

## Pituitary Adenoma Apoplexy: Review of Personal Series

### Abstract

**Background:** Pituitary apoplexy is a life-threatening event with unspecific clinical background and no standardized treatment. **Materials and Methods:** The authors retrospectively analyzed seventeen patients affected by pituitary adenoma apoplexy and treated in a 10-year period. Thirteen patients underwent surgery through transsphenoidal route while four patients have been treated conservatively. **Results:** The endoscopic surgical procedure showed a better result in term of complete removal of the tumor while in the “conservative” group less frequent evidence of hormones’ deficiency has been registered. Once a residual lesions was observed a strict radiological follow-up is mandatory. **Conclusions:** According to dedicated literature and pre- and post-operative evidence of personal series, the authors try to provide an algorithm that could help in the standardization of the diagnostic and therapeutic pathways in patients with pituitary adenoma apoplexy.

**Keywords:** Pituitary adenoma, pituitary apoplexy, pituitary gland, transsphenoidal surgery

### Introduction

Pituitary adenoma apoplexy is a serious event caused by the abrupt expansion of an ischemic and/or hemorrhagic macroadenoma.<sup>[1]</sup> It represents a medical emergency with the possible surgical indication.

It is a rare event that occurs in 0.6 up to 10% of pituitary adenomas with 0.2–0.6 events per 100 person-year in a patient with nonfunctioning adenomas.<sup>[2,3]</sup> It presents a slight prevalence in male.<sup>[1]</sup> In 70% of patients with pituitary apoplexy the adenoma, frequently represented by nonfunctioning macroadenomas or prolactinomas, was previously undiagnosed.<sup>[4]</sup> Rarely an apoplectic event within the sellar region could also happen in patients with hypophysitis or other sellar mass such as craniopharyngioma, Rathke’s cleft cyst and metastasis.<sup>[5,6]</sup> There are no certified predisposing factors but nowadays could be hypothesized a relation between apoplexy and situations that could change vascular supply to the sellar region such as previous surgery (cardiac or laparoscopic surgery), radiotherapy, spinal anesthesia, hypertension, and physical activity. Anticoagulant therapy, liver failure, dopaminergic treatment, dynamic hypophyseal testing with releasing

hormones, pituitary radiation therapy, pregnancy, and head trauma could facilitate hemorrhagic pituitary events.<sup>[7-14]</sup>

Patients with pituitary apoplexy could present sudden or subacute onset of a headache, vomiting, progressive decrease of consciousness with the association of symptoms due to pituitary hormones deficiencies or to the II, III, IV, or VI cranial nerves involvement.<sup>[1,15]</sup>

A computed tomography (CT) scan and above all a magnetic resonance imaging (MRI) of the brain are mandatory to diagnose a pituitary apoplexy [Figure 1]. Laboratoristically, a pituitary hormones’ deficiency happened in about 80% of the patients with frequent adrenocorticotrophin (ACTH) and gonadotropin involvement.<sup>[16,17]</sup>

Conservative treatment is usually represented by an immediate fluid, electrolytes, and steroids replacement (especially in case of ACTH deficiency). In patients with worsening neurological symptoms or with intracranial hypertension emergency surgery is needed. However, it is currently unclear if, in the acute phase, conservative, or surgical management carries the best outcome so the decision to conservatively or surgically manage this patients should be usually performed by a multidisciplinary team.<sup>[16]</sup> With these paper, we would like,

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supported by the dedicated literature, to report our personal experience in pituitary apoplexy treatment and to suggest a therapeutic algorithm that could be useful in these patients' management.

## Materials and Methods

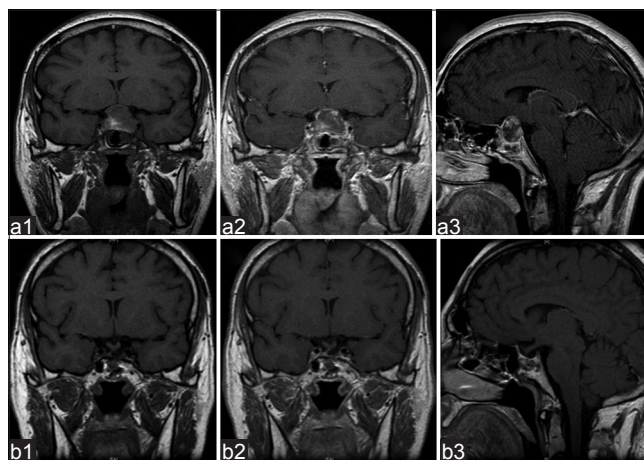
From January 2000 to December 2010, 357 patients with pituitary adenoma were managed by the pituitary team at Neurosurgical Department of Umberto I General Hospital in Ancona. In this group, 17 patients (12 males and 5 females) were admitted to the emergency department due to a pituitary adenoma apoplexy.

We focused our attention on this group, preoperatively evaluating age, sex, risk factors, and symptoms as shown in Table 1.

Patients with pituitary apoplexy were then divided into two groups according to a conservative or surgical treatment performed.

The outcome (mean follow-up of 9.5 years) was evaluated from a clinical and radiological point of view. Clinically authors focused the attention on recovery time from the surgical procedure and need of a substitutive hormones

therapy. Besides, a radiological follow-up, using an MRI performed at least 3 months after surgery, was performed to discover the possible presence of a residual. Data



**Figure 1:** A 70-year-old man with a headache and vomiting and preoperative magnetic resonance imaging evidence (a1-a3) of pituitary apoplexy within a pituitary macroadenoma. He was submitted to an endoscopic assisted adenoma removal through a transphenoidal approach performed within 48 h from the onset of symptoms. The patient experienced a clinical improvement in 1 week and a magnetic resonance imaging performed 3 months after surgery (b1-b3) show complete removal of the tumor

**Table 1: Patients admitted to Neurosurgical Department of Ancona between 2000 and 2010 for pituitary apoplexy**

Number	Age	Sex	Risk factors	Clinical pictures	Treatment	Clinical results	Residual	Hormonal therapy
1	53	Male	No	Ophthalmoplegia (left III cranial nerve)	Surgery (micro)	Resolved after 3 months	No	Yes
2	38	Female	No	Headache and rigor nuchalis	Conservative	Resolved after 1 week	No	No
3	72	Male	Hypertension	Ophthalmoplegia (right III cranial nerve)	Conservative	Resolved after 1 week	<1 cm	No
4	42	Male	No	Ophthalmoplegia (left III cranial nerve)	Surgery (micro)	Resolved after 3 months	No	No
5	45	Male	Radiotop on residual	Headache and vomiting	Conservative	Resolved after 1 week	<1 cm	Yes
6	65	Male	No	Visual acuity deficit	Surgery (micro)	Resolved after 1 week	No	Yes
7	56	Male	No	Ophthalmoplegia (left III and VI cranial nerve)	Surgery (micro)	Resolved after 6 months (VI)	<1 cm	No
8	62	Male	No	Visual acuity deficit	Surgery (micro)	Resolved after 2 weeks	<1 cm	Yes
9	58	Female	No	Ophthalmoplegia (left III cranial nerve)	Surgery (endo)	Resolved after 1 month	No	No
10	70	Male	No	Headache and vomiting	Surgery (endo)	Resolved after 1 week	No	No
11	67	Female	No	Ophthalmoplegia (right III cranial nerve)	Surgery (endo)	Resolved after 1 month	No	No
12	59	Male	No	Headache, vomiting and visual acuity deficit	Surgery (endo)	Resolved after 1 week	No	Yes
13	71	Male	No	Ophthalmoplegia (right III cranial nerve) and visual acuity deficit	Surgery (endo)	Resolved after 2 months	No	No
14	38	Female	No	Headache and vomiting	Conservative	Resolved after 1 week	<1 cm	No
15	73	Female	Hypertension	Ophthalmoplegia (left III and VI cranial nerve)	Surgery (endo)	Resolved after 6 months (VI)	No	No
16	58	Male	No	Ophthalmoplegia (left III and VI cranial nerve)	Surgery (endo)	Resolved after 6 months (VI)	No	No
17	72	Male	Hypertension	Bilateral ophthalmoplegia	Surgery (endo)	Resolved after 6 months (VI)	<1 cm	Yes

obtained from these evaluations were used to compare all these parameters in the two groups.

Consent to data publication of each patient enrolled in the study was obtained.

## Results

In our series, a male prevalence was observed (M:F 12/5) with a mean age of 58.8 years. In four patients (23.4%) risk factors for apoplexy, represented by hypertension (three patients) and previous radiation therapy, have been observed. No other predisposing factor has been documented.

Sixteen pituitary apoplexy patients out of 17 had an undiagnosed pituitary adenoma. In the patient where a pituitary adenoma was already known apoplexy happened after the radiotherapy performed on a residual with sudden onset of a headache and vomiting.

Clinically, a preoperative ocular motility defect was present in ten cases (58.8%) due to a III cranial nerve palsy (six patients) or to a combined III and VI cranial nerve palsy (four patients). A headache and vomiting were observed in five patients.

Once the apoplexy diagnosis was performed, thirteen patients out of seventeen (76.5%) underwent surgical macroadenoma removal through a transnasal transsphenoidal approach, performed with a microscopic technique in five patients and with an endoscopic one in the others. In the conservative group, three patients out of four had prolactinomas.

All patients of the surgical group that showed deteriorated visual acuity and visual field defect at presentation experienced a complete recovery within 3 months. The oculomotor palsy usually needs 3 months for a complete restoration while a sixth cranial nerve palsy usually improved after 6 months.

No patients of the conservative group had diabetes insipidus while only one needed substitutive hormone therapy instead of five patients in the surgical group (three patients submitted to a microscopic approach and two to and endoscopic one) with one of them affected by diabetes insipidus needing a desmopressin (DDAVP) treatment [Figure 2].

In our series, no patient died and no surgical complication had been documented. Only one patient with cavernous sinus infiltration at diagnosis, after an adenoma removal through a microscopic approach, needed subsequent radiation therapy for MRI residual evidence. Patients who had been treated with endoscopic-assisted technique at MRI follow-up showed a complete removal of macroadenoma even with cavernous sinus infiltration in all but one cases.

## Discussion

Pituitary apoplexy usually represents a life-threatening emergency. The first case was described at the end of 19<sup>th</sup> century by Bailey but the definition “pituitary apoplexy” was created only in 1950 by Brougham, Heusner, and Adams.<sup>[18]</sup>

Its symptoms could mimic other frequent neurological pathologies such as subarachnoid hemorrhage, bacterial meningitis or stroke eventually leading to a delayed or even a missed diagnosis. Although the apoplexy etiology has not yet been clarify, nowadays, the most likely cause seems to be a transient blood flow modification to the adenoma due to a vascular occlusion caused by the tumor growth with a subsequent increasing risk of hemorrhage due to an abnormal vascularization. A sudden and prolonged superior hypophyseal artery compression can, on the other hand, justify the ischemia eventually followed by reperfusion damages.

Once suspected, an MRI of the brain is mandatory to gain a correct diagnosis of pituitary apoplexy. CT scan is diagnostic in 21%–28% of cases while an MRI represents the gold standard confirming the diagnosis in over 90% of affected people.<sup>[19-21]</sup> Sometimes, an angio-MRI could be useful to distinguish vascular malformations from a pituitary lesion.<sup>[22]</sup> It is also important to underline that before the hemorrhagic event a pituitary adenoma was an undiagnosed lesion in more than 50% of these patients.<sup>[19,23]</sup> It demonstrates how bigger dimensions of the adenoma that are frequently associated subsequent symptoms are not a risk factor for apoplexy that could frequently happen even in very small and asymptomatic tumors. In these situations, in fact, probably the typical characteristic vascular modifications that could provoke apoplexy anticipate the compression on neighboring neurovascular structures or on

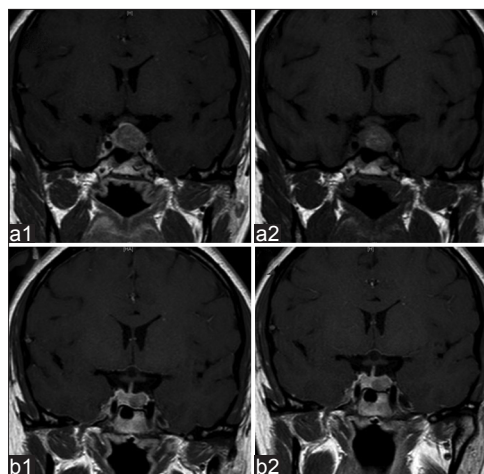


Figure 2: Pre- (a1 and a2) and post-operative magnetic resonance imaging (b1 and b2) performed in a 38-year-old female submitted to a conservative treatment due to a pituitary apoplexy

the normal gland that often caused the typical symptoms of an adenoma.

Nowadays, the dedicated literature does not allow to obtain official guidelines about treatment of this problem. In fact, it is usually impossible to perform control case studies or randomized trial. At the same time, general agreement was founded about the importance of an immediate fluid and steroids administration to gain a hemodynamic stability and to reduce the effects of hormone deficiencies. In the past, many studies were performed aiming at treatment standardization in patients with pituitary apoplexy.

In our series, all patients of the surgical group were submitted to the procedure within 72 h from the clinical onset [Figure 3]. The neurological signs and symptoms (i.e., ocular palsy and visual field defect) improved 3 months after surgery although abducens nerve palsy usually need more time to recover. All cases presented a complete resolution of clinical findings after the 6<sup>th</sup> month. In the conservative group, usually preoperative symptoms demonstrated an improvement after only 1 week. This difference is not statistically significant in this study, but probably, in our opinion, it could be confirmed in larger series. In fact, patients with pituitary adenoma submitted

to a surgical treatment usually have bigger tumors with subsequent relevant compression and palsy of the neurovascular structures that obviously need longer time to recover instead of what happened in people submitted to conservative treatment. This difference could be further supported considering the possible morbidity of a surgical procedure compared to pharmacological treatment.

Pituitary apoplexy in a patient with a conservative treated macroadenoma was particularly frequent in a patient with prolactinomas. Many important reports, in fact, underlined that medical therapy of prolactinomas could be associated with an increased risk of apoplexy.

Emergency surgery should be reserved for patients with progressive deterioration of consciousness, hypothalamic involvement, and progressive visual worsening. In this case, it is demonstrated that a significant postoperative clinical improvement is a consequence of a surgical procedure performed as soon possible, preventing permanent neurological consequences.

Decompressive surgery can be delayed but performed within the 1<sup>st</sup> week when visual acuity defect appear stable. If ophthalmoplegia is improving or stable, conservative strategy could be considered. It could be reasonable to repeat an MRI within 10 days to evaluate therapeutic choice in case of residual lesion.

According to literature, more than half of affected patients require substitutive hormone therapy with no significant difference between surgical and medical group. Our series showed the need of substitutive hormonal therapy in 25% of conservative treated patients and 34.8% of the surgical ones.

Analyzing endoscopic assisted patients, we found a better outcome on postapoplexy events in term of hormone deficiency (20% treated with substitutive therapy) and presence of residual lesion comparing with people submitted to a microscopic technique. This series is

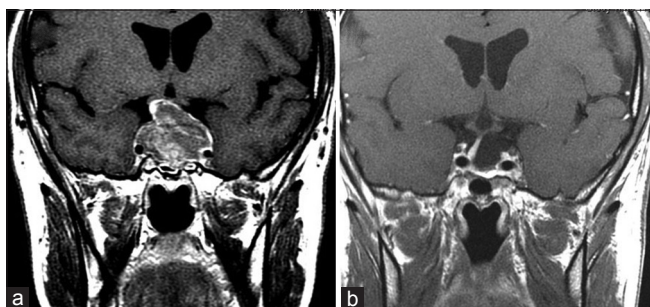


Figure 3: A 53-year-old man with preoperative radiological evidence (a) of large pituitary macroadenoma with apoplexy and clinical presence of ophthalmoplegia due to left III cranial nerve involvement. He was submitted to an early microsurgical procedure of adenoma asportation with postoperative evidence of complete tumor removal (b)

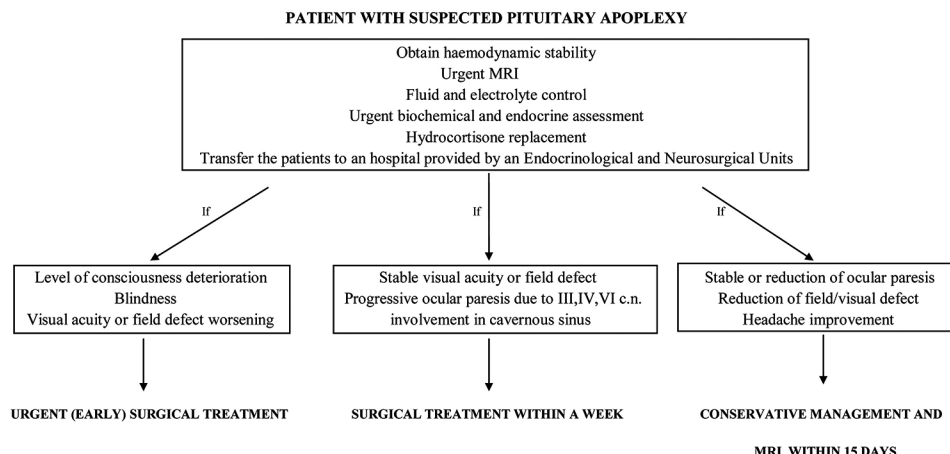


Figure 4: An algorithm for the management of pituitary apoplexy

small, and these results are not significant, but probably it could be confirmed in larger studies considering the better accuracy and clarification of the surgical field granted by the endoscope. In fact, it could allow a most accurate preservation of the normal gland and instead of the operating microscope, better visualization of hidden corners of the surgical fields where sometimes adenoma remnants could be discovered.

According to with dedicated literature and our personal series evidence, we suggest a strategic algorithm that, in our opinion, could be useful in pituitary apoplexy treatment, as shown in Figure 4.

## Conclusions

With this paper we report our experience in the pituitary adenoma apoplexy management and, reviewing the dedicated literature, we provide an algorithm that could standardized diagnostic and therapeutic pathways in this life-threatening pathology.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

- Dubuisson AS, Beckers A, Stevenaert A. Classical pituitary tumour apoplexy: Clinical features, management and outcomes in a series of 24 patients. *Clin Neurol Neurosurg* 2007;109:63-70.
- Fernández-Balsells MM, Murad MH, Barwise A, Gallegos-Orozco JF, Paul A, Lane MA, *et al.* Natural history of nonfunctioning pituitary adenomas and incidentalomas: A systematic review and metaanalysis. *J Clin Endocrinol Metab* 2011;96:905-12.
- Sivakumar W, Chamoun R, Nguyen V, Couldwell WT. Incidental pituitary adenomas. *Neurosurg Focus* 2011;31:E18.
- Randall BR, Couldwell WT. Apoplexy in pituitary microadenomas. *Acta Neurochir (Wien)* 2010;152:1737-40.
- Chhiber SS, Bhat AR, Khan SH, Wani MA, Ramzan AU, Kirmani AR, *et al.* Apoplexy in sellar metastasis: A case report and review of literature. *Turk Neurosurg* 2011;21:230-4.
- Husain Q, Zouzias A, Kanumuri VV, Eloy JA, Liu JK. Idiopathic granulomatous hypophysitis presenting as pituitary apoplexy. *J Clin Neurosci* 2014;21:510-2.
- Bhattacharyya A, Tymms DJ, Naqvi N. Asymptomatic pituitary apoplexy after aortocoronary bypass surgery. *Int J Clin Pract* 1999;53:394-5.
- Bonicki W, Kasperlik-Zaluska A, Koszewski W, Zgliczynski W, Wislawski J. Pituitary apoplexy: Endocrine, surgical and oncological emergency. Incidence, clinical course and treatment with reference to 799 cases of pituitary adenomas. *Acta Neurochir (Wien)* 1993;120:118-22.
- Chen Z, Murray AW, Quinlan JJ. Pituitary apoplexy presenting as unilateral third cranial nerve palsy after coronary artery bypass surgery. *Anesth Analg* 2004;98:46-8.
- da Motta LA, de Mello PA, de Lacerda CM, Neto AP, da Motta LD, Filho MF. Pituitary apoplexy. Clinical course, endocrine evaluations and treatment analysis. *J Neurosurg Sci* 1999;43:25-36.
- Dökmetsas HS, Selçuklu A, Colak R, Unlühizarci K, Bayram F, Kelestimur F. Pituitary apoplexy probably due to TRH and GnRH stimulation tests in a patient with acromegaly. *J Endocrinol Invest* 1999;22:698-700.
- Hiroi N, Ichijo T, Shimojo M, Ueshiba H, Tsuboi K, Miyachi Y. Pituitary apoplexy caused by luteinizing hormone-releasing hormone in prolactin-producing adenoma. *Intern Med* 2001;40:747-50.
- Lee DH, Chung MY, Chung DJ, Kim JM, Lee TH, Nam JH, *et al.* Apoplexy of pituitary macroadenoma after combined test of anterior pituitary function. *Endocr J* 2000;47:329-33.
- Uchiyama H, Nishizawa S, Satoh A, Yokoyama T, Uemura K. Post-traumatic pituitary apoplexy – Two case reports. *Neurol Med Chir (Tokyo)* 1999;39:36-9.
- Bi WL, Dunn IF, Laws ER Jr. Pituitary apoplexy. *Endocrine* 2015;48:69-75.
- Glezer A, Bronstein MD. Pituitary apoplexy: Pathophysiology, diagnosis and management. *Arch Endocrinol Metab* 2015;59:259-64.
- Briet C, Salenave S, Chanson P. Pituitary apoplexy. *Endocrinol Metab Clin North Am* 2015;44:199-209.
- Rolih CA, Ober KP. Pituitary apoplexy. *Endocrinol Metab Clin North Am* 1993;22:291-302.
- Ayuk J, McGregor EJ, Mitchell RD, Gittoes NJ. Acute management of pituitary apoplexy – Surgery or conservative management? *Clin Endocrinol (Oxf)* 2004;61:747-52.
- Sibal L, Ball SG, Connolly V, James RA, Kane P, Kelly WF, *et al.* Pituitary apoplexy: A review of clinical presentation, management and outcome in 45 cases. *Pituitary* 2004;7:157-63.
- Bills DC, Meyer FB, Laws ER Jr., Davis DH, Ebersold MJ, Scheithauer BW, *et al.* A retrospective analysis of pituitary apoplexy. *Neurosurgery* 1993;33:602-8.
- Rajasekaran S, Vanderpump M, Baldeweg S, Drake W, Reddy N, Lanyon M, *et al.* UK guidelines for the management of pituitary apoplexy. Pituitary apoplexy guidelines development group: May 2010. *Clin Endocrinol* 2011;74:9-20.
- Semple PL, Jane JA Jr., Laws ER Jr. Clinical relevance of precipitating factors in pituitary apoplexy. *Neurosurgery* 2007;61:956-61.