

Pituitary Apoplexy in Pituitary Adenoma: About 16 Cases

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Abstract

Introduction: Pituitary apoplexy is a rare condition caused by hemorrhage or infarction of the pituitary gland, often in the context of a pituitary adenoma. This study aimed to examine the epidemiological, clinical, paraclinical, therapeutic, and progressive characteristics of pituitary apoplexy caused by pituitary adenoma. **Patients and Method:** We conducted a retrospective descriptive study, analyzing 16 medical files of patients hospitalized for pituitary apoplexy out of 160 cases of pituitary adenomas in the Neurosurgery Department of the National University Hospital Center of Fann over a 6-year period, from January 1, 2014, to December 31, 2020. **Results:** We collected 16 cases of pituitary apoplexy over 6 years. The average age of our patients was 42.5 years, ranging from 17 to 79 years. Males were most represented, accounting for 80% of cases, with a sex ratio of M/F = 4. The clinical presentation included tumor syndrome (headache and neurological signs), endocrine signs, and general signs. In this study, 93.75% of patients underwent surgery via a transsphenoidal approach under endoscopy, with one case of incomplete excision (6.25%). Complications were mainly diabetes insipidus and nasal obstruction, occurring in 31.25% and 18.75% of cases, respectively. **Conclusion:** Pituitary apoplexy is a rare but serious complication of pituitary adenomas. It requires prompt diagnosis, confirmed by medical imaging. Hormone replacement therapy and tumor excision provide satisfactory results.

Keywords

Apoplexy, Pituitary Adenomas, Endoscopy

1. Introduction

Pituitary apoplexy is a rare condition caused by acute or sub-acute hemorrhage or infarction of the pituitary gland, often in the context of a pituitary adenoma [1].

Prevalence and incidence are difficult to estimate as many subacute cases present with subtle symptoms and remain undiagnosed. However, a prevalence of 62 cases per 1,000,000 inhabitants [2] and an incidence of 1.7 cases per 1,000,000 per year [3] have been reported.

Previous studies have shown that pituitary apoplexy occurs in 21% of patients with pituitary adenomas [1], with hemorrhagic infarction or subclinical or asymptomatic apoplexy being the most common. To date, 25% of all pituitary adenomas present with hemorrhagic and/or necrotic areas [4]. Pituitary apoplexy is a potentially life-threatening clinical syndrome, including sudden onset headache, oculomotor paralysis, visual disturbances, hormonal dysfunction, and altered state of consciousness [1] [2].

The main endocrinological consequence of this condition is anterior pituitary insufficiency in two-thirds of cases. This can be partial, affecting one or more lineages, or complete, leading to anterior pan-hypopituitarism, affecting all lineages. Involvement of the posterior pituitary is much less common [5]. Apoplexy generates a specific appearance on magnetic resonance imaging (MRI) of the pituitary gland, with hyperintense and hypointense zones in the sella turcica on T1 - T2 weighted images, respectively, suggesting apoplexy [1] [6].

Treatment of acute and severe forms of apoplexy may involve surgical intervention with decompression and replacement therapy with glucocorticoids. In contrast, conservative management may be applied to patients with milder apoplexy without visual or neurological disorders [1] [4] [5] [7] [8].

The aim of our work is to study the epidemiological, clinical, paraclinical, therapeutic and evolutionary characteristics of pituitary apoplexy on pituitary adenoma.

2. Patients and Method

This was a retrospective descriptive study that analysed 16 medical records of patients hospitalised for pituitary apoplexy out of a total of 160 cases of pituitary adenoma treated in the neurosurgery department of the Fann National University Hospital Centre over a 6-year period from January 1 2014 to December 31 2020.

We included all records of patients hospitalised and operated on for apoplexy of pituitary adenoma confirmed on the basis of clinical, paraclinical, intraoperative (haemorrhagic necrosis intraoperatively) and histological data.

The following data were collected: Epidemiological (age, sex, and circumstances of occurrence); Clinical: reasons for consultation, consultation time); Paraclinical (type of imaging, signs of haemorrhagic necrosis, relationship with the chiasma and cavernous sinus); Therapeutic (approach, associated treatment); Complications, quality of excision, visual and endocrine evolution.

The variables were analysed descriptively. Quantitative variables were described in terms of number of patients, number of missing values, mean, and extremes, and qualitative variables were described in terms of number of patients, number of missing values, mean, and extremes.

The data was entered using Word 2016 and the graphs and figures were analysed using Excel. The study was submitted to the Ethics Committee of the Fann National Teaching Hospital for approval, and confidentiality was maintained.

3. Results

Out of 160 pituitary adenoma cases, we collected 16 cases of pituitary apoplexy over 6 years, comprising 10%. The average age of patients was 42.5 years, ranging from 17 to 79 years. Males were most common, accounting for 80% of cases, with a male-to-female ratio of 4:1. All cases of apoplexy occurred in the context of pituitary adenoma. The average diagnostic time was 2.5 days, with 56.25% of patients diagnosed after more than 7 days.

Clinically, visual disturbances and intracranial hypertension were most common at 87.5% and 62.5%, respectively, followed by endocrine disorders at 37.5% and neurological signs at 31.3%. Radiologically, brain CT and MRI were performed in 62.5% of cases, while brain CT alone was performed in 37.5% of cases. Tumor diameter ranged from 10 mm to 60 mm, with an average of 26.42 mm. (Figure 1)

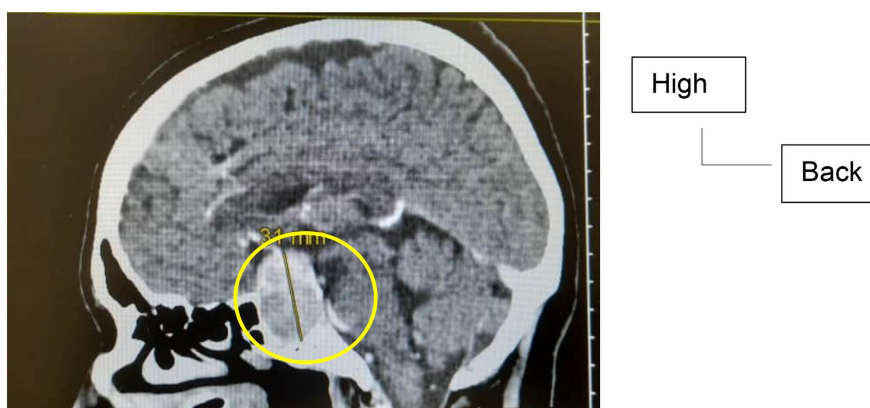


Figure 1. Brain CT showing areas of intra-tumor necrosis suggesting pituitary apoplexy on a pituitary macroadenoma (circled in yellow).

We note that 9 patients, or 56.25%, were operated on within 1 to 7 days, and 6 patients, or 37.5%, were operated on after 7 days. All our patients received analgesic-based treatments. Hormonal supplementation was introduced for all patients.

Distribution of cases according to surgical treatment

Fifteen patients, or 93.75%, benefited from surgical treatment. The transsphenoidal approach was used for all patients who underwent surgery. We recorded one case of incomplete excision, or 6.25%. In our series, out of 16 cases of PA operated on, complications included transient diabetes insipidus and nasal obstructions in 31.25% and 18.17% of cases, respectively.

Hyposmia, meningitis, CSF leak, and epistaxis each accounted for 6.25%, as shown in Table 1.

Table 1. Distribution of cases according to complications.

Complications	Numbers	Percentages
Transient diabetes insipidus	5	31.25%
Nasal obstruction	3	18.7%
Hyposmia	1	6.25%
Meningitis	1	6.25%
CSF leak	1	6.25%
Epistaxis	1	6.25%

Regular monitoring was conducted at the 3rd month, 6 months, and annually (remotely) for all patients. We note that 12 out of 16 cases, or 75%, underwent control imaging (CT or MRI of the brain), with 1 case of tumor residue, accounting for 6.25% in **Figure 2**.

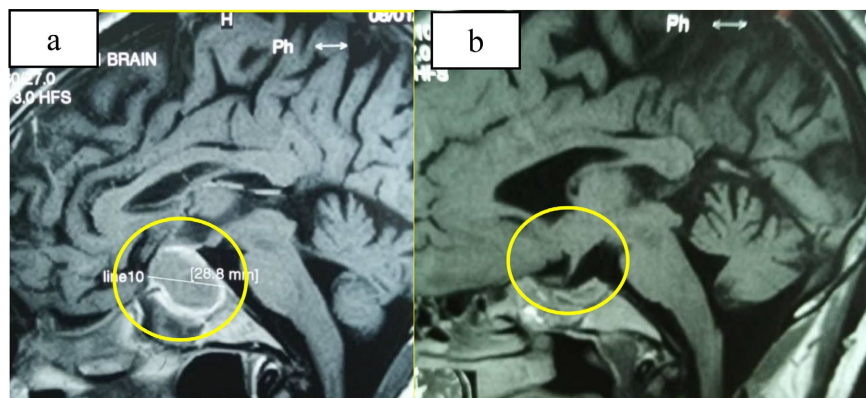


Figure 2. (a, b) Brain MRI: Sagittal T1 pre-operative MRI showing, intra-tumoral hyposignal suggesting a PA (2.a yellow circle), and sagittal T1 post-operative MRI showing complete excision (b: yellow circle).

In our series, we recorded 11 out of 16 cases of visual recovery, 6 out of 16 cases of hormonal remission, and 1 case of death, as reported in **Table 2**.

Table 2. Distribution of cases according to prognosis.

Prognosis	Numbers	Percentages
Visual recovery	11	68.75%
Hormonal remission	6	37.5%
Mortality	1	6.25%

4. Discussion

Over six years, from January 1, 2014, to December 31, 2020, we recorded 16 cases of pituitary apoplexy out of 160 cases of pituitary adenomas, equating to 10% or 2.5 cases per year. The incidence of pituitary apoplexy varies from 0.6% to 22%, depending on diagnostic criteria [9]. Soto-Ares *et al.* (2002) reported a frequency

of 10% to 15% of pituitary apoplexy in their series [10].

In our series, the average age of patients was 42.5 years, ranging from 17 to 79 years, which is comparable to data in the literature [11] [12]. We recorded 80% male cases compared to 20% female cases, with a male-to-female ratio of 4:1. It is often reported that pituitary apoplexy occurs more frequently in men than in women [7] [11] [13]. In our series, 2 patients, or 12.5%, were followed for pituitary adenoma, including one with a recurrence after surgery. These incidents often result in acute accidents with dramatic consequences for both visual and endocrine function. All cases of pituitary apoplexy in our series occurred in the context of pituitary adenomas. Pituitary apoplexy is more likely because these tumors can outgrow their blood supply, compressing the pituitary arteries and predisposing them to ischemia or hemorrhage [13]-[15]. A known history of pituitary adenoma facilitates the diagnosis of pituitary apoplexy.

Clinical/paraclinical data:

We recorded 10 cases of intracranial hypertension (62.5%), 14 cases of visual disturbances (87.5%), 6 cases of endocrinological disorders (37.5%), and 5 cases of neurological disorders (31.3%). The clinical manifestations of pituitary apoplexy vary, starting with intense, sudden headaches, most often retro-orbital or frontal, and sometimes diffuse, present in 62.5% of cases. Vision abnormalities occur in 87.5% of cases, including DVA in 43.75%, visual blurring and temporal hemianopia in 25% each, and bilateral blindness in 18.75%. This reduction in visual acuity and alteration of the visual field is due to tumor expansion compressing the chiasm and/or optic nerves. Deterioration can range from simple bitemporal hemianopia to total blindness [16].

In our series, disorders of consciousness were found in 25% of cases, with 18.75% having a Glasgow score between 14 and 11. One patient had a Glasgow score between 10 and 7, and 6.25% had an initial Glasgow score less than 7. According to the literature, they are present in 17% to 38% of cases, which corroborates our results [17] [18].

In other cases, it can lead to a deep coma after a few hours with a fatal outcome, as reported in our series.

A motor deficit of the limbs was found in 3 patients or 18.75% (2 cases or 12.5% with paresis and 1 case with plegia or 6.25%). In our series, damage to the three pairs of oculomotor nerves was observed in 5 patients or 31.3%, and damage to the VI in 6.25% of cases. The three pairs of oculomotor cranial nerves can be affected by compression or tumor invasion of the cavernous sinus. The third cranial pair is the most frequently affected [19] [20]. In our series, endocrine signs included amenorrhea/galactorrhea in 6 cases or 37.5% and android obesity in 3 cases or 18.75%. Acromegaly and erectile disorders each represented 1 case or 6.25%.

In our series, brain computed tomography (CT) was performed in 6 cases (37.5%), and the combination of brain CT and magnetic resonance imaging (MRI) in 10 cases (62.5%).

MRI allows for the determination of expansion and its relationship with surrounding structures. It detected hemorrhage in 9 out of 10 cases in the Onesti

series [21] and in all 3 cases in the Bills series [22]. It is generally accepted that MRI should be performed at least 12 hours after symptom onset to avoid false negatives, as hemorrhages may not be visible during the peracute phase [21] [23]. Currently, the diffusion sequence helps overcome this limitation [24].

CT scanning is less sensitive in detecting hemorrhage, showing signs in less than half of the cases [25] [26]. However, it is still used when MRI is contraindicated or when additional information is needed.

In our series, pituitary apoplexy occurred in the context of pituitary macroadenoma in 100% of cases, with a mean diameter of 26.42 mm (lesion diameters varied from 10 to 60 mm). Endocrine disorders are very common, with sudden anterior pituitary insufficiency. The medical emergency involves the administration of hydrocortisone, which is always necessary in the initial phase [10]. Manifestations of posterior pituitary insufficiency, such as diabetes insipidus, are rare (2% of cases) [27]. All our patients had an ophthalmological assessment. Visual acuity was affected in 9 out of 16 cases (56.25%): 6 patients had progressively reduced visual acuity (37.5%), and 3 patients presented with blindness (18.75%)—1 unilateral (6.25%) and 2 bilateral (12.5%). The fundus examination showed optic atrophy in 3 cases (18.75%)—2 bilateral (12.5%) and 1 unilateral (6.25%)—and papilledema in 5 cases (31.25%), including 1 unilateral (6.25%). The visual field was affected in 9 cases (56.25%): disrupted bilaterally in 5 cases (31.25%) and unilaterally in 2 cases (12.5%). This reduction in visual acuity and alteration of the visual field is due to the expansion of the tumor, causing compression of the chiasm and/or the optic nerves. Deterioration can range from simple bitemporal hemianopia to total blindness [16].

Therapeutic data/complications:

In our series, all patients benefited from treatment with analgesics and proton pump inhibitors. Hormonal supplementation was introduced in all patients: hydrocortisone in 100% of cases and levothyroxine in 11 out of 16 cases. Corticosteroid replacement therapy must be administered as soon as pituitary apoplexy is diagnosed to avoid acute adrenal insufficiency. Surgery is not always indicated. In pituitary apoplexy manifesting only as headaches or oculomotor disorders, surgical indications are similar to those for an uncomplicated adenoma. Surgery in the acute phase is often deemed unnecessary since spontaneous regression of oculomotor disorders is common [9] [11]. Close monitoring during the first days is necessary, as the clinical picture may worsen.

Treatment includes hormone replacement therapy, hydro-electrolyte resuscitation, and sometimes compensation for diabetes insipidus. In our series, we had a very serious case. According to Cardoso [9], surgical treatment does not seem to influence the mortality rate from pituitary apoplexy. In our study, almost all patients benefited from excision surgery via the trans-sphenoidal route under endoscopy in 15 cases, or 93.75%. Among them, 9 patients, or 56.25%, were operated on within 1 - 7 days, and 6 patients, or 37.5%, were operated on after 7 days.

The preferred approach is the transsphenoidal route. Craniotomy is reserved

[21] [22] for cases where this approach is insufficient, such as “hourglass” shapes, tumors with irregular extensions, or large associated intracerebral hematomas. Visual disturbances most often prompt surgery in cases of pituitary apoplexy. The authors are nearly unanimous on the need to operate on patients with visual disorders [21] [22] [28].

The main series finds improvement rates between 80% and 100% for both visual acuity and the visual field. It is performed urgently when there is severe chiasmatic pain, disturbances of consciousness due to the lesion’s volume, or clinical deterioration despite medical treatment. Factors limiting the possibility of complete excision via the transsphenoidal route include the invasion of the cavernous compartments, tumor consistency, the vertical extension of the tumor, and complex suprasellar extensions. We recorded 1 case of incomplete excision, or 6.25%.

In our series, 50% of patients experienced complications. Diabetes insipidus occurred in 5 cases (31.25%), nasal obstructions in 3 cases (18.75%), followed by hyposmia, epistaxis, meningitis, and CSF leak in 1 case each (6.25%). Gaillard *et al.*, in their series [12], found 12% transient diabetes insipidus and 1.45% prolonged diabetes insipidus; 21% experienced CSF leaks intraoperatively versus 3.5% postoperatively. Dehdashti [13] found 2.5% transient diabetes insipidus and 1% prolonged diabetes insipidus; 4.15% CSF leak intraoperatively versus 0.83% postoperatively. Konan *et al.* [29] reported 12.5% transient diabetes insipidus and 3.6% prolonged diabetes insipidus; 19.6% postoperative CSF leak and 3.6% meningitis. Thus, our data are close to those reported in the literature.

Monitoring/prognosis:

In our study, regular follow-ups were conducted at the 3rd month, 6th month, and annually. We were primarily interested in visual and hormonal recovery and mortality. In 12 out of 16 cases, or 75%, control imaging (CT or brain MRI) was performed, with 1 case of tumor residue, or 6.25%.

Early decompression promotes the resumption of pituitary function. Simple headaches associated with oculomotor disorders do not necessarily require surgical treatment; these disorders often regress spontaneously [28] [30]. The authors largely agree on the need to operate on patients with visual disorders [1] [9] [21] [31]. Major studies report improvement rates between 80% and 100% for both visual acuity and visual field.

In our series, we found that preoperative blindness significantly reduces the chances of recovery. Furthermore, the visual prognosis was better in patients operated on within the first 7 days following apoplexy. However, a late diagnosis should not lead to delaying surgery.

We recorded one death and one loss to follow-up in our series, each accounting for 6.25%. Bonicki [32] also reported two deaths due to extensive pituitary apoplexy, with large extra-sellar extension causing significant cerebral edema and severe hypothalamic insufficiency. Several other cases of pituitary apoplexy with fatal outcomes have been reported in the literature [33]. In extremely serious cases, intensive resuscitation is required.

5. Conclusion

We studied 16 cases of patients with pituitary apoplexy in the context of pituitary adenomas who underwent medical-surgical treatment. It is recognized as a rare but serious complication of pituitary adenomas. The clinical signs observed are neurological, endocrine, and ophthalmological. This condition is a diagnostic and therapeutic emergency. Brain imaging confirms the diagnosis, and the combination of hormone replacement therapy and trans-sphenoidal tumor excision yielded encouraging results, with a favorable outcome and visual recovery.

Author's Contributions

All authors contributed to the study conception and design, and all authors read and approved the final manuscript.

Ethics approval

The study was approved by the institutional review board of the National Teaching Hospital Fann of Dakar. The patients provided informed consent for the inclusion of their clinical data in this study.

Data Availability

The authors confirm that the data supporting the findings of this study are available within the article and the rest of the data is available on request from the authors.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

- PA:** pituitary apoplexy
DVA: Decreased visual acuity
CT: Computed tomography scan
MRI: Magnetic resonance imaging