




# Immune Thrombocytopenic Purpura Presenting with Pituitary Apoplexy: A Case Report and Literature Review

Omar Nabulsi<sup>1</sup>  Mohamed Abouelleil<sup>1</sup> Leah Lyons<sup>1</sup> Meggen Walsh<sup>1</sup> Justin Singer<sup>1</sup>

<sup>1</sup> Department of Neurosurgery, Spectrum Health, Grand Rapids, Michigan, United States

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**Address for correspondence** Omar Nabulsi, BA, Department of Neurosurgery, Spectrum Health, 25 Michigan St. NE, Grand Rapids, MI 49503-2560, United States  
(e-mails: omarnabulsi8@gmail.com; mohamed.abouelleil@spectrumhealth.org).

## Abstract

### Keywords

- pituitary apoplexy
- immune thrombocytopenic purpura
- pituitary adenoma
- pituitary mass resection

**Background** Pituitary apoplexy is a rare condition that usually occurs in the setting of a pituitary adenoma. It can present with symptoms of visual disturbances, vertigo, headache, and neurological impairments. Computed tomography (CT) scans can aid in identifying pituitary apoplexy and ruling out other diseases. We present a unique case of pituitary apoplexy in the setting of immune thrombocytopenic purpura (ITP).

**Case Description** A 61-year-old man with a past medical history significant for myocardial infarction presented to the emergency department with symptoms of diplopia and headache 36 hours after onset. The patient was found to have severe thrombocytopenia with a platelet count below 20,000. A CT of the head revealed a possible pituitary adenoma with compression of the optic chiasm. The patient's platelet count continued to decrease throughout his admission and dropped below 7,000 on day 2 of admission. The patient was given platelet transfusion along with intravenous immunoglobulins. The patient underwent endoscopic transsphenoidal resection of the pituitary mass. Pathology of the mass revealed immature platelets characteristic of immune ITP in the setting of pituitary apoplexy.

**Conclusion** While ITP in the setting of pituitary apoplexy is a rare entity, we believe that clinicians should have pituitary apoplexy on their differential diagnosis in patients with ITP.

## Introduction

Pituitary apoplexy is a rare clinical condition caused by acute hemorrhaging, infarction, or ischemia of the pituitary gland. It typically occurs within a pituitary adenoma and at times is more appropriately referred to as a pituitary tumor apoplexy. It can present with symptoms, such as severe sudden-onset headache, visual impairment, and neurological impairment, and may include nausea or vertigo.<sup>1</sup> Impairment in visual

acuity and visual field may be due to involvement of the optic nerve or optic chiasm and may present with ophthalmoplegia.<sup>2</sup> Additionally, hemorrhaging or infarction of the pituitary gland often cause hormonal dysfunction, necessitating exogenous correction as an untreated corticotrophic deficiency can be fatal.<sup>3</sup>

Pituitary apoplexy is often first identified via computed tomography (CT) scan due to an emergent symptom

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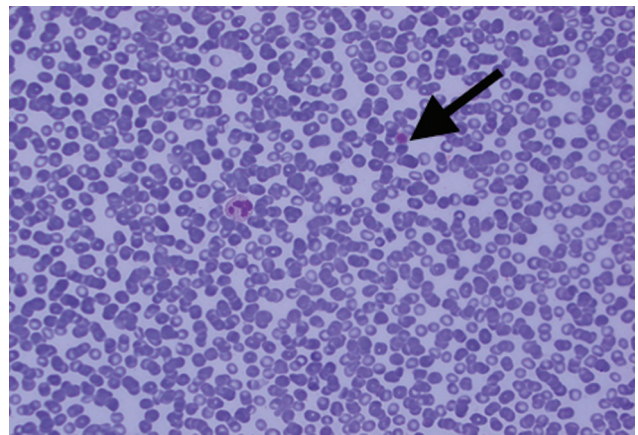
presentation. CT scans can provide important differential characteristics, rule out diseases, such as subarachnoid hemorrhage or craniopharyngioma, and help identify an acute hemorrhagic infarct.<sup>4</sup> However, the greater sensitivity of magnetic resonance imaging (MRI) scans enables them to better characterize suspected apoplexy since CT scans only provide nonspecific information in the absence of a hemorrhagic episode or a pre-existing adenoma.<sup>4</sup> The advantage of MRI scans for suspected pituitary apoplexy is further illustrated by the fact that CT scans can miss the appearance of apoplexy in up to 54 to 79% of patients.<sup>1</sup> MRI scanning also provides crucial information in the acute and subacute phase of pituitary apoplexy, a significant insight when considering a conservative management course.<sup>4</sup>

Recent epidemiological analyses highlight the rarity and complexity of pituitary apoplexy. The prevalence of pituitary apoplexy is ~6.2 cases per 100,000 persons, with an incidence of only 0.17 cases per 100,000.<sup>3</sup> An estimated 2 to 7% of patients with an adenoma experience apoplexy.<sup>1</sup> Although most patients (between 50 and 80%) with apoplexy are diagnosed without a prior diagnosis of pituitary adenoma, apoplexy is often the presenting symptom of an underlying tumor.<sup>1</sup> It should also be noted that sex seems to play a role in pituitary apoplexy diagnosis, with diagnosed males being about double the amount of diagnosed females; the age range remains broad with a slight peak in patients in their 50s and 60s.<sup>1</sup> We present a unique case of pituitary apoplexy in the setting of immune thrombocytopenic purpura (ITP).

## Case Presentation

A 61-year-old man presented to our emergency department, complaining of intermittent diplopia and a mild headache over the previous 36 hours. His past medical history was significant for congestive heart failure and myocardial infarction, resulting in multiple stent placements with aspirin therapy. A head CT was ordered and showed a possible pituitary adenoma with possible compression of the optic chiasm. MRI revealed a 2.3-cm pituitary macroadenoma with sedimentation of blood products creating a fluid level abutting the optic chiasm. Subsequent laboratory work revealed thrombocytopenia with a count below 20,000/ $\mu$ L and was otherwise unremarkable. Pituitary laboratories were ordered, revealing a mild hyperprolactinemia attributed to a stalk effect. The patient remained neurologically intact except for the complaint of diplopia. An ophthalmologic exam revealed no evidence of abnormality with visual acuity unchanged. A hematology and oncology consultation classified the patient's thrombocytopenia as ITP.

On day 2 of hospital admission, the patient's platelet count dropped to 7,000/ $\mu$ L, necessitating a platelet transfusion along with intravenous immunoglobulins. The patient was also treated with an intravenous administration of corticosteroids. The patient elicited an appropriate response to the treatment, and his platelet count improved to over 100,000/ $\mu$ L. The patient then underwent a transsphenoidal resection of the pituitary mass once his platelet count had normalized, 5 days after his initial presentation. Intraoperative, the mass was



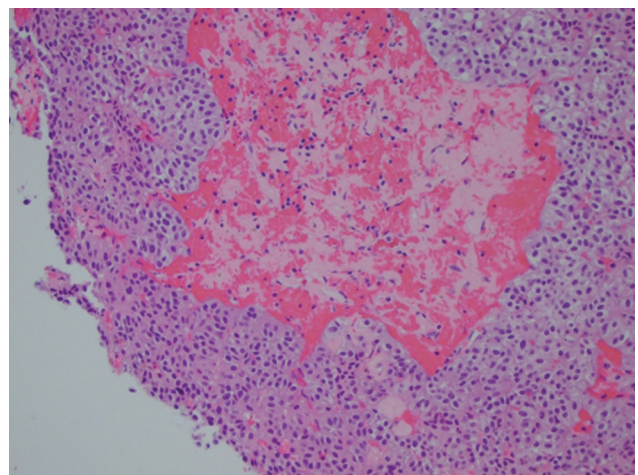
**Fig. 1** A Wright-stained peripheral blood smear depicting moderate to marked thrombocytopenia with elevated immature platelet fraction (arrow) that is suggestive of peripheral platelet consumption with appropriate bone marrow compensation.

found to have a hemorrhagic appearance that was most consistent with the patient's clinical acute deterioration and acute onset of severe headache. Pathology report of a peripheral blood smear identified enlarged, immature platelets, characteristic of ITP (**Fig. 1**). Additionally, the pathology report of the resected specimen was consistent with a pituitary adenoma with hemorrhage due to the specimen showing hemorrhage within the tumor cells (**Fig. 2**). Further analysis confirmed the presence of pituitary adenoma with apoplexy.

The patient reported postoperative improvement in symptoms of headache and diplopia, and he experienced no complications thereafter as his platelet count was normalizing. The patient was discharged on postoperative day 2 and was scheduled for neurosurgical and endocrinologic follow-up.

## Discussion

Historically, pituitary apoplexy was universally considered to be a neurosurgical emergency. Transsphenoidal surgical



**Fig. 2** Specimen of the resection depicting a single monomorphic cell type, lack of lobular configuration, no significant reticulin deposition, and a hemorrhage within the tumor cells consistent with pituitary adenoma with hemorrhage.

decompression was routinely used for most patients with pituitary apoplexy, and it has historically resulted in low morbidity and mortality.<sup>5</sup> Verrees et al found that surgical intervention performed within 72 hours of symptom onset allowed for a full return to normal pituitary function in 73% of patients.<sup>6</sup> Rutkowski et al reported similar improvements in pituitary hormone recovery with additional moderate improvements in visual deficits, but they concluded that the timing of surgical intervention did not significantly influence functional outcomes.<sup>7</sup>

More recently, however, the management of pituitary apoplexy has become increasingly controversial. Successful management of pituitary apoplexy must address systemic, neurologic, ophthalmologic, and endocrinologic abnormalities. In determining whether a surgical or conservative course is most appropriate, the patient's presentation, clinical stability, response to glucocorticoids, and access to an experienced neurosurgeon should all be considered.<sup>5</sup> For patients with a mild presentation of pituitary apoplexy, conservative management can often provide a prompt and favorable outcome. In a retrospective analysis of 33 patients with pituitary apoplexy, where 18 patients received only medical treatment and 15 patients had surgical intervention in addition to the medical treatment, hormonal and visual outcomes showed comparable results.<sup>5</sup> Select patients undergoing conservative management have even experienced spontaneous recovery and tumor disappearance.<sup>3</sup>

Nevertheless, conservative management may not be appropriate for all patients, and a multidisciplinary team of specialists in neurosurgery, endocrinology, and ophthalmology should apply this approach selectively when appropriate. Close monitoring of pituitary function with corticosteroid administration, intensive supportive measures for hemodynamic stability, and regular assessments in neurological and visual functioning are essential for optimal management and outcome.<sup>5</sup>

The exact pathophysiological underpinnings of pituitary apoplexy are difficult to ascertain, and various underlying mechanisms have been proposed to explain how spontaneous hemorrhage, necrosis, or infarction of adenomatous tissue may lead to apoplexy. The contribution of the unique vascular supply of the portal venous system to the proliferation and progression of apoplexy has drawn investigative interest.<sup>2</sup> There are also some acute events generally recognized as precipitating risk factors for pituitary apoplexy, such as cardiac surgery or other surgery, trauma, hypertension, hypotension, infusion of insulin or hypothalamic releasing factors, anticoagulation therapy, and pregnancy.<sup>1,8</sup> Much of the investigation into pituitary apoplexy involves studying the characteristics of the adenoma, which can be prone to hemorrhage and necrosis. As for intrinsic factors, pituitary adenomas have a high metabolic demand; reduced availability of glucose, therefore, greatly inhibits the cells' chances of survival.<sup>9</sup> Additionally, their limited angiogenesis and vascular network can potentially underlie spontaneous infarction characteristic of apoplexy, and an intrinsic vasculopathy can render the tissue susceptible to hemorrhage.<sup>4</sup> In non-adenomatous tissue, the mechanism of hemorrhage or in-

farction presents a greater challenge, leading some investigators to consider extrinsic contributing factors, such as certain medications or systemic diseases. It has previously been reported that diseases such as diabetes and arterial hypertension can possibly predispose persons to pituitary apoplexy. However, Goyal et al contend that the claim is unsubstantiated in light of recent evidence.<sup>4</sup>

The high degree of complexity and variability of pituitary apoplexy makes it an important clinical topic with significant implications for medical intervention and patient outcome. In fact, its most frequent presenting symptom—the sudden onset of a severe headache in the retro-orbital region—is commonly associated with conditions such as subarachnoid hemorrhage, cervical artery dissection, and cerebral dural sinus thrombosis, making pituitary apoplexy a condition that is often initially overlooked.<sup>4</sup> Timely diagnoses are also hindered by the fact that pituitary apoplexy can occur in nonadenomatous or microadenomatous pituitary tissue.

Pituitary apoplexy can also occur secondary to idiopathic thrombocytopenic purpura. A review of the literature reveals three cases of this association without other underlying medical conditions or pharmacologic influences. The first case reported in the literature describes a 70-year-old male patient with pituitary apoplexy secondary to idiopathic thrombocytopenic purpura.<sup>10</sup> In the case reported by Maïza et al regarding a 59-year-old male patient, pituitary apoplexy occurred due to severe thrombocytopenia, which developed as a complication of a macroprolactinoma.<sup>11</sup> Finally, Tsuji et al reported another rare case of an 83-year-old female patient with primary immune thrombocytopenia accompanied by pituitary apoplexy.<sup>12</sup> These cases have been reviewed and summarized in **Table 1**.

The rare co-occurrence of pituitary apoplexy with ITP presents significant challenges clinically in determining the optimal management of the two conditions for the best possible outcome. While pituitary apoplexy uncommonly presents in the setting of ITP, apoplexy should remain on the clinician's differential and be excluded for patients with severe headache and visual changes with concomitant thrombocytopenia, especially if they have a negative CT scan of the head for acute intracranial hemorrhage.

The first case reported in the literature of pituitary apoplexy occurring secondary to thrombocytopenia was in October 2000 by Wongpraparut et al.<sup>13</sup> Their case presented a patient with acute myeloid leukemia, whose chemotherapy resulted in thrombocytopenia and the subsequent occurrence of pituitary apoplexy. In investigating symptoms of sudden-onset severe headache, nausea, vomiting, and blurred vision, an initial head CT scan came back negative. After physical examination revealed bitemporal visual field defects and decreased visual acuity, a repeat CT scan revealed a hemorrhagic mass in the pituitary compressing the optic chiasm. Transnasal sphenoidotomy decompression surgery was performed, and symptoms and visual defects improved postoperatively.

Prothrombotic states have not previously been indicated as precipitating factors for pituitary apoplexy. In a report by Kruljac et al, an elderly woman began receiving prophylactic

**Table 1** Characteristics of pituitary adenoma with immune thrombocytopenia purpura in the literature

Case report	Age (y)	Sex	Microscopic features	Platelet count	Symptoms
This study	61	Male	A single monomorphic cell type, lack of lobular configuration, no significant reticulin deposition, a hemorrhage within the tumor cells consistent with pituitary adenoma with hemorrhage	20,000/ $\mu$ L	<ul style="list-style-type: none"> <li>• Intermittent diplopia</li> <li>• Headache</li> </ul>
Lenthall et al <sup>10</sup>	70	Male	A bone marrow aspirate showed megakaryocytes consistent with peripheral platelet consumption or destruction	1,000/ $\mu$ L	<ul style="list-style-type: none"> <li>• Frontal headache</li> <li>• Blurred vision</li> <li>• Signs of meningism and bitemporal hemianopia</li> </ul>
Maïza et al <sup>11</sup>	59	Male	Histopathological exam and immunostaining led to diagnosis of necrotic prolactin-secreting pituitary adenoma	4,000/ $\mu$ L	<ul style="list-style-type: none"> <li>• Occurrence of purpura</li> </ul>
Tsuji et al <sup>12</sup>	83	Female	Unknown	10,000/ $\mu$ L	<ul style="list-style-type: none"> <li>• Headache</li> </ul>

fractionated heparin therapy for sepsis, rhabdomyolysis, and overt disseminated intravascular coagulation.<sup>1</sup> After a week of heparin therapy, she began experiencing the sudden onset of vision loss, ptosis, diplopia, and severe headache. Heparin-induced thrombocytopenia type 2 was confirmed, and an MRI revealed a pituitary tumor mass with thickening of the sphenoid sinus mucosa and suggested focal ischemic necrosis. Kruljac et al demonstrated the first such case of heparin-induced thrombocytopenia triggering pituitary apoplexy.<sup>14</sup>

## Conclusion

We report a unique case of ITP presenting with pituitary apoplexy. Pituitary apoplexy should be considered in appropriate clinical circumstance in patients presenting with ITP.

### Conflict of Interest

None declared.

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