Pituitary apoplexy with acute complete bilateral third nerve palsy and papillary involvement: A case report

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Pituitary apoplexy (PA) is a rare, potentially life-threatening condition primarily associated with pituitary adenomas. It presents with sudden, severe symptoms due to inadequate blood supply, bleeding, or tissue death in the pituitary gland. This case report describes a case of PA in a 40-year-old female, and reviews the recent literature surrounding the subject. The patient presented with complete bilateral third nerve palsy and dilated non-reactive pupils. Her initial symptoms included retroorbital headache, fever, and double vision, which rapidly progressed to oculomotor nerve palsy. MRI revealed hemorrhagic PA. High-dose steroids were initiated, leading to the resolution of ptosis. Additionally, surgical intervention was performed. PA typically affects older males with known adenomas, making this case unusual due to the patient's age, gender, and absence of prior adenoma history. Differentiating PA from other intracranial pathologies is crucial, and MRI plays a pivotal role in accurate diagnosis.

Keywords: *pituitary; apoplexy; oculomotor nerve palsy; headache; ptosis; transnasasl surgery.*
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Pituitary apoplexy (PA) is a rare medical condition characterized by a sudden onset of symptoms resulting from inadequate blood supply, bleeding, or tissue death in the pituitary gland. This condition is most commonly associated with pituitary adenomas. In many cases, PA represents both a medical and surgical emergency. Rapid identification and assessment are crucial to enhance patient outcomes. When considering only symptomatic cases, the incidence is approximately 10%. If we also take into account non-symptomatic intratumoral bleeding detected through neuroimaging studies, the incidence rises to 26%. This condition predominantly affects males with an average age of 50 to 60 and typically manifests with neuro-ophthalmic symptoms such as sudden-onset headaches, nausea, ophthalmoplegia, and visual disturbances. The visual symptoms occur due to direct pressure on the optic nerves or chiasm, while hormonal disruptions result from the abrupt cessation of hormone release. Many patients experience double vision, which arises from the external compression of one or more of the nerves controlling eye movement, with the oculomotor nerve being the most frequently affected. Patients may exhibit drooping eyelids and outward deviation of the affected eye, often accompanied by dilation of the pupil. Several theories regarding the pathophysiology of PA have been proposed. One suggests that the superior hypophyseal artery and its branches become compressed against the diaphragma sella, leading to ischemia in the anterior pituitary gland and the tumor. Another theory posits that the thin vascular network within the pituitary is compressed as it resides within the limited space of the sella, causing ischemia, tissue death, and bleeding. Finally, another theory suggests that the tumor's rapid growth surpasses its vascular supply, resulting in ischemia and tissue death [1]. Despite initial management involving fluid and electrolyte replenishment and the use of glucocorticoids with or without thyroid hormone replacement, the optimal approach to further treatment remains uncertain [2, 3]. In this context, we present a case of PA where the patient exhibited an acute and complete bilateral third nerve palsy with papillary involvement.

Case Report

A 40-year-old woman presented to our emergency department with complete bilateral ptosis and bilateral exotropia. She reported experiencing a fever and runny nose nine days before her visit, followed by a sudden left-sided, unilateral retroorbital headache that resolved after using over-the-counter analgesics. Six days before her arrival, upon waking up, she discovered an inability to open her eyes and mentioned feelings of dizziness and double vision when manually lifting her eyelids. She did not report any nausea or vomiting. Subsequently, she sought consultation with a neurologist, but her condition did not improve, leading to a referral to our facility.

Upon examination, the patient displayed isolated bilateral complete oculomotor nerve palsy, along with dilated and non-reactive pupils. Her visual acuity was measured at accurate finger counting from a distance of 6 meters in both eyes, and a standard visual field assessment revealed no signs of bitemporal hemianopia. All other sensory and motor examinations were within normal parameters. Her laboratory results were all within the normal range. Following an MRI with and without contrast, she received a diagnosis of hemorrhagic PA (Fig. 1).

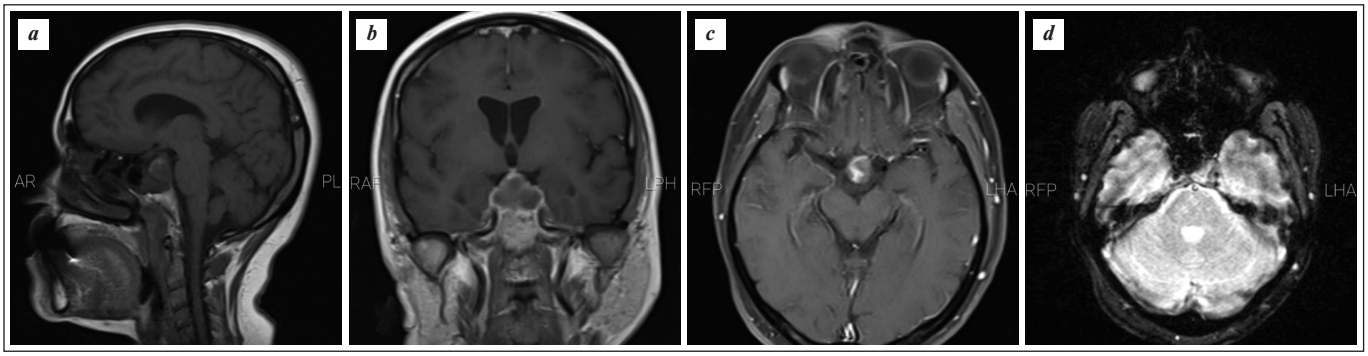

Fig. 1. *Hyperintensity in pituitary gland in T1 sequence (a). Heterogenous enhancement in enlarged pituitary gland (b and c). Hypointensity in pituitary region in GRE sequence (d)*

Subsequently, she commenced treatment with high-dose intravenous Dexamethasone at 8 mg every 8 hours, resulting in the resolution of ptosis in her left eyelid within 24 hours (Fig. 2). Treatment also included high-dose steroids and a transnasal, transsphenoidal resection of the lesion.

Discussion

Here, we presented a distinctive case of a 40-year-old female presenting with no significant past medical or surgical history or drug use with an isolated bilateral complete third cranial nerve palsy, primarily suggesting an acute vascular disease process. Patient's complete blood count, biochemical and coagulation studies, as well as a hormonal panel consisting of GH, FSH, LH, Prolactin, Progesterone, Testosterone, IGF1, ACTH, PTH, Cortisol, T3, T4, and the latter two's free counterparts were all in the normal range of values. Her Brain MRI showed a hyperintense pituitary region suggestive of hemorrhagic PA.

PA is a rare event occurring in approximately 1.6–2.8% of macroadenoma patients [4]. This phenomenon exhibits a male predilection with a gender ratio of 2:1 and typically manifests at an average age of 57 [4, 5]. Remarkably, about 60% of those afflicted by PA are unaware of their underlying pituitary adenoma before the acute event, underscoring the stealthy nature of this condition [4]. It's worth noting that our patient was female and younger than the typical age for PA at age 40, and she had no past medical history of adenoma.

PA's clinical presentation spans a broad spectrum, with the most common symptom being a sudden, intense headache, often localized retro-orbitally [2, 4]. Visual deficiencies, ranging from 50% to 82% of cases, represent the second most frequent symptom [4]. Patients may also experience nausea, vomiting, ocular paralysis, and symptoms mimicking meningism [6]. In the presented case, the patient presented with an isolated bilateral CNIII palsy, and it was upon further inquiry that she described a classic PA headache which rather exceptionally had subsided quickly, and the patient had no symptoms for two days before the sudden onset of her presenting complaint. However, there are the patients can present with, as illustrated in other reported PA cases during the past year (see Table).

In the emergency setting, patients exhibiting symptoms indicative of PA typically undergo computed tomography (CT). While CT can help diagnose bland and hemorrhagic infarctions within pituitary adenomas, other pathologies share similar radiological findings. These may include hyperdense lesions in the pituitary region, such as aneurysms, meningiomas, germinomas, lymphomas, craniopharyngiomas, and Rathke cleft cysts [4]. Therefore, magnetic resonance imaging (MRI) is pivotal in diagnosing PA, as it offers a more detailed examination. MRI can identify the presence of an adenoma and its hemorrhagic degeneration, with its features correlating accurately with pathological and operative findings [4]. In the acute phase of PA, usually within the first week, the lesion appears isointense on T1-weighted images and hypointense on T2 sequences, with a corresponding high signal on diffusion-weighted imaging. In the subacute phase (7–21 days), the lesion becomes hyperintense on both T1 and T2 due to methemoglobin content. The chronic phase (>21 days) is characterized by hypointensity on both T1 and T2, resulting from hemosiderin and ferritin. Following intravenous gadolinium administration, slight and inhomogeneous contrast enhancement may occur, albeit it can be challenging to differentiate from normal residual pituitary tissue [4].

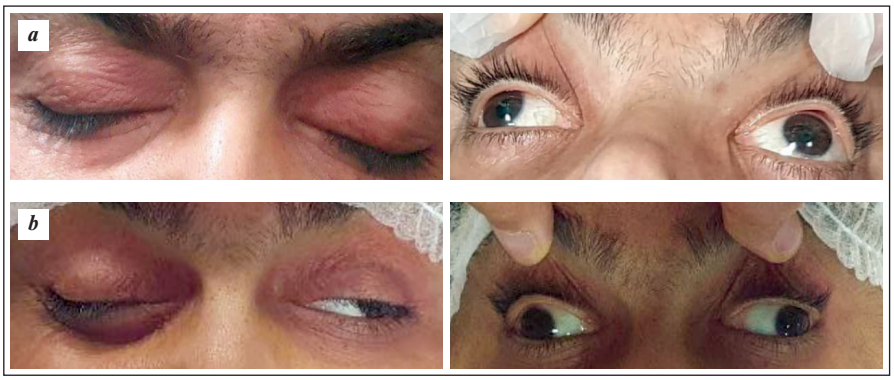

Fig. 2. *PA: Bilateral complete ptosis along with bilateral isolated oculomotor nerve palsy at admission (a). One day after the treatment with IV Dexamethasone 8 mg Q 8h the ptosis of the left eye was partially improved; although, the eye movement examinations revealed no changes (b)*[1]

[1]Цветной рисунок к этой статье представлен на сайте журнала: nnp.ima-press.net

A review on the cases of PA that are reported unitl 2023 in PubMed, demonstrates a extent of the presentations

Age / Sex	Signs and Symptoms	Laboratory Findings at Admission	Imaging Findings at Admission	Treatment	Reference
41-year-old / Female	• Acute headache • Diplopia • Nausea • Vomiting	No significant changes	CT: • Oval formation in sellar and suprasellar region • Unevenly hypodense, hyperdense material • Enhanced margin with contrast injection MRI: • Cystic sellar and suprasellar formation • T2 hyperintense • T1 hypointense • Peripheral ring enhancement with contrast, cavernous sinus infiltration • Optical chiasma compression	Surgical: Trans-sphenoidal endoscopic removal of the sellar lesion	[4]
62-year-old / Female	• Acute headache • Visual impairments (Not defined)	Not reported	CT: • Intrasellar mass with areas of intralesional hyperdensity • Peripheral contrast enhancement MRI: • Hyperintense intrasellar lesion in T1 and T2 • Peripheral contrast enhancement	Surgical: Trans-sphenoidal resection of the lesion	[4]
44-year-old / Male	• Disorientation • Confusion • Headache • Fever • Nuchal rigidity	Blood sample: ↑ WBC count ↑ Lactic Acid ↓ Hemoglobin ↓ Hematocrit ↓ Mg^{2+} ↓ Na^{+} ↓ IGF-1 ↓ LH CSF sample: • Xanthochromia ↑ WBC count ↑ PMNs ↑ Protein	MRI: • Expansile sellar turcica mass • T1 hyperintensity • Optic chiasm compression	Surgical: Transsphenoidal pituitary tumor resection Pharmaceutical: • IV Ceftriaxon • Acyclovir • Vancomycin (due to suspicion of meningitis) • Levothyroxin • Stress-dose steroids Other interventions: Fluid restriction	[6]
60-year-old / Male	• Persistent unrelieved headaches	Blood sample: ↓ TSH ↓ Free T4 ↓ Free T3 ↓ Testosterone ↓ LH ↓ IGF-I	CT: No significant changes MRI: • Loss of contrast enhancement in the pituitary lesion	Pharmaceutical: • IV Dexamethasone • Mannitol • Tramadol • Ketorolac • 3% hypertonic saline Other interventions: Fluid restriction	[10]
47-year-old / Female	• Sudden right eye pain • Right eye double vision and a squint	Blood sample: ↑ Prolactin ↑ FSH ↑ LH	MRI: • Frontal white matter chronic ischemia • Old microbleeds in left occipital and right temporal lobes • Sellar and suprasellar mass	Surgical: Transnasal, transsphenoidal resection of pituitary macroadenoma	[11]
48-year-old / Male	• Intense temporal headache • Right eye ptosis • Gaze palsy • Light response delay	Blood sample: ↑ Prolactin ↓ ACTH ↓ Cortisol ↓ LH ↓ Testosterone	CT: No significant changes MRI: • Enlarged sella • Suprasellar extension • Optic chiasm compression	Surgical: Not described. Pharmaceutical: Stress dose steroids	[12]
29-year-old / Female	• Weight gain • Fatigue • Irregular menstrual cycles • Decreased visual acuity	Blood sample: ↑ Prolactin ↑ Total cortisol ↓ LH	MRI: • Pituitary fossa cystic lesion • Optic chiasm compression	Surgical: Trans-nasal transsphenoidal resection of the lesion	[13]

Continuing of table

Age / Sex	Signs and Symptoms	Laboratory Findings at Admission	Imaging Findings at Admission	Treatment	Reference
74-year-old / Male	• Acute onset frontal headache • Eye pain with radiation posteriorly • Mild blurred vision • Transient diplopia • Vomiting	Blood sample: ↓ Na^+	CT: • Subtle ischemic changes in the left capsular basal ganglia region MRI: • Large pituitary lesion • Internal hemorrhag • Neural compression	Other interventions: Fluid restriction of 1L/day	[14]
28-year-old / Male	• Severe headache • Intermittent fever • Bilateral temporal visual field loss	Not reported	CT: • Pituitary hemorrhagic tumor with homogenous density in the sella turcica	Surgical: Not described	[15]
56-year-old / Male	• Chronic worsening frontotemporal headache • Acute left eye ptosis	No significant changes	MRI: • Sellar and suprasellar lesion with T1 hyperintensity • T2 signal void	Surgical: Pituitary adenectomy	[3]
50-year-old / Male	• Painful left eye ptosis • Slow right eye light response	No significant changes	MRI: • Pituitary fossa sellar lesion • High T1 signal at the periphery, extending suprasellar and laterally • T2 signal void	Surgical: Transsphenoidal pituitary adenectomy	[3]
56-year-old / Male	• Acute headache • Double vision • Bilateral ptosis • Bilaterally exotropic gaze with inability to adduct bilaterally • Dilated left pupil • Light response delay	Not reported	MRI: • The third cranial nerves compression by hemorrhagic bilateral pituitary adenoma	Not reported	[5]
82-year-old / Male	• Sudden binocular diplopia • Headache • Complete ptosis of both eyes • Impaired vestibulo-ocular and papillary reflexes	Blood sample: ↓ Na^+ 9-hours urine sample: ↓ Cortisol	MRI: • Macroadenoma in pituitary with hemorrhage, bordering bilateral cavernous sinuses and optic chiasm	Surgical: Trans-sphenoidal total excision of pituitary tumor	[16]

MRI is crucial for the differential diagnosis of PA. It is essential to exclude conditions like aneurysms, which present as round, hypointense lesions on T2-weighted images, and craniopharyngiomas, characterized by solid, cystic, and calcified components. Additionally, Rathke cleft cysts can be distinguished by their T1 hyperintensity and midline location [4]. Once diagnosed, PA demands prompt treatment. The optimal approach remains a subject of debate, although initial hemodynamic stabilization, resolving electrolyte abnormalities, and replacing cortisol and thyroid hormones as needed are consensual management steps [2]. Fortunately, our patient had no evidence of hemodynamic instability or symptoms of hormonal deficiency upon presentation, and her normal lab values were a reassurance to proceed to the consecutive decision of whether she would need urgent surgical treatment. Much effort has been made to compare surgical and conservative approaches to treating patients with PA. Based on the guidelines proposed by the PA guidelines development group, this decision is predicated on the main pillars of the patient's level of consciousness, visual acuity, and field defects. Ocular paresis alone isn't identified as grounds for immediate surgical treatment [7, 8]. Of note, several studies have proposed a general lack of difference in outcomes of patients who are managed surgically vs. the patients who are conservatively treated, including a recent prospective multicenter study by Mamelak et al. that demonstrated similar 3-month results between the groups mentioned above [8, 9]. Fortunately, our patient had no evidence of decreased LOC, reduced visual acuity, or visual field defects, and after consulting with the hospital's neurosurgery department, conservative treatment with high-dose steroids was chosen as the main element of her management, which led to a quick reduction in the ptosis of her left eye.

In conclusion, this case highlights the diverse clinical manifestations of PA, which can present with isolated bilateral complete third nerve palsy and dilated, non-reactive pupils. While PA typically occurs in older males and is associated with macroadenomas, this case involved a younger female with no prior adenoma history. Early diagnosis through neuroimaging, such as MRI,

is crucial in differentiating PA from other intracranial pathologies. In this case, conservative management with high-dose steroids was effective in resolving the patient's symptoms. The decision to pursue surgical intervention in PA should be based on the patient's level of consciousness, visual acuity, and field defects. As demonstrated here, an individualized approach is essential in achieving favorable outcomes in PA cases.

Statement of Ethics. The patient provided informed consent for the publication of this case report, including the use of medical history, clinical details, and diagnostic images. Patient anonymity has been preserved, and all procedures were conducted by ethical standards and institutional guidelines and the approval of the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences .

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