Pituitary apoplexy in a patient on antiplatelet therapy: A case report

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Abstract. Pituitary apoplexy is a rare but life-threatening neurosurgical emergency, typically caused by acute hemorrhage or infarction of a pituitary adenoma within the sella turcica. It presents clinically with the sudden onset of severe headache, visual impairment and ophthalmoplegia. The present study reported the case of a 45-year-old male who experienced intermittent headaches and progressive right-sided visual deterioration over two months, with acute worsening in the preceding 6 h. The patient's medical history included coronary stent implantation and the patient had been on enteric-coated aspirin therapy for ~4 months. Magnetic resonance imaging and computed tomography of the head confirmed the diagnosis of pituitary apoplexy. The patient underwent emergency endoscopic transsphenoidal surgery, leading to significant improvement in right-sided vision. At the 6-month follow-up, the patient exhibited complete recovery with no evidence of tumor recurrence on imaging. This case highlights the importance of timely diagnosis and surgical intervention in achieving favorable outcomes in pituitary apoplexy and serves as a reminder for clinicians to consider the risk of hemorrhage in patients on long-term antiplatelet therapy.

Introduction

Pituitary apoplexy (PA) is a rare clinical syndrome, occurring in ~2-12% of pituitary adenomas (1,2), a tumor with an overall incidence of 3.9-7.4 per 100,000 person-years in the general population (3). It predominantly affects individuals aged 50-69 years and exhibits a significant male predilection, with a male-to-female ratio ranging from 1.1:1 to 2.3:1 (2,4). Several factors may trigger PA, including surgery, pregnancy, thrombocytopenia, head trauma, anticoagulation, infections and other iatrogenic causes (4-7). Common symptoms include sudden, severe headache, vision loss, blindness, cranial nerve palsy, altered consciousness, hypotension, hypoglycemia and other manifestations of pituitary dysfunction. Given its acute and life-threatening nature, PA is considered a neurosurgical emergency. However, the optimal treatment remains undefined, with management primarily relying on the expertise of a multidisciplinary team. A systematic review of 708 patients with PA across 13 clinical series (1993-2024) reported that 30.6% of patients received conservative management (serial neurologic assessments, visual function monitoring, renal/metabolic surveillance with electrolyte panels, pharmacologic therapy with glucocorticoids or dopamine agonists for prolactinoma-associated cases), while 69.4% underwent surgical intervention as the primary approach (4). The current study presents a rare case of PA in a patient who had been taking aspirin for ~4 months following coronary stent implantation and discusses its clinical features, management and outcome.

Case report

In November 2022, a 45-year-old male was admitted to Chongqing General Hospital (Chongqing, China) with a 2-month history of intermittent headaches and progressive right-sided vision impairment, which had acutely worsened over the past 6 h. At 4 months before admission, the patient had been diagnosed with acute myocardial infarction due to triple-vessel coronary artery disease and subsequently underwent coronary stent implantation. Following the procedure, the patient was placed on enteric-coated aspirin tablets for antiplatelet therapy. In addition, the patient had a history of left eye trauma at the age of 23 years, resulting in severe visual impairment, with only light perception remaining.

On initial physical examination, the left eye had no light perception, while visual acuity in the right eye was limited to finger counting at a distance of 30 cm. On the second day of hospitalization, endocrine evaluation revealed decreased levels of prolactin (1.74 ng/ml; normal range, 2.64-13.13 ng/ml) and testosterone (1.23 ng/ml; normal range, 1.75-7.81 ng/ml), while all other hormonal parameters were within normal limits. The coagulation profile obtained on hospital day 1 included normal values for all measured parameters: Prothrombin time, 10.40 sec (normal range, 9-14 sec); activated partial

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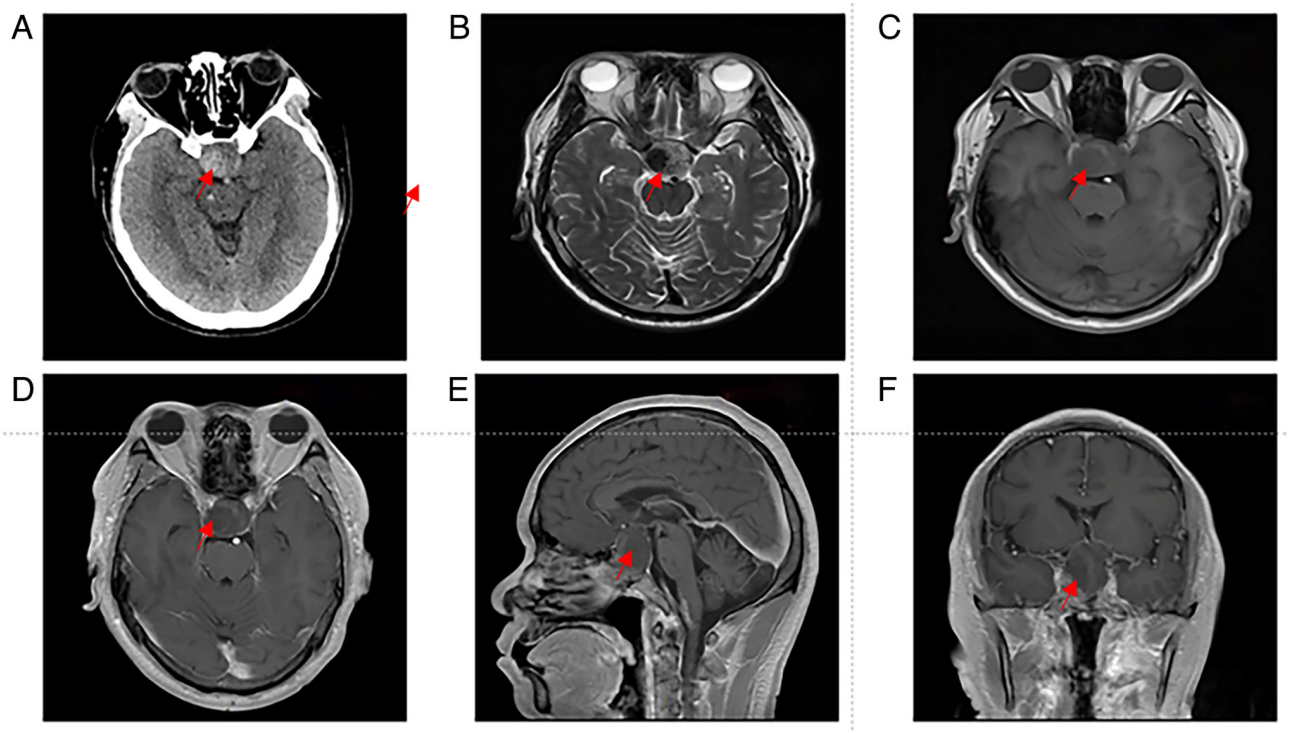

Figure 1. Preoperative images. (A) Preoperative computed tomography. (B-F) Preoperative magnetic resonance imaging. (B) T2-weighted image. (C) T1-weighted image. Gadolinium-enhanced (D) transverse, (E) sagittal and (F) coronal images. The red arrows indicate the lesion.

thromboplastin time, 31.40 sec (normal range, 20-40 sec); thrombin time, 12.50 sec (normal range, 10-18 sec); fibrinogen, 4.54 g/l (normal range, 2-4 g/l); and international normalized ratio, 0.93 (normal range, 0.80-1.20), collectively indicating normal coagulation function. The complete blood count on the first day of hospitalization demonstrated increased levels of white blood cells ($11.78x10^9$/l; normal range, $3.50\text{-}9.50x10^9$/l) with otherwise normal parameters, including erythrocytes ($5.12x10^{12}$/l; normal range, $4.30\text{-}5.80x10^{12}$/l), hemoglobin (149 g/l; normal range, 130-175 g/l), platelets ($191x10^9$/l; normal range, $100\text{-}300x10^9$/l), and platelet indices: Mean volume (11.60 fl; normal range, 9-13 fl), distribution width (16.80 fl; normal range, 9-17 fl), plateletcrit (0.22%; normal range, 0.11-0.28%) and large cell ratio (38.40%; normal range, 11-45%). The increased white blood cells indicated that the patient was in a stress state following disease onset.

Preoperative visual field assessment was not performed. Computed tomography (CT) of the head performed on hospital day 1, revealed a sellar mass measuring 2.7x2.9x4.1 cm, exhibiting iso- to slightly hyperdense characteristics (Fig. 1A). On the second day of hospitalization, magnetic resonance imaging (MRI) showed an irregular mass in the sellar region, measuring ~2.6x2.9x4.2 cm (Fig. 1B-F). The lesion appeared iso- to slightly hypointense on T1-weighted imaging (Fig. 1C) and iso- to slightly hyperintense on T2-weighted imaging (Fig. 1B), while post-contrast imaging revealed localized nodular enhancement (Fig. 1D-F). After comprehensive preoperative evaluation, the patient underwent transsphenoidal endoscopic total resection of the lesion on the second day of hospitalization.

On postoperative day 3, CT scans showed no evidence of bleeding in the sellar region (Fig. 2A). To prevent coronary stent thrombosis, the patient was started on low-molecular-weight heparin. On postoperative day 3, endocrine evaluation revealed decreased levels of cortisol (2.16 μg/dl; normal range, 4.26-24.85 μg/dl), adrenocorticotropic hormone (2.68 pg/ml; normal range, 7.2-63.4 pg/ml) and human thyroid-stimulating hormone (0.322 μIU/ml; normal range, 0.560-5.910 μIU/ml), while all other hormonal parameters remained within normal limits. To manage adrenal insufficiency, the patient was promptly initiated on intravenous hydrocortisone (100 mg) on postoperative day 3. Additionally, a daily oral prednisone regimen was prescribed, with 5 mg administered in the morning and 2.5 mg in the afternoon. By postoperative day 5, the patient reported significant improvement in right-sided vision. Visual field testing showed a right-eye visual acuity of 0.5, with 3/4 visual field defects, while light perception in the left eye was restored. On postoperative day 9, endocrine evaluation revealed slightly decreased free triiodothyronine (3.31 pmol/l; normal range, 3.53-7.37 pmol/l) and free thyroxine (6.52 pmol/l; normal range, 7.98-16.02 pmol/l), while other hormonal levels remained normal. Consequently, prednisone was discontinued.

Surgically resected tumor tissues underwent routine histopathological examination with hematoxylin and eosin staining. Subsequent to specimen collection, tumor tissues were fixed in 4% formaldehyde at room temperature for 24 h, followed by paraffin embedding. The embedded blocks were sectioned into 4-μm slices and deparaffinized in xylene at 60˚C for 2 h. For staining, sections were sequentially treated with 0.5% hematoxylin (3 min) and 0.5% eosin (3 min) at room temperature. Histopathological evaluation was subsequently performed using light microscopy, with representative microphotographs captured for documentation. As indicated in Fig. 3, a pituitary neuroendocrine tumor was confirmed, which was likely a null cell adenoma.

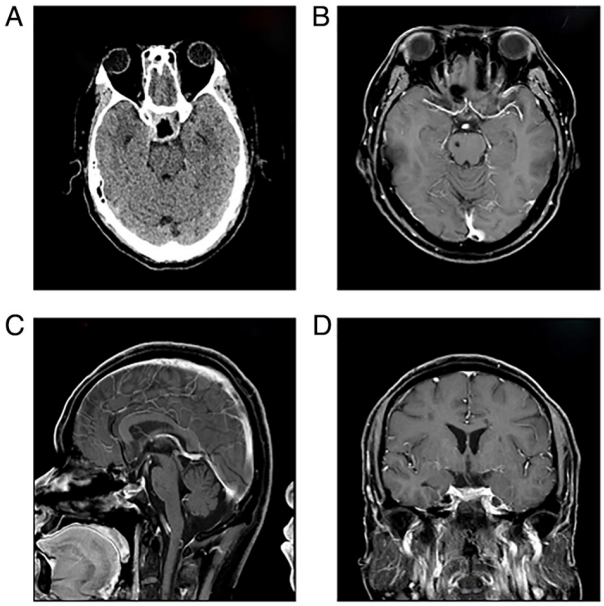

Figure 2. Postoperative imaging. (A) Postoperative computed tomography on postoperative day 3. (B-D) Postoperative gadolinium-enhanced magnetic resonance imaging at 6 months after surgery. (B) Transverse, (C) sagittal and (D) coronal images.

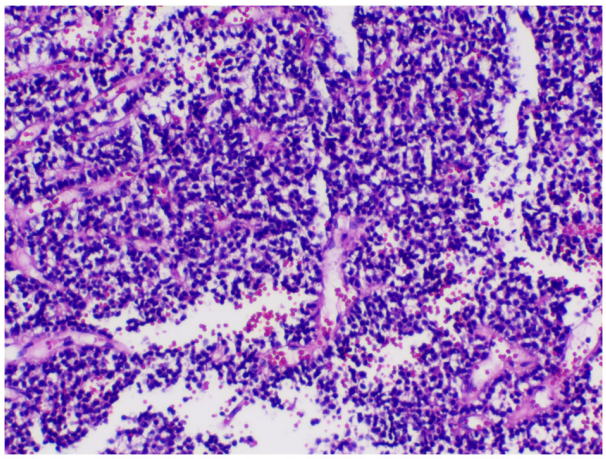

Figure 3. Image of histopathology (hematoxylin and eosin staining; magnification, x200).

At 6 months post-operatively, follow-up MRI showed no evidence of tumor recurrence (Fig. 2B-D), and endocrine assessment confirmed the recovery of pituitary function. However, the patient declined further vision and visual field examinations, stating that he had fully recovered. At 1 year post-operatively, a telephone follow-up indicated that the patient remained asymptomatic and continued to decline additional evaluations, including MRI, vision and visual field examinations, and endocrine evaluation.

Discussion

Apoplexy is a rare but serious complication of pituitary adenomas. Several case reports have documented occurrences of PA following cardiac surgery, involving cardiopulmonary bypass, mitral and aortic valve replacement and stent placement (7-12). Table I shows the major characteristics of previous cases. All patients were male with a minimum age of 53 years. With the exception of one case managed conservatively, all patients underwent surgical intervention for PA, with operative timing ranging from 2 h to 2 weeks post-diagnosis. Postoperative assessment revealed functional recovery in all surgical cases, although the extent of improvement varied significantly among individuals. The key distinguishing feature of the present case compared to previous reports is the timing of PA onset and different triggering factors driving PA development. While prior cases typically occurred within the immediate postoperative period, the present study reported a rare case of PA in a patient who had been taking aspirin for ~4 months following coronary stent implantation. Regarding previously reported perioperative PA occurrences during cardiac surgery, it was hypothesized that cardiac surgery may increase the susceptibility of abnormal pituitary tissue to hypoperfusion or ischemia, while also elevating the risk of hemorrhage from the fragile vasculature of adenomas, particularly due to heparin-induced anticoagulation (2,10). In the present case, the patient's aspirin use may represent one of the contributing factors to PA development. Aspirin (acetylsalicylic acid) is a well-established inhibitor of platelet aggregation (13,14). Its primary mechanism involves the irreversible inhibition of cyclooxygenase (COX) activity within platelets, specifically targeting the COX-1 isoform. COX-1 catalyzes the conversion of arachidonic acid to thromboxane A2 (TXA2). TXA2 serves as a crucial mediator of platelet activation and vasoconstriction. Deficiency in TXA2 production significantly inhibits both platelet aggregation and activation processes. Aspirin exerts its effect by acetylating a specific serine residue in the COX-1 active site, thereby permanently blocking TXA2 synthesis. This irreversible inhibition persists throughout the platelet's lifespan.

The diagnosis of PA can be readily confirmed through clinical symptoms, endocrine evaluations and imaging studies. However, the optimal management approach remains a subject of ongoing debate. Earlier guidelines from the UK recommended surgical decompression for patients presenting with significant neuro-ophthalmic symptoms or reduced consciousness (15). By contrast, conservative management with close monitoring is generally preferred for patients without neuro-ophthalmological symptoms, hemodynamic stability or altered consciousness (4). A meta-analysis comparing 259 surgical and 198 conservative cases, along with a multicenter international prospective registry study from 2024 involving 67 surgical and 30 medical cases, demonstrated that both surgical and non-surgical approaches can lead to the restoration of visual and endocrine functions, yielding comparable clinical outcomes in PA (16,17). The impact of surgical timing on neurological recovery remains an area of active investigation, though findings are inconsistent. Certain studies suggest that early surgical intervention significantly improves visual acuity, visual fields and pituitary function recovery (18-20), while others report no significant effect of surgical timing on visual outcomes in patients with PA (21,22). These discrepancies may be attributed to factors such as variations in sample size, differing definitions of early vs. late surgery (based on the interval

Table I. Major characteristics of previous studies.

Author/s, year	Age, years	Sex	Cardiac surgery	Time after surgery	Treatment for PA	Surgery time after cardiac surgery	Outcome of PA	(Refs.)
Semenov *et al*, 2000	82	Male	Coronary artery bypass surgery	Immediate post-operative	Transsphenoidal surgery	13 days	Right visual field defect and need for hormone replacement therapy at 15-month follow-up	(7)
Cooper *et al*, 1986	63	Male	Coronary artery bypass surgery	12 h	Transsphenoidal surgery	2 weeks	Ophthalmoplegia resolved at 2-month follow-up	(8)
	62	Male	Mitral and aortic valve replacement	12 h	Transsphenoidal surgery	21 h	Sixth cranial nerve paresis and slight right ptosis at three weeks post-operatively	
	55	Male	Coronary artery bypass surgery	Immediate post-operative	Transsphenoidal surgery	18 h	Slight ptosis at 2-month follow-up	
Fuchs *et al*, 1998	53	Male	Coronary stent implantation	NA	Conservative management	NA	Ophthalmoplegia improved markedly at 3-month follow-up	(9)
	65	Male	Coronary stent implantation	On postoperative day 1	Transsphenoidal surgery	Emergency operation	Right eye blindness and left visual field defect at 3-month follow-up	
Loubani *et al*, 2001	60	Male	Coronary artery bypass surgery	On postoperative day 1	Surgery	On postoperative day 5	Minor visual defect on the right. MRI shows complete resolution of the pituary adenoma at 1-year follow-up	(10)
Mattke *et al*, 2002	64	Male	Coronary artery bypass surgery	Immediate post-operative	Transsphenoidal surgery	9 days	Visual acuity and visual field defects were both markedly improved after surgery	(11)
Chen *et al*, 2004	62	Male	Coronary artery bypass surgery	3 h	Transsphenoidal surgery	4 days	Almost recovery and no residual pituitary tumor at four-month follow-up	(12)

PA, pituitary apoplexy; NA, not available.

between symptom onset and surgery) and potential biases inherent in observational studies. Given the rarity of PA, conducting randomized controlled trials is particularly challenging. However, despite being derived from observational research, these findings provide valuable insights into PA management.

In the present case, emergency surgical intervention was performed at 14 h after symptom onset. The decision to proceed with surgery was based on four critical factors: i) The patient had severe bilateral visual impairment, with the right eye affected by PA and the left eye already compromised due to prior trauma. Emergency transsphenoidal decompression was prioritized to maximize the chances of visual recovery in the PA-affected right eye; ii) although spontaneous tumor regression following PA has been reported in certain studies (2,16), there are no reliable predictors to identify patients who would benefit from conservative management; iii) the procedure was performed by a highly experienced neurosurgical team specializing in pituitary surgery, significantly reducing the risk of complications such as cerebrospinal fluid leakage or iatrogenic damage to functional pituitary tissue; and iv) no surgical contraindications were identified during the comprehensive preoperative evaluation. As anticipated, the patient experienced significant visual improvement without any major postoperative complications.

In conclusion, PA is a rare complication, particularly in this case, where it occurred after nearly four months of continuous aspirin use following coronary stent implantation. However, complete recovery was achieved through a multidisciplinary approach, including transsphenoidal endoscopic surgery, endocrine management and cardiovascular therapy. This case also broadens the understanding of the pathophysiological mechanisms and temporal occurrence of PA. Traditionally associated with the perioperative period due to intraoperative heparinization and hemodynamic fluctuations, PA may also develop after prolonged exposure to antiplatelet therapy, suggesting a potential risk factor in its pathogenesis. While routine screening and prophylactic measures may not be cost-effective given the low incidence of pituitary adenomas and PA, it is crucial for clinicians to educate patients undergoing long-term antiplatelet therapy after coronary stent implantation. If symptoms suggestive of PA-such as headaches or visual disturbances-arise, prompt referral to a high-volume pituitary disease center with specialized expertise is essential.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

CS, DZ, JW, JL and NW designed the study. CS, DZ, JW and NW collected and analyzed the clinical data. CS and DZ reviewed previous cases. CS, DZ, JW, JL and NW wrote and revised the paper. CS and NW confirmed the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All procedures were performed in in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of this manuscript and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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