# Two rare cases of pituitary apoplexy in adult females: a tricky diagnosis

Umberto Tupputi<sup>1</sup>, Valentina Testini<sup>2,3</sup>, Maria Grazia Rita Manco<sup>3</sup>, Maria Teresa Paparella<sup>3</sup>, Roberto Bellitti<sup>2</sup>, Giuseppe Guglielmi<sup>2,3.4</sup>

<sup>1</sup>Radiology Unit, "Bonomo" Hospital, Andria, Italy; <sup>2</sup>Radiology Unit, "Dimiccoli" Hospital, Barletta, Italy; <sup>3</sup>Department of Clinical and Experimental Medicine, Foggia University School of Medicine, Foggia, Italy; <sup>4</sup>Radiology Unit, Hospital "Casa Sollievo Della Sofferenza", San Giovanni Rotondo, Foggia, Italy

**Abstract.** We reported two cases of women who suffered from a rare case of pituitary apoplexy, rare and potentially fatal clinical condition due to a hemorrhagic infarction of the pituitary gland due to a pre-existing macroadenoma. The onset of symptoms is often insidious and includes generic symptoms such as headache, vomiting, and visual disturbances. In this case report we discuss the typical computed tomography and magnetic resonance imaging features of this rare clinical condition in order to help radiologists in the timely diagnosis for a more rapid and correct diagnostic framing. (www.actabiomedica.it)

Key words: Pituitary apoplexy, pituitary macroadenoma, neuroradiology, computed tomography, magnetic resonance imaging

### Introduction

Pituitary apoplexy (PA) was first described by Pearce Bailey in 1898 (1) and recognised as a defined clinical syndrome by Brougham et al. in 1950 (2).

It is a rare and potentially fatal clinical condition, characterized by the onset of a rapid and ingravescent symptomatology that varies from non-specific symptoms such as headache and vomiting to more specific symptoms of nervous system involvement such as diplopia, panipopituitarism and an alteration of the mental state (2-5).

This clinical condition is mainly caused by hemorrhagic infarction of the pituitary gland on a pre-existing macroadenoma, most often unrecognized and discovered in such circumstance as in this case (6-8).

#### Case presentation

The first case was a 41-year-old female patient admitted to our emergency department due to severe

headache, diplopia, nausea and vomiting, with vital signs in a normal range.

No significant changes were found in the lab tests. After that, the patient underwent a non-contrast head computed tomography (CT).

CT showed the presence of an expansive oval formation in the sellar and suprasellar region, with unevenly hypodense densitometry with a hyperdense contextual material that was levelled in the declive. After administration of contrast agent, an enhancement of the margin of the lesion was observed (Figure 1).

The subsequent magneticd resonance imaging (MRI) examination confirmed the presence of the known sellar and suprasellar formation with a predominantly cystic signal, hyper-intense in T2-weighted and hypointense in T1-weighted scans, with haemorrhagic areas in the declive area that showed hyperintense signal in the T1-weighted scans. After contrast agent administration, a characteristic peripheral ring enhancement was observed. Cavernous sinus infiltration



**Figure 1.** Axial (A), Coronal (B) and sagittal (C) non-contrast brain computed tomography (CT) show the presence of an expansive oval formation in the sellar and suprasellar region with unevenly hypodense densitometry with a hyperdense contextual material that was levelled in the declive. Axial (D), Coronal (E) and Sagittal (F) contrast brain CT that show the enhancement of the margin of the lesion in the sellar and suprasellar region.

and optical chiasma compression were also demonstrated (Figure 2).

After careful evaluation of the clinicalradiological findings in neurosurgery, the patient was subjected to removal of the known sellar lesion with a trans-sphenoidal endoscopic approach.

The subsequent histological examination of the excised mass confirmed the diagnostic hypothesis of apoplectic pituitary adenoma.

The second was the case of a 62-year-old woman who came to the emergency department for acute headache and visual impairment. Brain CT scan in basal conditions showed an intrasellar mass with areas of intralesional hyperdensity from a recent hemorrhagic focus. The administration of contrast agent showed peripheral contrast enhancement. (Figure 3) These findings were suggestive of pituary apoplexy. For diagnostic confirmation, the patient underwent a brain MRI after a few hours, which documented a hyperintense intrasellar lesion in the T1-weighted scans and T2-weighted scans sequences (Figure 4) and with peripheral post-contrast enhancement, findings that may be referred to a subacute hemorrhagic focus into a pituitary adenoma.

The patient underwent surgery, with a trans-sphenoidal resection of the lesion.

## Discussion

Pituitary apoplexy (PA) is a rare event that occurs in 1.6-2.8 % of patients with macroadenomas; it is more frequent in males, with a gender ratio of 2:1 and

3



**Figure 2.** Axial Magnetic Resonance FLAIR imaging (A), Coronal T2-weighed imaging TSE (B) and Sagittal T1-weighed imaging SE (C) confirm the presence of the known sellar and suprasellar formation with a predominantly cystic signal. After contrast administration, axial (D), Coronal (E) and Sagittal T1-weighed imaging (F) show the characteristic peripheral ring enhancement of the sellar and suprasellar formation.

an average age of onset of 57 years (5, 9-11). About 60% of patients with PA are unaware of having a pituitary adenoma prior to the acute event (12).

Pituitary apoplexy is manifested by a wide spectrum of clinical manifestations: the most common symptom is headache, often described as sudden, high-intensity and reported in the retro-orbital position (2-5, 13-15). The second most frequent symptom is visus deficiency, which varies from 50 to 82% of cases, followed by nausea, vomiting, ocular paralysis and meningism (12).

Most of the patients with symptoms related to PA will undergo computed tomography in an emergency setting. CT is useful to diagnose bland and hemorrhagic infarction within pituitary adenomas. Numerous other pathologies may mimic the CT radiological findings of PA; most common hyperdense lesions in the pituitary region are anuerisms, meningiomas, germinomas, lymphomas, Craniopharingioma and Rathke cleft cysts.

Therefore, although CT can exclude other diseases (i.e. subarachnoid haemorrhage), magnetic resonance imaging can give more details about a suspected PA. Contrast administration may show a rim of enhancement that can be suggestive but not diagnostic of pituitary apoplexy. CT doesn't differentiate cystic or degenerative changes from previous hemorrhage (16).

MRI is the most important tool in the diagnosis of PA, being able to identify the presence of an adenoma and its haemorrhagic degeneration (12). Semple



**Figure 3.** Axial (A) and coronal (B) non-contrast brain computed tomography (CT) show a hyperdense mass at the pituitary gland Axial (C) and coronal (D) CT after contrast administration show a rim of enhancement around the mass



**Figure 4.** Magnetic Resonance imaging (MRI) T1-weighed imaging sequences (A) show an hyperintense sellar lesion, typical of subacute phase On MR T2-weighed imaging GRE sequences (B), the lesion appears hyperintese, with fluid-fluid level suggestive with acute hemorrhage. MRI T1-weighed sequences after gadolinium administration (C) show a rim of contrast enhancement around the mass.

et al. demonstrated that MRI features of PA correlate with the pathologic reports and operative findings and that PA features can be accurately predicted from MR imaging (17).

MRI predominantly showed an intra- and suprasellar expanding mass with different signal intensities on T1-weighted images and T2-weighted images, depending on the presence of hemorrhage and on its stage.

In the acute phase (within the first week), the lesion appears isointense on T1 and hypointense on T2 sequences. The surronding dura may show reactive thickening and enhancement. In this phase, PA show high signal on diffusion weighted imaging with the corresponding low signal on apparent diffusion coefficient (ADC) maps corresponding to area of infract (18).

Subacute phase (7–21 days) will show a hyperintense lesion on T1 and on T2 because methemoglobin shortens the T1 relaxation time (19).

In the chronic phase (>21 days) macrophages digest the clot and hypointensityon both T1 and T2 will appear because of the presence of hemosiderin and ferritin (20).

After intra-venous gadolinium administration, a slight and inhomogeneous contrast enhancement is evident but often is difficult to differentiate from normal residual pituitary gland.

MRI is a crucial tool in differential diagnosis of pituitary apoplexy.

The first condition to be excluded is the aneurysm from the carotid siphon or from the anterior communicating artery that appear as round, hypointense lesions in T2-weighted images due to the flow void. In case of partial thrombosis, hyperintense signal on T1-weighted images may occur, therefore a study with MRI angiography allows to exclude this pathology (21).

Craniopharingioma is usually an intra-suprasellar lesion with variable solid, cystic and calcified components that can help to obtain the correct diagnosis.

Rathke cleft cysts (RCCs) occur with T1 hyperintensity due to variable protein content. The RCC, which can be intra- or suprasellar, is usually located along the midline and does not have a fluid debris level (22). Finally, other conditions that can simulate pituitary apoplexy are lipoma and dermoid cysts that can be easily discriminated by fat suppression imaging and for the different clinical syndrome compared to PA.

Once the diagnosis is made, pituitary apoplexy needs to be treated rapidly.

What is the best approach to the patient with PA is still widely debated.

The first intervention is generally conservative, consisting of hemodynamic stabilization, correction of electrolyte disturbances and corticosteroid administration (23). If conservative management is chosen, it is imperative that the patient be kept under close clinical monitoring to observe for clinical deterioration (24).

Surgical treatment consists of trans-sphenoidal resection of the lesion after stabilization of the general condition of the patient (25). It is necessary when local pressure on the hypothalamus is present that requires urgent surgical decompression to prevent permanent visual loss and possible death.

## Conclusion

Pituitary apoplexy is an endocrinal emergency, which requires immediate investigation and treatment. PA imaging is essential in diagnosis, therapeutic management and prognosis.

The radiologist must know the imaging characteristics of this disease and rule out other clinical mimics.

Abbreviations: FLAIR: Fluid Attenuated Inversion Recovery; TSE: Turbo Spin Echo; SE: Spin Echo; GRE: Gradient Echo

Ethics Approval and Consent to Participate: Written consent was obtained from the patient to publish the case report.

**Consent for Publication:** Written consent for publication was obtained from the patient.

**Consent Form for Case Reports:** Written informed consent was obtained from the patients concerned.

**Conflict of Interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

#### References

- 1. Bailey P. Pathological report of a case of acromegaly, with special reference to the lesions in the hypophysis cerebri and in the thyroid gland; and a case of haemorrhage into the pituitary. Philadelphia Med J 1898;1:789-792.
- Brougham M, Heusner AP, Adams RD. Acute degenerative changes in adenomas of the pituitary body: with special reference to pituitary apoplexy. J Neurosurg 1950;7:421-439.
- Wakai S, Fukushima T, Teramoto A, Sano K. Pituitary apoplexy: its incidence and clinical significance. J Neurosurg. 1981;55(2):187-193.
- 4. Cardoso ER, Peterson EW. Pituitary apoplexy: a review. Neurosurgery. 1984;14(3):363-373.
- 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(1):63-70.
- Ebersold MJ, Laws ER Jr, Scheithauer BW, Randall RV. Pituitary apoplexy treated by transsphenoidal surgery. A clinicopathological and immunocytochemical study. J Neurosurg. 1983;58(3):315-320.
- 7. Mohr G, Hardy J. Hemorrhage, necrosis, and apoplexy in pituitary adenomas. Surg Neurol. 1982;18(3):181-189.
- 8. Rovit RL, Fein JM. Pituitary apoplexy: a review and reappraisal. J Neurosurg. 1972;37(3):280-288.
- Bills DC, Meyer FB, Laws ER Jr, et al. A retrospective analysis of pituitary apoplexy. Neurosurgery. 1993;33(4):602-609.
- Fraioli B, Esposito V, Palma L, Cantore G. Hemorrhagic pituitary adenomas: clinicopathological features and surgical treatment. Neurosurgery. 1990;27(5):741-748.
- Onesti ST, Wisniewski T, Post KD. Clinical versus subclinical pituitary apoplexy: presentation, surgical management, and outcome in 21 patients. Neurosurgery. 1990;26(6):980-986.
- Boellis A, di Napoli A, Romano A, Bozzao A. Pituitary apoplexy: an update on clinical and imaging features. Insights Imaging. 2014;5(6):753-762.
- Pant B, Arita K, Kurisu K, Tominaga A, Eguchi K, Uozumi T. Incidence of intracranial aneurysm associated with pituitary adenoma. Neurosurg Rev. 1997;20(1):13-17.
- Randeva HS, Schoebel J, Byrne J, Esiri M, Adams CB, Wass JA. Classical pituitary apoplexy: clinical features, management and outcome. Clin Endocrinol (Oxf). 1999;51(2):181-188.

- 15. Couture N, Aris-Jilwan N, Serri O. Apoplexy of a microprolactinoma during pregnancy: case report and review of literature. Endocr Pract. 2012;18(6):e147-e150.
- Goyal P, Utz M, Gupta N, et al. Clinical and imaging features of pituitary apoplexy and role of imaging in differentiation of clinical mimics. Quant Imaging Med Surg. 2018;8(2):219-231.
- Semple PL, Jane JA, Lopes MB, Laws ER. Pituitary apoplexy: correlation between magnetic resonance imaging and histopathological results. J Neurosurg. 2008;108(5):909-915.
- Rogg JM, Tung GA, Anderson G, Cortez S. Pituitary apoplexy: early detection with diffusion-weighted MR imaging. AJNR Am J Neuroradiol 2002;23:1240-5.
- Wildemberg LE, Glezer A, Bronstein MD, Gadelha MR. Apoplexy in nonfunctioning pituitary adenomas. Pituitary. 2018;21(2):138-144. doi:10.1007/s11102-018-0870-x
- Albani A, Ferraù F, Angileri F, et al. Multidisciplinary Management of Pituitary Apoplexy. Int J Endocrinol. 2016;7951536.
- Bonneville F, Cattin F, Marsot-Dupuch K, Dormont D, Bonneville JF, Chiras J. T1 signal hyperintensity in the sellar region: spectrum of findings [published correction appears in Radiographics. 2021 Nov-Dec;41(7):E210]. Radiographics. 2006;26(1):93-113.
- Osborn AG. Pituitary apoplexy. In: Osborn A, Salzman KL, Barkovich AJ (eds) Diagnostic imaging. Brain, 2nd edn. 1972 Amirsys Inc, Salt Lake City, II-2-28-31
- Glezer A, Bronstein MD. Pituitary apoplexy: pathophysiology, diagnosis and management. Arch Endocrinol Metab. 2015;59(3):259-264.
- 24. Giritharan S, Gnanalingam K, Kearney T. Pituitary apoplexy – Bespoke patient management allows good clinical outcome. Clin Endocrinol 2016;85:415-22.
- 25. Rajasekaran S, Vanderpump M, Baldeweg S, et al. UK guidelines for the management of pituitary apoplexy. Clin Endocrinol 2011;74:9-20.

Correspondence:

Giuseppe Guglielmi, Prof., MD

Radiology Unit, "Dimiccoli" Hospital, Viale Ippocrate, 15, 70051 Barletta, Italy;

- Department of Clinical and Experimental Medicine,
- Foggia University School of Medicine,
- Viale L. Pinto 1, 71121, Foggia, Italy;

Department of Radiology, Fondazione IRCCS Casa Sollievo

- della Sofferenza, Viale Cappuccini 1,
- 71013 San Giovanni Rotondo, FG, Italy
- E-mail: giuseppe.guglielmi@unifg.it