaining four patients, identifiable tumor tissue was not grossly visible after hematoma removal, and the surrounding area was curetted to obtain any possible remaining tissue.

Histopathological and immunohistochemical findings

Of the 32 patients with pituitary bleeding, there were 27 (84.4%) patients with non-functioning pituitary adenoma, and five (15.6%) were diagnosed with functioning adenoma. In addition, there were 15 patients with silent adenoma; four belonged to group I (26.7%), eight were group II (80%), and three were group III (42.9%). Silent adenoma was associated with severity of pituitary hemorrhage ($p = 0.032$). In group II, tumors were not identified in two patients, due to bleeding-related necrosis, and all eight non-functioning adenomas were silent adenoma. Similarly, in group III, the pathological features in four patients were necrosis, while the remaining three patients with non-functioning tumors had silent adenomas.

The histopathological findings of hematoma in group II were studied. They consisted of fibrous tissue with hemosiderin-laden macrophages and old hemorrhage, suggestive of chronic-stage hemorrhage (Fig. 3). Upon pathological examination in group III, 4 cases (57.1%) presented with

Table 5. The characteristics of MR images in pituitary apoplexy

Characteristic	No. of patients (%)		
	Group I	Group II	Group III
Diameter of tumor			
Microadenoma (< 1 cm)	1 (6.7)	2 (20)	0
Macroadenoma (> 1 cm)	14 (93.3)	8 (80)	7 (100)
Volume of hemorrhage (mL)			
Volume < 1 mL	11 (73.3)	3 (30)	0
Volume > 1 mL	4 (26.7)	7 (70)	7 (100)
Age of hemorrhage			
Acute state	4 (26.7)	6 (60)	6 (85.7)
Subacute state	3 (20)	4 (40)	1 (14.3)
Chronic state	8 (53.3)	0	0

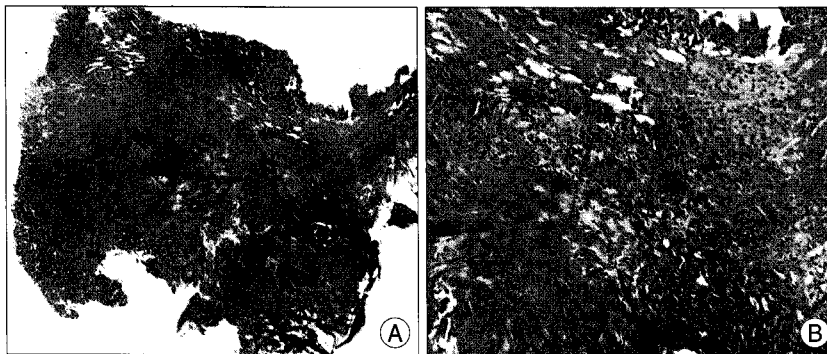


Fig. 3. Histopathological findings in chronic stage of pituitary hemorrhage. A : The tumor tissue is totally composed of dense fibrotic tissue with focal hemorrhage (H&E \times 80). B : On high magnification, fibroblasts are haphazardly arranged and infiltrating inflammatory cells and old hemorrhagic foci are noted (H & E \times 200).

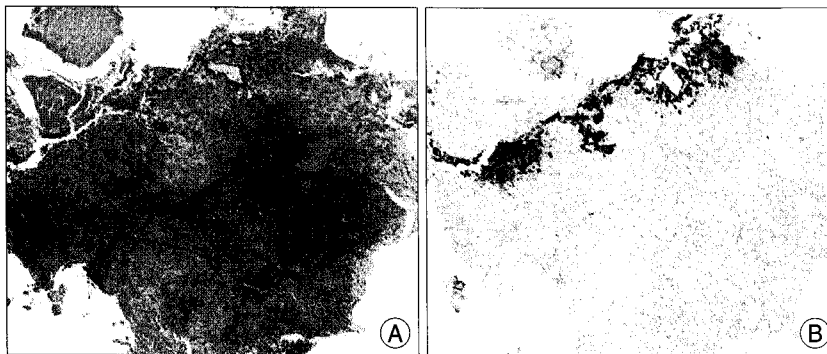


Fig. 4. Histopathological findings in pituitary hemorrhage presented with infarction. A : The tumor tissue shows marked hemorrhagic infarction (H & E \times 80). B : Focal remaining tumor cells are immunoreactive for adrenocorticotrophic hormone (ACTH) (IHC for ACTH \times 80).

necrotic tissue and 2 patients presented with infarction (Fig. 4, Table 6).

Surgical outcomes

There were no deaths due to apoplexy or surgery. Surgery resulted in full or partial improvement of the following : headache in all patients; visual field defect in 83.3% of patients; visual acuity in 66.6% of patients; and cranial nerve palsy in 85.7% of patients.

Of the seven patients with hypopituitarism, postoperative endocrinological improvements were achieved in two

patients, but five patients (i.e., one in group I, one in group II and three in group III) experienced persistent hypopituitarism and required endocrinal replacement therapy.

Postsurgical hypopituitarism developed in two patients (i.e., one each in groups II and III). Postoperative DI was noted in six patients but was transient in the five patients. Of the four patients with prolactinoma in group I, hyperprolactinemia persisted postoperatively in one case (for whom bromocriptine was prescribed). Adjuvant therapy with stereotactic radiosurgery was performed in one patient with tumor extension to the parasellar area.

DISCUSSION

“Pituitary apoplexy” refers to a clinical syndrome consisting of a constellation of signs and symptoms that are attributed to the rapid expansion of an infarcted or hemorrhagic pituitary gland^{1,13,14,19,21,24}. However, there is no comprehensive definition for “pituitary apoplexy”; some authors use a broad definition that includes any case of pituitary adenoma that show evidence of hemorrhage or bloody fluid in surgery, upon histopathological inspection, or on neuroimaging²⁴. Some hemorrhage is extensive and may eventually destroy most or all of the pituitary adenoma; patients present with mild symptoms, or even be asymptomatic. These cases of asymptomatic or mild symptomatic

pituitary hemorrhage or infarction have been termed “subacute pituitary apoplexy” or “subclinical pituitary apoplexy”^{7,15,19}. In these cases, diagnosis is often delayed or neglected¹⁵. In our study, the patients in group I presented symptoms consistent with subclinical apoplexy; on the other hand, patients in group II can be considered to be compatible with the definition of clinical apoplexy, through careful history-taking of abrupt headaches. Thus, an accurate and prompt diagnosis with careful history-taking is necessary for appropriate management.

Males are more commonly affected by pituitary apoplexy

Table 6. Immunohistopathological findings

Histologic finding	Group I (n = 15)	Group II (n = 10)	Group III (n = 7)
Necrosis	2 (13.3%)	2 (20%)	4 (57.1%)
Functioning adenoma	5 (33.3%)	0	0
PRL	4	0	0
GH	1	0	0
Non-functioning adenoma	8 (53.4%)	8 (80%)	3 (42.9%)
FSH	2	2	2
FS + LH	0	2	0
ACTH	1	0	1
PRL	1	2	0
PRL + GH	0	1	0
GH	0	1	0
Null cell	4	0	0

PRL : prolactin, GH : growth hormone, FSH : follicle stimulating hormone, ACTH : adrenocorticotrophic hormone, LH : luteinizing hormone

than women; in some series, the male to female ratio is as divergent as 2 : 1^{6,16,18}. The age range of affected individuals stretches from the first decade through the eighth decade, with most cases presenting among individuals in the fifth or sixth decade^{5,16}. Among our patients, the overall ratio of males to females was nearly equal. However, in group III—those who presented with aggressive clinical symptoms—most patients were male and in their fifth or sixth decade.

The prevalence of pituitary apoplexy presenting with clinical syndrome in several large series of surgically treated pituitary adenoma cases varied between 0.6% and 10% and is usually below 5%^{7,12,13,15,19,24}. However, the incidence of pituitary adenoma hemorrhage including asymptomatic intratumoral hemorrhage or subclinical apoplexy is much higher, and has been observed in 14 - 22% of surgically resected adenomas^{12,16,19,24}. These hemorrhages are usually detected only through imaging or pathological studies, but they may exhibit a size of hemorrhage that ranges from small to extensive^{15,19}. In our study, the incidence of pituitary apoplexy including subclinical cases, was 36.3%, which was higher than those seen in other series.

In general, pituitary apoplexy occurs spontaneously in previously asymptomatic patients. Numerous studies have discussed the predisposing factors of pituitary apoplexy^{5,13,16}. Biousse et al.² reported an increased demand on the pituitary that was coupled with blood pressure fluctuations associated with cardiac surgery, systemic hypotension, and hypertension as an inciting factors in the pituitary apoplexy generation. Additionally, changes in intracranial pressure associated with sneezing, coughing, closed head trauma, and lumbar puncture may provoke pituitary bleeding^{2,5}. Pituitary apoplexy has also been instigated by dynamic pituitary testing with thyrotropin-releasing hormone, gonadotropin-releasing hormone, and corticotropin-releasing hormone by increasing intratumoral blood flow and provo-

king bleeding in immature vessels^{13,16,24}. Among 16 (50%) patients in the study, predisposing factors were identified; several factors (such as head trauma, cerebral infarction) were found to be to the aforementioned changes. However, some factors that seem to be associated with cerebral hemorrhage, such as hypertension and DM, had no statistically significant relationship with pituitary hemorrhage in this study ($p = 0.717$ for hypertension; $p = 0.203$ for DM). Additionally, it is not clear whether infectious disease in this study, tsutsugamushi

fever is associated with pituitary apoplexy. Further research is required to determine these relationships.

The actual pathophysiological mechanism of pituitary apoplexy is not definitively known. Suggested possibilities include ischemia of the tumor, as a result of outgrowing its blood supply^{5,6,13,16}; kinking of the superior hypophyseal artery against the diaphragm sellae; or the presence of vasculopathy or abnormal blood vessels, with a tendency to hemorrhage⁵. In our study, there were 14 (43.8%) pituitary apoplexy patients with a volume under 1 mL; the majority of them (11 patients, 34.4%) were categorized as being in group I. In small-size apoplexy, Robit and Fein¹⁷ suggest that the trabecular arteries arising from the superior hypophyseal artery may be compressed by the diaphragm sellae, thereby causing ischemia and secondary necrosis of the tumor. Presumably, however, the mass was insufficient to compress the surrounding parasellar structure.

Earlier studies suggest that growth hormone and ACTH-secreting pituitary adenomas are more likely to present with apoplexy than others¹⁵. However, a recent study reported that more than 70% of cases of adenoma with apoplexy were of the non-functioning pituitary adenoma variety¹⁹. In our study, 84.4% of patients with apoplexy had non-functioning adenoma. It is unlikely that non-functioning adenoma has any unusual intrinsic characteristics to increase the risk of hemorrhage or infarction; however, because non-functioning tumors lack specific clinical markers, such as evidence of hormone hypersecretion—they can go undetected for many years, until they become large enough to cause tumor ischemia. It is in this subset of patients where apoplexy represents the first clinical manifestation of previously unrecognized pituitary adenoma.

Some authors have insisted that silent adenomas, particularly silent corticotroph adenomas and silent somatotroph adenomas, are more likely to be associated with apoplexy or

invasiveness and exhibit a higher rate of recurrence than other tumors^{4,20,25}. In this study, silent adenomas were found more frequently in group II and III patients than in group I patients; furthermore, null-cell adenoma was found in group I only. These findings suggest that hemorrhages of silent adenoma are more aggressive than hemorrhages of other non-functioning types of adenoma.

MRI is more effective than computed tomography in identifying the imaging features of pituitary apoplexy and is the investigative tool of choice⁹. Pituitary apoplexy may present with various MRI features of hemorrhage. In the acute stage, the appearance of hemorrhage typically presents a high signal intensity on T1-WI and a low signal intensity on T2-WI^{3,8,9,14}. Enhanced MRI images do not provide additional information with regard to hemorrhage in the presence of blood⁹. Signal intensity changes occur in subacute hemorrhage due to the degradation of hemoglobin into methemoglobin; in such cases the signal should appear bright on both T1-WI and T2-WI^{3,10}. In the chronic phase (i.e., over 15 days), sedimentation of blood products may create a fluid level within the mass—a feature that is highly suggestive of hemorrhagic pituitary apoplexy^{3,8,14,17}. In our study, we found that preoperative findings of pituitary hemorrhage on the MRI sequences correlated well with clinical symptoms and operative findings.

In cases of subacute or chronic hematoma in radiological and operative findings, bleeding in the pituitary adenoma remaining in the pituitary fossa seems to undergo pathological changes with time, such as immature fibrosis of the neomembranes or trabeculae, and limited organization of the hematoma²². As with the pathophysiology of chronic subdural hematoma, the chronic form of hematoma is enlarged and compresses the surrounding tissues, thus causing persistent symptoms.

The immediate management of pituitary apoplexy consists of supportive care, fluid electrolyte monitoring, and replacement of hormones such as corticosteroids^{1,11,14,19,23}. Patients with pituitary hemorrhage without any symptoms related to hemorrhage (group I) do not require any surgical treatment for the hemorrhage, on the other hand, patients with headache with accompanying neurological deficit due to hemorrhage (group III) are not difficult to diagnose and for the patients can be given a prompt treatment plan for the clinically obvious apoplexy. However, for patients with headache without neurological deficit (group II), a detailed evaluation is required to determine whether the headache is related to the hemorrhage or is non-specific; in such cases, early surgery should be considered, because headache is not readily cured by medical treatment. In our study, the patients in group III with diminished levels of consciousness,

deteriorating vision, and sudden onset blindness underwent emergency surgery. For most patients in group II, surgery was elective and was performed early (i.e., within one week of diagnosis). Patients in group I had elective surgery according to treatment for pituitary adenoma. We observed both low morbidity and significantly improved outcomes of neuro-ophthalmic signs, similar to results in other series. There is a consensus that prompt surgical decompression of pituitary lesion as indicated in pituitary apoplexy with severe neuro-ophthalmic signs is preferable^{5,15,23}. However, the role of urgent surgery in patients with no or mild neuro-ophthalmic signs (such as patients in groups I, II in this study) remains controversial, because there have been no prospective randomized controlled trials in the management of pituitary apoplexy. Sibal et al.²¹, in their relatively large study, suggested that conservative management is safe for most patients with pituitary apoplexy with no or mild neuro-ophthalmic signs in the acute stage; they suggested that immediate surgical decompression is not normally indicated in pituitary apoplexy patients with no or mild neuro-ophthalmic signs, and that early but not necessarily emergency surgery should be selected.

CONCLUSION

Pituitary hemorrhage may present with a wide spectrum of symptoms and signs, all of which are affected by size, stage of hematoma, and immunohistochemical reactivity to pituitary hormones. Persistent headache is related to the chronic stage of hematoma compressing the surrounding structures; symptom relief is contingent upon surgical decompression. Urgent surgery is needed for patients afflicted by neurological deficits.

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