

Pituitary apoplexy: clinical features, management and outcome. Clinical study and review of the literature

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Abstract: *Background:* Pituitary apoplexy is a clinical syndrome secondary to rapid expansion of the content of the sella and extension to suprasellar region, cavernous sinus, sphenoid sinus secondary to a bleeding, ischemic or mixed episode taking place in a pituitary adenoma. This episode will determine a significant compression of the optic nerves, optic chiasm, cavernous sinus and hypothalamus, which translates clinically most often by headache, visual disturbances, decreased level of consciousness and ophthalmoplegia. *Material and methods:* This paper presents a retrospective study over a period of five years, from January 2009 to December 2013 and includes 98 patients diagnosed with pituitary apoplexy and treated in the Third Department of Neurosurgery, Emergency Clinical Hospital Bagdasar-Arseni. Of the 98 patients, 62 were females (63.3 %) and 36 were males (36.7 %) with a ratio of female to male of 1.7:1. The patients were aged between 17 and 75 years old, average age being approximately 50 years. Follow-up period ranged from 2 months to 5 years. The main symptoms at presentation was sudden, intense headache, this symptom was encountered in 90 patients (91.83%), vomiting showed by 76 patients (77.55%), decreased visual acuity observed in 57 patients (58.16%), visual field deficits in 74 patients (75.51%), cranial nerves palsy (III, IV, VI) observed in 14 patients (14.28 %). *Conclusions:* Pituitary apoplexy is a disease that can endanger patients' lives. The clinical presentation may vary from minor symptoms to major neurological deficits and even death so early diagnosis and treatment are vital.

Key words: apoplexy, pituitary adenoma.

Background and epidemiological considerations

Pituitary apoplexy is one of the major neurosurgical emergencies especially due to

compression of the optic nerves and chiasm and associated hormonal imbalance. In this paper, we present a retrospective study conducted over a period of 5 years which includes patients diagnosed with pituitary

apoplexy and treated in the Third Department of Neurosurgery from Emergency Clinical Hospital Bagdasar-Arseni, Bucharest.

In this paper, we propose to draw attention to the importance of early diagnosis and treatment of these patients given the sometimes disastrous consequences of this condition on visual and endocrine function. Also, we will make an analysis of the literature for a better understanding of this neurosurgical pathology.

Pituitary apoplexy is a clinical syndrome secondary to rapid expansion of the content of the sella and extension to suprasellar region, cavernous sinus, sphenoid sinus secondary to a bleeding episode, ischemic or mixed episode (ischemic and hemorrhagic) taking place in a pituitary adenoma. The hemorrhagic, ischemic or mixed episode will determine a significant compression of the optic nerves, optic chiasm, cavernous sinus and hypothalamus, which translates clinically most often by headache, visual disturbances, decreased level of consciousness and ophthalmoplegia. (1)

The first subtemporal decompression for a pituitary adenoma was practiced by Paul, a British neurosurgeon in 1892, in an acromegalic patient with intracranial hypertension. In 1898, Bailey described the first case of pituitary adenoma associated with intratumoral hemorrhage. In 1906, Hounsfield reported a series of 10 patients with pituitary tumors treated by temporal and subfrontal approaches. A milestone in the treatment of these tumors was marked by Schloffer, in 1907, when he approached sella turcica via an extensive lateral rhinotomy with resection of

the septum and turbinates. In 1909, Cushing used a variation of Schloffer's technique, he adopted sublabial incision, later described by Halstead and Kanavel. Brougham et al, first described the signs and symptoms associated with hemorrhage in a pituitary tumor and named it pituitary apoplexy; the suffix "plexi" comes from Greek term meaning to strike or to have a stroke. Another important step in the treatment of this pathology is the transnasal transfenoidal approach, first described by Hirsch in 1910. In 1960, Hardy used operating microscope in a transnasal transsphenoidal approach of a microadenoma. From 1990, endoscopes is a tool widely used in surgical treatment of sellar tumors. (27)

Pituitary tumors represent about 10-15 % of all primary brain tumors, a much higher frequency, of 20-25%, is found for microadenomas discovered incidentally at autopsy. Regarding pituitary apoplexy clinically evident, it has a frequency of 1-2%, maximum 10 % in some studies of total pituitary tumors, the frequency is about 28 % if we take into consideration clinically silent pituitary apoplexy when diagnosis is established in histopathological examination. (2) (27)

Approximately 50% of apoplectic events occur in patients who were not previously diagnosed with a pituitary tumor. The age range of affected patients is situated between first and eighth decades of life with the most cases in the fifth or sixth decade. Most of the published studies demonstrated a higher frequency of pituitary apoplexy among male compared to female population. (24)

Material and methods

This paper presents a retrospective study over a period of five years, from January 2009 to December 2013 and includes 98 patients diagnosed with pituitary apoplexy and treated in the Third Department of Neurosurgery, Emergency Clinical Hospital Bagdasar-Arseni. Of the 98 patients, 62 were female (63.3%) and 36 were male (36.7%) with a ratio of female to male of 1.7:1. Thus, we observe a slightly higher frequency in female population compared to studies published so far. The patients were aged between 17 and 75 years old, average age being approximately 50 years, this aspect is in line with studies published to

date. Follow-up period ranged from 2 months to 5 years.

Clinical presentation

The main symptom at presentation was sudden, intense headache, this symptom was encountered in 90 patients (91.83%). Other signs and symptoms were: vomiting showed by 76 patients (77.55%), decreased visual acuity observed in 57 patients (58.16%), visual field deficits in 74 patients (75.51%), cranial nerves palsy (III, IV, VI) observed in 14 patients (14.28%). None of the patients in our study did not show altered consciousness on admission (figure 1).

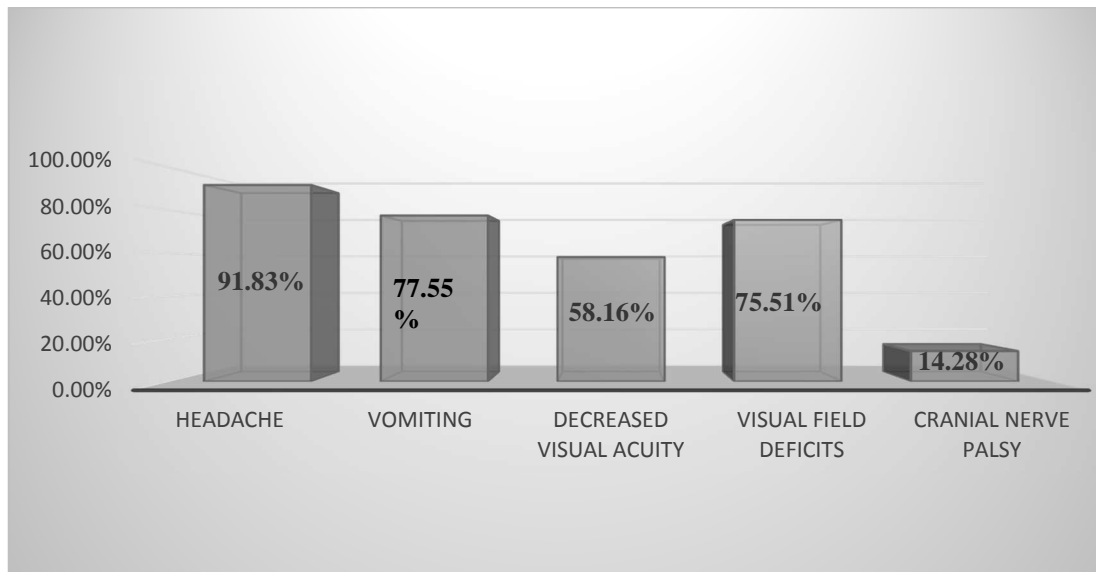


Figure 1 - Clinical status at admission.

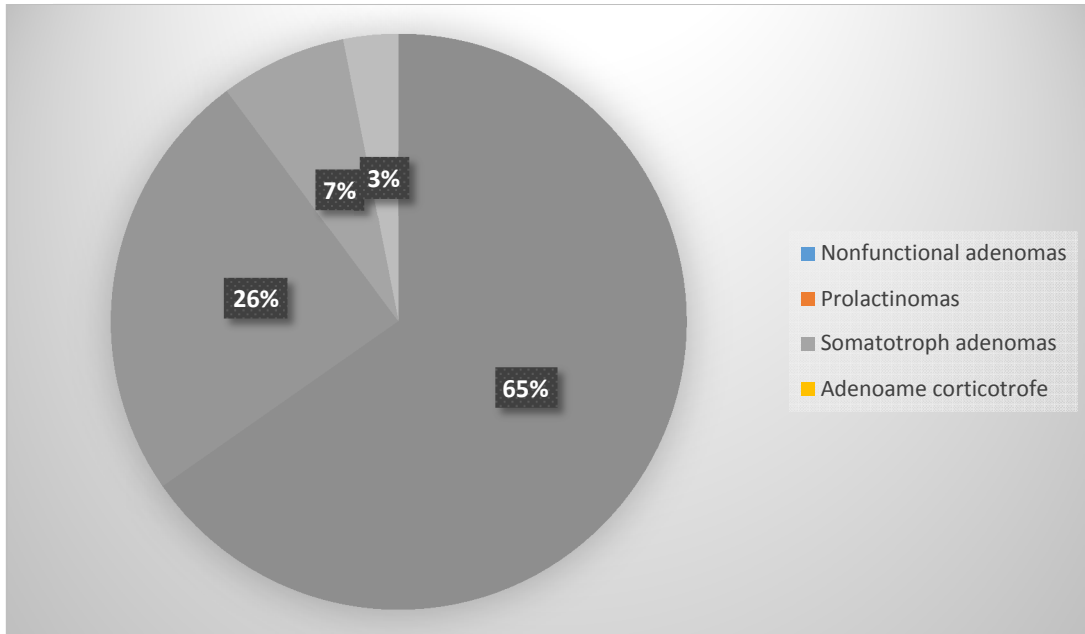


Figure 2 - Endocrinological status at admission.

Endocrinological findings

Endocrinological evaluation was performed in all patients in the study, 64 patients had clinically nonfunctioning pituitary tumors (65.3%), 24 patients had prolactinomas (24.5%), 7 patients were known with GH secreting pituitary adenomas (7.1 %) and 3 patients had ACTH secreting pituitary adenomas (3.1%). Pituitary apoplexy occurs with no predilection to a certain category of pituitary adenomas. A greater frequency of pituitary apoplexy in the studied population with clinically nonfunctioning pituitary tumors is due to higher overall frequency of this type of tumor than a certain predisposition (figure 2).

Imaging evaluation

For imaging diagnosis of our patients we used CT scan and MRI with and without

gadolinium; we also used this investigations to evaluate the postoperative status of our patients.

Treatment

In all cases included in our study, surgery treatment was practiced emergency. The time between diagnosis and surgery was of one to ten days. In all cases we used transnasal transsphenoidal approach. In cases with corticoid insufficiency, corticosteroid hormone replacement therapy was instituted. During surgery, and in the immediate postoperative period was performed monitoring of urine output and in patients with diabetes insipidus, treatment with desmopressin was made.

Patient outcomes

In the immediate postoperative period the best recovery was observed for cranial nerve

palsy (nerves III, IV and VI). As regards of visual function (decreased visual acuity or visual field deficits) recovery was partial after surgery.

Of the 57 patients with impaired preoperative visual acuity we observed its improvement after surgery in 46 patients (80.7%), from 74 patients with visual field deficits at admission, postoperative improvement was noted in 63 patients (85.1%). Regarding paresis of cranial nerves III, IV, VI, it was almost completely recovered after surgery, 12 of 14 patients with severe preoperative paresis (85.7%).

Our study shows that the recovery was better in cases where surgery was done in the first week after symptoms onset. This applies especially to recover deficits in visual acuity or visual field, in terms of recovery oculomotor nerve palsy, good results were obtained when surgery was made more than one week after the onset of the symptoms.

Of the 98 patients included in the study, 56 were operated during the first week after onset of the signs and symptoms and 42 patients were operated at less than a week. Of the 56 patients operated in the first week, 54 had improvement of visual function (96.4%) while the percentage of recovery for patients operated more than a week is 50% (21 patients with improved visual function after surgery).

Postoperative endocrinological status

Of the 98 patients operated, all patients with hypopituitarism did not fully recover after surgery, so hormone replacement therapy on various axes was necessary in most patients. Thus in our series of patients, 60 patients (61.2 %) required corticosteroid

replacement therapy, 41 patients (41.8%) received thyroid hormone replacement, gonadotroph hormone replacement was necessary in 24 patients (25.5%) and desmopressin treatment in 7 patients (7.1%).

Discussion

Pituitary apoplexy is a clinical syndrome caused by the rapid expansion of a pituitary adenoma secondary to ischemia and /or intratumoral hemorrhage which causes compression of the cavernous sinus, chiasm and optic nerves. Clinical syndrome is characterized by brutal installed headache, vomiting, vertigo, meningism, deceased level of consciousness, ophthalmoplegia, visual field deficits, and decreased visual acuity. (3-5)

All types of pituitary tumors can develop intratumoral apoplexy. Approximately 50% of apoplectic events occur in patients who had not been previously diagnosed with pituitary tumors, this leads to a delay in diagnosis. Wakai et al noticed in their retrospective study that 16.6% of their patients with pituitary adenomas show bleeding or intratumoral hematoma but only 6.8% had a clinical apoplectic episode. Deb and al observed intratumoral hemorrhage in 17.1% of patients, but only 5.4% had clinical signs and symptoms of pituitary apoplexy. (6, 7)

The most common signs and symptoms present at admission were: headache (frontal or retroocular), visual field restriction, decreased visual acuity, ophthalmoplegia, nausea, vomiting, vertigo, meningism, deceased level of consciousness, facial pain or numbness, fever, hemiparesis, Horner syndrome, seizures.(8)

Hormonal status

Hormonal imbalance is often found in pituitary apoplexy. Hypopituitarism is caused by increased intrasellar pressure, destruction of the pituitary gland by an existing adenoma or secondary to apoplectic event. Vedhuis and Hammond noted that after an episode of pituitary apoplexy, 88% of patients had growth hormone deficiency, 76% had inadequate secretion of luteinizing hormone, 67% had prolactin inappropriate secretion, 66% had inappropriate secretion of ACTH and 33 % had estradiol deficiency. (1, 26, 28)

Diabetes insipidus is rare and occurs in pituitary apoplexy secondary to tumor compression of the infundibulum made by edematous or hemorrhagic material so that it is prevented release of antidiuretic hormone from hypothalamus. Another possibility is the compression of the inferior hypophysial artery in the intracavernous portion by hemorrhagic material. Baha and Verrees found that diabetes insipidus occurs in only 2-3% of patients with pituitary apoplexy. (1)

Precipitating factors

Precipitating factors have been identified in about 50% of the cases diagnosed with pituitary apoplexy. The most common are: treatment with bromocriptine, estrogen therapy, anticoagulation, pregnancy, head trauma, bowel and other general surgery, diabetic ketoacidosis, cardiac bypass, radiotherapy, hypertension or hypotension, atherosclerosis. (1, 9, 10, 27)

Fluctuations in blood pressure associated to cardiac bypass and surgical interventions can lead to pituitary apoplexy. Fragmentation of atherosclerotic plaques and engaging of

particles within the pituitary vasculature may lead to gland infarction. Infections, childbirth, and surgery may be associated with pituitary apoplexy secondary to increased gland activity in response to increased need for stress hormones in these circumstances. Sneezing, coughing or ketoacidosis change blood flow and blood osmotic values precipitating pituitary apoplexy. (11, 12, 25)

Numerous studies have shown a higher rate of hemorrhage or ischemia in pituitary tumors due to large discrepancy between the development of local circulation and tumor size; however small tumors can also develop apoplexy events. (11, 12, 25)

Imaging studies

CT scan has a detection rate of 21-46 % for pituitary apoplexy. The main detected issues are: hemorrhagic area, specific hyperdense, recent hemorrhage, mixed density when bleeding is associated with acute ischemic area. Another aspect is subarachnoid hemorrhage, CT scan can detect invasion of the basal cisterns with blood, complication that can accompany a series of pituitary apoplexy. The CT scan bone window gives us important information about sella turcica and paranasal sinuses. (3, 13) (figure 3).

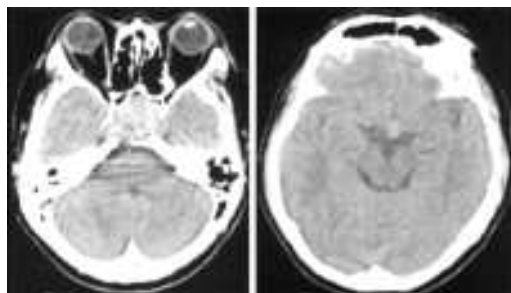


Figure 3 - Pituitary apoplexy – CT scan

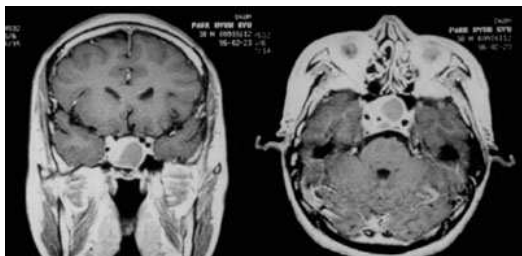


Figure 4 - Pituitary apoplexy – MRI images

MRI has a detection rate of 100 % for pituitary apoplexy. This imaging investigation has greater sensitivity and achieves better detection of the tissue. The issues detected in patients with pituitary apoplexy are specific heterogeneous density hemorrhage, edema and ischemia in the pituitary gland. (14) (figure 4).

MRI is the most effective imaging investigation for pituitary apoplexy. Piotin et al wrote down that MRI imaging for this condition can be very varied. (15)

Arita et al drew attention to parasellar dural changes. These changes are caused by changes in dural blood flow. He also noted about sphenoidal sinus mucosal thickening due to local venous obstruction. Another cause could be sphenoid sinus mucosal inflammation induced by inflammatory substances produced by tumor necrotic tissue. (16, 17)

Differential diagnosis

Differential diagnosis of pituitary apoplexy can be done with subarachnoid hemorrhage secondary to aneurysm rupture, viral or bacterial meningitis, spontaneous bleeding (hypertension, amyloidosis, metastatic or primary pituitary tumor), cavernous sinus thrombosis, carotid-cavernous fistula,

migraine, optic neuritis, diabetic oculomotor palsy, temporal arthritis, vertebrobasilar insufficiency, transtentorial herniation. (18)

Treatment

The standard treatment for pituitary apoplexy includes high-dose of corticosteroid hormone which will lead to improvement of symptoms and surgical decompression using a transsphenoidal approach. Pituitary gland is capable to secrete suitable amounts of hormones even when only 10% of the gland remains functional. (19, 20)

The treatment of choice for pituitary apoplexy is represented by surgical intervention which also decompress cavernous sinus and suprasellar structures; it is recommended especially when there is impairment of visual acuity or visual field, impaired consciousness or when there is progression of symptoms. Transsphenoidal approach is safe and effective because it does not make a direct manipulation of the optic tract especially for pituitary apoplexy in the acute phase when there is an important compression of the optic pathway. (10, 21)

Transcranial approaches are recommended when there is an important hemispheric hemorrhage extension, presence of hemorrhage and/or necrosis that extends beyond the intact diaphragm or when there is a sphenoid sinus less aerated. The main transcranial approaches used are pterional, subfrontal, and subtemporal. (22, 23, 27)

The main complications of transsphenoidal surgery are: damage to the hypothalamus, visual tract damage, vascular lesions, CSF fistula, cavernous sinus injury (internal carotid artery, cranial nerves III, IV,

VI), iatrogenic hypopituitarism, brainstem injury, and nasal complications (mucocele, sinusitis, fracture of hard palate or cribriform plate, nasal deformity). (22, 27)

Conclusions

Pituitary apoplexy is a disease that can endanger patients' lives. The clinical presentation may vary from minor symptoms to major neurological deficits and even death so early diagnosis and treatment are vital.

Abbreviations

CT – computerized tomography
IRM – magnetic resonance imaging

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