First described in case reports by Bailey in 1898,\textsuperscript{1} Bleibtreu in 1905,\textsuperscript{2} and Dingley and Lond in 1932,\textsuperscript{3} and finally described as a clinical syndrome by Brougham and colleagues in 1950,\textsuperscript{4} pituitary apoplexy refers to the potentially life-threatening acute hemorrhage or infarction of a pituitary tumor. Its presentation, related to meningeal irritation and compression of the optic chiasm and parasellar structures, is variable\textsuperscript{5-7} but typically includes the sudden onset of headache, nausea, vomiting, ophthalmoplegia, altered mental status, and hormonal dysfunction.\textsuperscript{8} Pituitary apoplexy has an incidence of 0.6-16.6\% in pituitary adenomas\textsuperscript{6,9-12} and may occur spontaneously but is also associated with trauma, anticoagulation, radiation therapy, mechanical ventilation, and surgery.\textsuperscript{13} Pituitary apoplexy after cardiac surgery is an exceptionally rare perioperative complication, and all but one reported case have been managed surgically. Additionally, while spontaneous remission of endocrinopathies following pituitary apoplexy of hormonally-active tumors is well-described,\textsuperscript{14-17} resolution of non-functioning tumors following apoplexy is rare.\textsuperscript{8,18,19} A case is presented in which no surgical management of pituitary apoplexy was required as the apoplectic event led to the spontaneous resolution of a previously undiagnosed nonfunctioning pituitary macroadenoma following cardiac surgery.

A 71 year-old man with a past medical history significant for type II diabetes mellitus, hypercholesterolemia, and unstable angina underwent five vessel coronary artery bypass grafting (CABG) with no intraoperative complications. The patient was anticoagulated with intravenous heparin (400 units/kg) and then put on the cardiopulmonary bypass machine for 122 minutes, with a cross clamp time of 78 minutes. During the bypass procedure, the hematocrit, mean arterial pressure, and blood flow decreased to as low as 18\%, 44 mmHg, and 3.8 L/minute/metre\textsuperscript{2}, respectively. Despite reversal with protamine intraoperatively and in the post-operative recovery room, his coagulation profiles remained elevated (normal values in parentheses: PT 19.4 (10.6 – 13.5), INR 2.0 (0.8 – 1.2), and APTT 43.7 (22.4 – 38.8)). He did not receive anticoagulation post-operatively but was started on clopidogrel bisulfate. He developed a severe headache on the night immediately after the operation and in the morning complained of double vision. He was found to be drowsy with a right third nerve palsy – he demonstrated ptosis on the right with impaired ability to adduct or elevate the right eye and had a dilated and non-reactive right pupil. There was no evidence of papilledema and he had normal visual fields to confrontation.

An urgent computed tomography (CT) scan of the brain demonstrated a sellar mass with suprasellar extension. There was no hemorrhage, attenuation, or alteration within this lesion, and the patient was started on dexamethasone. The patient’s headache gradually improved over the next 24 hours. A non-contrast magnetic resonance imaging scan performed on the day after CABG demonstrated a mass in the sella turcica with suprasellar extension and increased signal intensity peripherally indicative of hemorrhage. Imaging performed 2 months post-cardiac surgery (C, D) demonstrated reduction in the size of the sellar tumour. By 7 months post-cardiac surgery, there was complete resolution of the tumour (E, F).

**Figure:** Coronal (A) and sagittal (B) non-contrast magnetic resonance images performed on the day after CABG demonstrated a mass in the sella turcica with suprasellar extension and increased signal intensity peripherally indicative of hemorrhage. Imaging performed 2 months post-cardiac surgery (C, D) demonstrated reduction in the size of the sellar tumour. By 7 months post-cardiac surgery, there was complete resolution of the tumour (E, F).
which appeared to be a pituitary macroadenoma. Magnetic resonance imaging (MRI) (Figure A, B) demonstrated that the tumour was causing mild compression of the optic chiasm and extended to the cavernous sinuses bilaterally without encasing either carotid artery. On T2-weighted images, the lesion was isointense but peripherally showed increased signal intensity on T1-weighted images suggestive of hemorrhage.

The patient was treated with dexamethasone (4 mg intravenously q6h) because of presumed cortisol deficiency. Surgical decompression of the pituitary fossa was deferred since the patient’s third nerve palsy was improving on a daily basis. Laboratory investigations subsequently revealed low testosterone but no other indications of pituitary dysfunction (normal values in parentheses): thyroid stimulating hormone (TSH) 2.27 mU/L (0.4-5.25), free T4 9.2 pmol/L (10.3-25.7), prolactin 2µg/L (3-15), testosterone <0.7 pmol/L (7.3-26.0), FSH 1 U/L (1.4-18.1), LH <1 U/L (1.5-9.3), growth hormone (GH) 5.3 µg/L (0-3), cortisol 344 nmol/L (250-850). The patient was discharged from hospital on the eighth post-operative day on a tapering dose of dexamethasone since his cortisol levels were within the normal range.

Follow-up examination two months post-operatively found that the patient’s third nerve palsy had resolved and his neurological examination was normal, including normal visual fields to confrontation. Imaging studies (Figure C, D) revealed significant reduction in the size of the pituitary macroadenoma with no compression of the optic chiasm. Laboratory tests again revealed low testosterone (1.7 pmol/L) and so the patient was started on Androgel. Repeat imaging seven months post-operatively revealed no evidence of the macroadenoma, and imaging two and three years following cardiac surgery confirmed its persistent absence (Figure E, F).

DISCUSSION

As a perioperative complication of cardiac surgery, pituitary apoplexy is rare and has been reported hitherto in only 21 cases since the 1950s.20-35 A pathological study26 suggested that the incidence of pituitary apoplexy following cardiac surgery is likely more common than has been reported hitherto; the pituitaries of 15.2% of patients who died within ten days of cardiac surgery demonstrated ischemic necrosis compared to unselected autopsy cases in which only 1.4% showed similar pituitary abnormalities.

To the best of our knowledge, there is only one reported case in which pituitary apoplexy associated with cardiac surgery is documented to have led to spontaneous complete resolution of a pituitary macroadenoma. Loubani and Galliñanes27 reported the case of a 60-year-old man who developed bilateral blindness and pupillary meiosis and dissociated eye movements with alternating right and left divergence the day after elective CABG. Although magnetic resonance imaging on the first post-operative day showed only an enlarged pituitary gland with isointense signal on the T1- and T2-weighted images, repeat imaging the next day demonstrated hemorrhage into a pituitary infarction. The patient was treated with hormone-replacement therapy and gradually recovered vision over the next week in hospital. By one year post-cardiac surgery, the patient had only a minor visual field defect in the right lower temporal field and imaging demonstrated complete resolution of the pituitary adenoma. Bhattacharyya and colleagues22 have described the case of a 56-year-old man who underwent CABG with no intraoperative or immediate post-operative complications. He presented three months post-surgery with symptoms of hormone deficiency. Computed tomography demonstrated recent hemorrhage in a pituitary adenoma. He was treated medically with hormone replacement therapy, but no imaging evidence was provided of complete resolution of the tumour. Additionally, Altezani and colleagues21 have shown considerable decrease in the size, although not complete resolution, of a pituitary adenoma following apoplexy managed conservatively in a 72-year-old man after redo CABG surgery.

The etiology of pituitary apoplexy associated with cardiac surgery is likely multifactorial. Pituitary adenomas are predisposed to hemorrhage and necrosis. Although typically slow-growing, adenomas can grow beyond their blood supply and can compress the hypothalamo-hypophysial portal vessels that supply them.36,37 Vasculopathic characteristics of adenoma blood vessels also render them particularly susceptible to apoplexy.36,37 Pathological examination of tumour vessels has shown abnormal sinuoids, thin-walls, hyaline changes and fibrinoid necrosis,28,37,38 all of which cause the vessels to be abnormally fragile and thus more susceptible to injury.5,8,39-40 Indeed, up to 25% of patients with pituitary adenomas have been found to have either imaging or surgical confirmation of hemorrhage or necrosis.7

Various aspects of cardiac surgery itself also predispose adenomas to apoplexy. During the bypass procedure, hematocrit, mean arterial pressure, and blood flow can drop to as low as 20%, 30 mmHg, and less than 2.2 L/minute/metre², respectively.24 Transient increases in intracranial pressure associated with positive pressure ventilation also contribute to reduced cerebral perfusion pressure.39 Hypotension predisposes adenomas to infarction and subsequent hemorrhage and was the postulated mechanism of apoplexy in other situations, such as following hemodialysis,41 large volume liposuction surgery,42 and abdominal aortic aneurysm surgery.43 Hemodilution with crystalloid during bypass can also decrease plasma oncotic pressure and result in an increase in interstitial pressure in adenomas.24,28 Ischemia of the pituitary adenoma may result from embolization of atheroma, air bubbles, or pieces of plastic from the bypass tubing.44,45 Biouss and colleagues39 suggest that surgical stress associated with cardiac surgery may cause excessive stimulation of the pituitary due to the production of larger amounts of steroids, and Semple and colleagues36 postulate that any increase in the metabolic activity of tumours can diminish their blood supply. Lastly, anticoagulation associated with bypass surgery additionally predisposes adenomas to hemorrhage. Heparin is used for anticoagulation before the onset of bypass, but heparin reversal is incomplete in over half of patients.46 Decreased platelet counts and partial platelet dysfunction are also noted during bypass.24 The use of thrombolytic and antithrombotic medications, such as aspirin, heparin, clopidogrel, ticlopidine, and IIb-IIIa receptor antagonists, during acute coronary syndromes has been associated with pituitary apoplexy,38,47,48 and, similarly, has been suggested to be important in the development of apoplexy after cardiac surgery.20-35 It is possible that a combination of hypotension, reduced blood flow, decreased hematocrit, and...
anticoagulation during our patient’s bypass procedure led to the pituitary apoplexy.

Several practical guidelines to management of pituitary apoplexy have been suggested. Immediate surgical treatment is suggested in patients with an impaired level of consciousness, blindness, or progressively deteriorating vision. Surgical treatment is also recommended if patients do not demonstrate clinical improvement within the first few days after apoplexy. Among the concerns that are especially relevant for surgical management of pituitary apoplexy post-cardiac surgery are those related to performance of the neurosurgical procedure while a patient may still be anticoagulated as part of their post-cardiac surgery care and the increased risk of perioperative morbidity and mortality associated with performing a surgical procedure soon after cardiac surgery. Conservative management is appropriate for patients with rapidly improving, absent, or only mild neuro-ophthalmological signs. Regardless of the type of management, patients require close monitoring and long-term follow-up to identify tumour recurrence, which has been reported to be as high as 6% and 22% for patients treated surgically or only medically, respectively. Our patient continues to be seen in follow-up on an annual basis with repeat magnetic resonance imaging in order to monitor for possible tumour recurrence.

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