International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Immune Thrombocytopenic Purpura Complicated by Pituitary Apoplexy: 5th Case Worldwide

S. Belmaati Cherkaoui[1], S. Wahbi[2], A. Essafi[3], Z. El Azime[4], H. Aynaou[5], H. Salhi[6]

[1,2] Medical Doctor, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition. Hassan II University Hospital Center, Fez, Morocco
[3,4,5] Assistant Professor, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition. Hassan II University Hospital Center, Fez, Morocco & Laboratory of epidemiology, Research in health sciences, Faculty of Medicine and Pharmacy, USMBA, Fez, Morocco
[6] Head of Department, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition. Hassan II University Hospital Center, Fez, Morocco & Laboratory of epidemiology, Research in health sciences, Faculty of Medicine and Pharmacy, USMBA, Fez, Morocco

Abstract

Background: Pituitary apoplexy (PA) is an uncommon condition that may arise as a consequence of immune thrombocytopenic purpura (ITP). It is typically observed in the context of pituitary adenoma. The condition may manifest with symptoms of intracranial hypertension, namely, headaches of a "helmet-like" character, visual acuity decline, and vertigo. This case report describes a rare occurrence of pituitary apoplexy in a patient diagnosed with immune thrombocytopenic purpura (ITP).

Aim: Despite the rarity of this pathological coexistence, it highlights the potential link between immune thrombocytopenic purpura (ITP) and the emergence of pituitary apoplexy (PA).

Case description: A 34-year-old male patient with no previous medical history, referred to the hospital with hemorrhagic symptoms, including epistaxis and gingivorrhagia. Lab tests revealed a severe thrombocytopenia of 1,000 elements/mm³. Etiological investigation set up a diagnosis of ITP, and platelet transfusion along as intravenous immunoglobulin therapy were initiated. Subsequently, the patient presented to the emergency department with ptosis, diplopia, a sudden decline of visual acuity, and headaches. Cerebral imaging showed a pituitary adenoma with signs of hemorrhage and compression of the optic chiasm. A conservative management approach was therefore adopted and the clinical course was characterized by the involution of the ischemic adenomatous material, development of an empty Sella turcica, persistence of the other pituitary hormones deficiency and the resolution of the polyuria-polydipsia syndrome. Platelet counts returned to normal following the initiation of treatment.

Result: The patient was satisfied after the improvement of ophthalmological symptoms and the resolution of thrombocytopenia after treatment.

Conclusion: We presented a rare emergence of ITP with severe thrombocytopenia complicated by apoplexy of a pituitary macroadenoma. This case highlights the critical importance of considering pituitary apoplexy in the differential diagnosis when evaluating patients with ITP.

Keywords: Autoimmune Thrombocytopenic Purpura, Pituitary Apoplexy, Magnetic Resonance Imaging.

1. Introduction :

The prevalence of pituitary apoplexy (PA) is estimated at 6.2 cases per 100,000 people, while the incidence is as low as 0.17 cases per 100,000 [1]. It's main clinical manifestation is primarily distinguished by ocular symptoms, such as visual acuity sudden decline, visual field defects, and oculomotor impairment as a result of cranial nerve and cavernous sinus involvement [2]. Cerebral computed tomography (CT) is still the initial radiological exam for such clinical presentations. Although it is nonspecific, it can help to rule out other conditions, such as craniopharyngioma [3]. In this context, hypothalamic-pituitary magnetic resonance imaging (MRI) is a more sensitive and specific method, with a sensitivity of up to 90% in detecting PA, allowing for a good correlation between radiological and histological findings [4]. The occurrence of hemorrhagic complications in the presence of a pituitary adenoma may be associated with hematological disorders [5].

The current case report presents an unusual clinical association between PA and immune thrombocytopenic purpura (ITP), an association that has rarely been previously described in the literature. Based on our knowledge, this is the fifth case worldwide to prove the coexistence of pituitary apoplexy and ITP, suggesting a potential close relationship between these two pathological entities.

2. Case Presentation:

A 34-year-old male patient with no past medical history presented with epistaxis, spontaneous gingivorrhagia, and diffuse purpuric skin lesions. A complete blood count (CBC) revealed thrombocytopenia, with an initial platelet count of 15,000 elements per mm^3, declining markedly within days to 1,000 elements per mm^3. Given the severity of the thrombocytopenia, the patient received a platelet transfusion and intravenous immunoglobulin therapy. A comprehensive etiological workup yielded a diagnosis of immune thrombocytopenic purpura (ITP). Concurrently, the patient developed intermittent diplopia, a sudden visual acuity decline, and headaches resistant to conventional analgesics. Additionally, the patient's history indicated the onset of hypogonadism, characterized by decreased libido and erectile dysfunction, along with asthenia. Clinical examination found a conscient patient with Glasgow Coma Scale (GCS) score of 15, normal blood pressure, no signs of dehydration, and right eye ptosis, with no other neurological impairments. The patient had no evidence of acrofacial dysmorphic syndrome, Cushing's syndrome stigmata, or signs of hypermetabolism. However, polyuria-polydipsia syndrome was identified, with an estimated fluid intake of 9 liters per day and output of 7 liters per day. The initial cerebral CT scan demonstrated a pituitary adenoma compressing the optic chiasm.

Hypothalamic-pituitary MRI revealed the existence of a pituitary macroadenoma, measuring 30 x 20 x 24 mm in diameter (AP x T x H), hyperintense on T1 and T2-weighted images. Additionally, the macroadenoma exhibited hemorrhagic features described as T1 and T2 hyperintense, with late and peripheral enhancement post-contrast, and evidence of compression of the optical chiasm. Visual field testing indicated the presence of deficits in the right temporal quadrant and the left hemi temporal region. Endocrinological analysis revealed undetectable cortisol levels at 0 µg/dl, a decreased ACTH, hypogonadotropic hypogonadism with low testosterone levels at 1.1 ng/ml and low levels of FSH and LH, central hypothyroidism with FT4 at 0.64 ng/l (Normal range 0.78-1.48), normal prolactin, and hypotonic urine on urinary ionogram.

After six days of treatment, consisting of platelet transfusion, intravenous immunoglobulin administration,

and corticosteroid therapy, platelet count returned to normal. The neurological symptoms markedly improved spontaneously with resolution of diplopia, improvement of ptosis and visual acuity, and regression of visual field defects

Considering this progression, a follow-up MRI scan revealed an empty Sella turcica, while a second visual field test highlighted significant improvement, with minimal persistence of left temporal quadrant involvement. These clinical, radiological, and ophthalmological findings justified a conservative approach to the apoplexy, with hormonal supplementation of all deficient axes. The polyuria-polydipsia syndrome showed spontaneous improvement.

For the thrombocytopenia, the therapeutic outcome was satisfactory, with platelet counts exceeding 120,000 elements/mm³. Even after the interruption of corticosteroid therapy, platelet counts remained within the normal range.

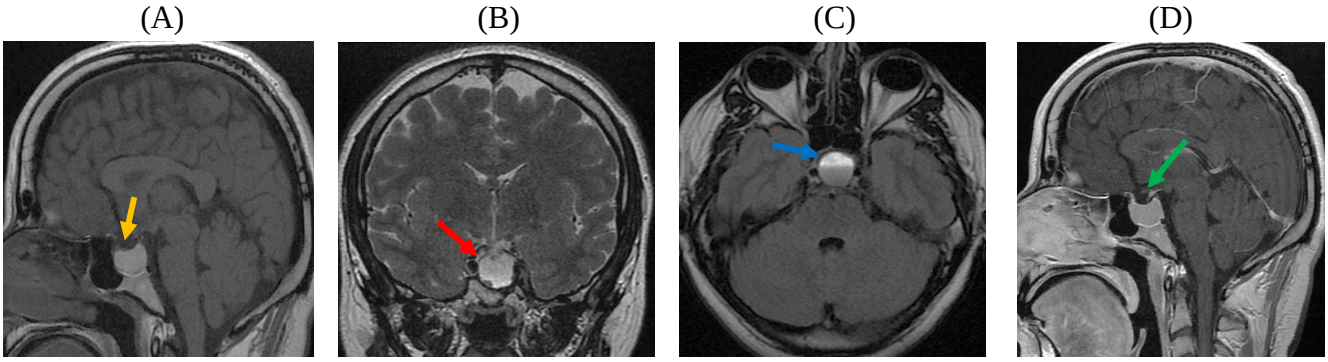

Figure 1: Pituitary MRI in sagittal T1-weighted imaging (A), coronal T2-weighted (B), Flair (C), sagittal T1 after Gadolinium injection (D): showing an intra-sellar pituitary lesion, described as hyperintense on T1 (yellow arrow), T2 (red arrow), and Flair, demonstrating a fluid-fluid level (blue arrow), with late and peripheral enhancement post-contrast (green arrow), The lesion shows compression of the optical chiasm, downward displacement of the sellar floor, and upward displacement of the pituitary stalk, while supporting the permeability of the cavernous sinuses and lateral internal carotid arteries consistent with a pituitary macroadenoma in apoplexy. (Department of Radiology, Hassan II University Hospital Center, Fez, Morocco)

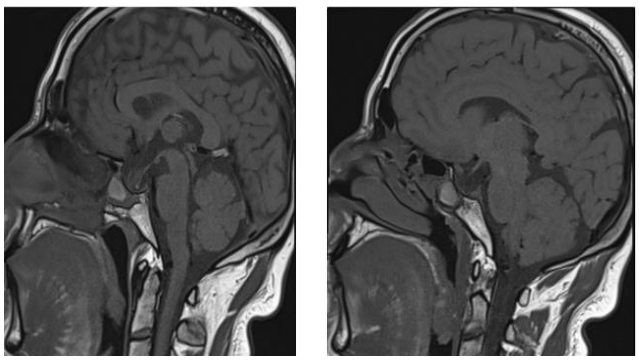

Figure 2: Follow-up pituitary MRI in sagittal T1-weighted imaging revealing an empty Sella turcica

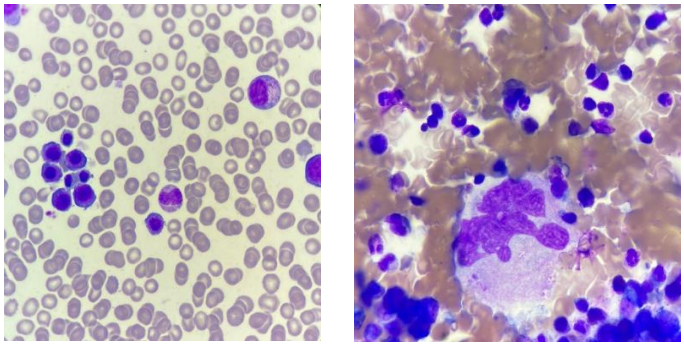

Figure 3: Bone marrow aspirate with images showing hypercellular and hemodiluted marrow with megakaryocytic hyperplasia characteristic of immune thrombocytopenic purpura (ITP)

3. Discussion:

The pituitary gland is characterized by a notably dense vascular network. The anterior pituitary receives its blood supply from the superior hypophyseal artery, which originates from the internal carotid artery and travels along the infundibulum to enter the anterior pituitary. Additionally, it is perfused by portal vessels that stem from the hypothalamus. The inferior hypophyseal artery, also a branch of the internal carotid artery, supplies the posterior pituitary [6].

In the literature, the prevalence of pituitary apoplexy (PA) varies significantly depending on the definition used. It can reach 15-20% of all pituitary adenoma cases if it's based on histopathological criteria, such as necrotic and/or hemorrhagic areas in pituitary tissue. However, the prevalence reaches only 1% when it's definition is established on clinical criteria by the sudden onset of ophthalmological or neurological symptoms related to hemorrhage and/or necrosis in a pituitary adenoma [7].

The average age of individuals affected by PA is typically in their 50s. There is no gender predominance, and the likelihood of apoplexy occurrence is independent of the adenoma's histological type [7]. Historically, PA was widely regarded as a neurosurgical emergency, with transsphenoidal surgical decompression being the standard treatment for the majority of patients. [8].

Recently, the approach to managing PA has been the subject of significant debate, particularly regarding the decision between surgical and conservative treatment options. Several studies have shown that there is no significant difference between surgical and conservative approaches if the seven-day window has elapsed. In cases of mild PA, conservative management has been found to yield rapid and favorable outcomes. Some patients who received conservative treatment have even shown spontaneous recovery and the disappearance of the tumor [9]. In our patient, neurological and ophthalmological symptoms improved spontaneously under glucocorticoid therapy with close monitoring. The visual field defects improved spontaneously, and magnetic resonance imaging (MRI) confirmed the involution of adenomatous material, the absence of a residual mass, and an empty sella turcica appearance.

Several factors have been identified as potentially accelerating PA [10].

-Factors related to pituitary adenoma growth: estrogens, pregnancy, LHRH used for biological assessment of pituitary functions [11],

- Radiotherapy, hypertension, and diabetes mellitus and other factors that may impair microcirculation [12],

- Cranial trauma, lumbar puncture, and spinal anesthesia or other factors that can alter intracranial pressure, due to pituitary hypoperfusion.

-Factors leading to systemic hypoperfusion and, so, pituitary hypoperfusion: cardiac surgery,

hemodialysis,
- Factors that may influence blood coagulation including multiple myeloma, von Willebrand disease, the use of anticoagulant agents [13], antithrombotic agents [14] , and thrombocytopenia.

As far as we know, there have been four documented cases in the literature of an association between thrombocytopenia and apoplexy in the absence of any underlying comorbid medical conditions or pharmacological impacts.

The first case documented in the literature by Lenthall et al., 2001 describes a 70-year-old male presenting with PA, manifested by headaches and visual impairment. Bone marrow examination revealed megakaryocytes with peripheral platelet destruction, which is consistent with the diagnosis of idiopathic thrombocytopenic purpura (ITP) [5]. As in our case, a conservative approach was adopted due to prolonged platelet normalization time and the surgical contraindication related to perioperative hemorrhagic risk, with an evolution toward empty sella. The patient's clinical presentation spontaneously improved as the platelet count normalized, and magnetic resonance imaging also revealed empty sella.

Maïza et al., 2004 reported the second case of a 59-year-old patient who had a severe thrombocytopenia complicated by a PA. The clinical manifestation was purpura occurring after a surgery for a macroprolactinoma. Histological and immunohistochemical examination confirmed the presence of necrotic prolactin-secreting adenomatous tissue [7].

The third case, as reported by Tsuji et al., 2016 about an 83-year-old female patient with primary ITP, who developed PA, presented with headaches. Unfortunately, the available data about therapeutic management is insufficient [15].

The fourth case, as reported by Nabulsi et al., 2023 described a 61-year-old patient whose apoplectic episode occurred with diplopia and headaches. The initial platelet count was 20,000 elements/mm^3, indicative of ITP. The patient underwent surgical resection of the adenoma, and later histopathological examination confirmed the presence of hemorrhagic material in the surrounding tissue of the pituitary tumor cells [16].

To the best of our knowledge, our patient is the fifth worldwide case where PA occurred in the context of a likely pre-existing and unrecognized pituitary adenoma, consequent to thrombocytopenia due to ITP. Two additional cases have been reported in the literature. Wongpraparut et al., 2000 described a patient with myeloid leukemia who developed thrombocytopenia and PA during chemotherapy [17]. Kruljac et al., 2012 reported another case of thrombocytopenia-induced PA in a patient receiving heparin therapy [18]. Therefore, thrombocytopenia, irrespective of its etiology, seems to be a predisposing factor that could potentially trigger PA in patients with existing pituitary disorders, such as adenomas.

The conservative approach can be proposed to some patients who do not present consciousness impairment or vision loss. The authors who adopted this approach consider that neurosurgery may be possible if the neurological implications include unilateral oculomotor nerve paralysis [19], without exceeding an eight day delay, in accordance with the UK guidelines for the management of PA published in 2011 [20].

In the present case, the timing of correction of coexisting thrombocytopenia, the marked ophthalmic improvement, and the neuroradiological evolution toward empty sellae collectively justified the decision to abstain from surgical intervention. Subsequently, the patient's ophthalmological and neurological conditions showed improvement, although panhypopituitarism persisted, needing hormone replacement therapy.

Although there is no consensus on the management of this rare pathologic coexistence, the UK published

guidelines in 2011 to guide the decision between conservative and surgical management of PA. These guidelines advocate conservative management in the absence of neuro-ophthalmologic involvement, or in the presence of neuro-ophthalmologic involvement but with an initial trend toward improvement under close neurologic monitoring every 4-6 hours. However, severe neuro-ophthalmologic involvement, altered consciousness, or neurological impairment should add urgent imaging for possible decompressive surgery. Surgery should be performed by an experienced pituitary surgeon within the first 7 days of symptom onset unless there is immediate urgency [20].

However, new onset or worsening of visual or neurological deficits may call for surgery that was not initially indicated. In our patient, conservative management was decided after multidisciplinary discussion given the marked neuro-ophthalmologic and radiologic improvement, with no need for surgery in the short, medium or long term.

4. Conclusion:

Managing the combination of pituitary apoplexy (PA) and immune thrombocytopenic purpura (ITP) presents notable clinical challenges in optimizing treatment for both conditions. Although PA is a rare complication of ITP, it should be included in the differential diagnosis and carefully excluded in patients with severe headaches, visual disturbances, and thrombocytopenia.

References:

1. 1. Nass R, Evans WS: Physiologic and Pathophysiologic Alterations of the Neuroendocrine Components of the Reproductive Axis. In: Yen and Jaffe's Reproductive Endocrinology. Elsevier; 2019. 473-519.e12.10.1016/B978-0-323-47912-7.00020-2
2. 2. Pituitary Apoplexy: Practice Essentials, Background, Pathophysiology. Published Online First: 24 October 2023.
3. 3. 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. 10.1016/j.clineuro.2006.01.006
4. 4. Semple PL, Jane JA, Lopes MBS, Laws ER: Pituitary apoplexy: correlation between magnetic resonance imaging and histopathological results. J Neurosurg. 2008, 108:909–15. 10.3171/JNS/2008/108/5/0909
5. 5. Lenthall R, Gonugunta V, Jaspan T: Pituitary apoplexy with optic tract oedema and haemorrhage in a patient with idiopathic thrombocytopenic purpura. Neuroradiology. 2001, 43:156–8. 10.1007/s002340000390
6. 6. Reid RL: Pituitary Apoplexy: A Review. Arch Neurol. 1985, 42:712. 10.1001/archneur.1985.04060070106028
7. 7. Maïza JC, Bennet A, Thorn-Kany M, Lagarrigue J, Caron Ph: Pituitary Apoplexy and Idiopathic Thrombocytopenic Purpura: A New Case and Review of the Literature. Pituitary. 2004, 7:189–92. 10.1007/s11102-005-1760-6
8. 8. Nawar RN, AbdelMannan D, Selman WR, Arafah BM: Analytic Review: Pituitary Tumor Apoplexy: A Review. J Intensive Care Med. 2008, 23:75–90. 10.1177/0885066607312992
9. 9. Briet C, Salenave S, Bonneville J-F, Laws ER, Chanson P: Pituitary Apoplexy. Endocr Rev. 2015, 36:622–45. 10.1210/er.2015-1042
10. 10.Biousse V: Precipitating factors in pituitary apoplexy. J Neurol Neurosurg Psychiatry. 2001,

71:542–5. 10.1136/jnnp.71.4.542

11. 11.Freeman R, Wezenter B, Silverstein M, Kuo D, Weiss KL, Kantrowitz AB, Schubart UK: Pregnancy-associated subacute hemorrhage into a prolactinoma resulting in diabetes insipidus. Fertil Steril. 1992, 58:427–9. 10.1016/S0015-0282(16)55219-4
12. 12.Sussman EB, Porro RS: Pituitary apoplexy: the role of atheromatous emboli. Stroke. 1974, 5:318–23. 10.1161/01.str.5.3.318
13. 13.Nourizadeh AR, Pitts FW: HEMORRHAGE INTO PITUITARY ADENOMA DURING ANTICOAGULANT THERAPY. JAMA. 1965, 193:623–5. 10.1001/jama.1965.03090070073033
14. 14.Fuchs S, Beeri R, Hasin Y, Weiss AT, Gotsman MS, Zahger D: Pituitary Apoplexy as a First Manifestation of Pituitary Adenomas Following Intensive Thrombolytic and Antithrombotic Therapy. Am J Cardiol. 1998, 81:110–1. 10.1016/S0002-9149(97)00862-X
15. 15.Tsuji T, Mochinaga H, Yamasaki H, Tsuda H: [Primary immune thrombocytopenia accompanied by pituitary apoplexy]. Rinsho Ketsueki. 2016, 57:877–80. 10.11406/rinketsu.57.877
16. 16.Nabulsi O, Abouelleil M, Lyons L, Walsh M, Singer J: Immune Thrombocytopenic Purpura Presenting with Pituitary Apoplexy: A Case Report and Literature Review. J Neurol Surg Rep. 2023, 84:e61–4. 10.1055/a-2072-0147
17. 17.Wongpraparut N, Pleanboonlers N, Suwattee P, et al.: Pituitary apoplexy in a patient with acute myeloid leukemia and thrombocytopenia. Pituitary. 2000, 3:113–6. 10.1023/a:1009909908942
18. 18.Kruljac I, Čerina V, Pećina HI, Pažanin L, Matić T, Božikov V, Vrkljan M: Pituitary Metastasis Presenting as Ischemic Pituitary Apoplexy Following Heparin-induced Thrombocytopenia. Endocr Pathol. 2012, 23:264–7. 10.1007/s12022-012-9224-9
19. 19.Maccagnan P, Macedo CL, Kayath MJ, Nogueira RG, Abucham J: Conservative management of pituitary apoplexy: a prospective study. J Clin Endocrinol Metab. 1995, 80:2190–7. 10.1210/jcem.80.7.7608278
20. 20.Rajasekaran S, Vanderpump M, Baldeweg S, et al.: UK guidelines for the management of pituitary apoplexy. Clin Endocrinol (Oxf). 2011, 74:9–20. 10.1111/j.1365-2265.2010.03913.x