

Pituitary apoplexy after cardiac surgery in a patient with subclinical pituitary adenoma: case report with review of literature

Udar przysadki po operacji serca u chorego z podklinicznym gruczolakiem przysadki: opis przypadku i przegląd piśmiennictwa

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Abstract

Pituitary adenoma infarction associated with cardiac surgery occurs rarely but it is a serious, life-threatening acute clinical event. Several mechanisms have been proposed but no direct cause has been clearly identified.

We report a case of pituitary apoplexy occurring in a 74-year-old patient 6 hours after cardiac surgery. The patient presented with confusion, unilateral ptosis and ophthalmoplegia. Neurological examination revealed right oculomotor nerve palsy and decreased level of consciousness. Magnetic resonance imaging showed a hemorrhagic and necrotic pituitary macroadenoma. After prompt endocrinological replacement therapy with hydrocortisone and levothyroxine, the confusion of the patient resolved. Removal of a non-functional macroadenoma with large necrotic areas resulted in full recovery. The physician should be aware of pituitary adenoma infarction after open cardiac surgery and should remember that it can be fatal or cause permanent neurological or endocrine damage without proper treatment. Surgical and endocrine treatment can be life-saving procedures.

Key words: pituitary apoplexy, Sheehan's syndrome, cardiac surgery, pituitary adenoma.

Streszczenie

Zawał w obrębie gruczolaka przysadki związany z operacją serca występuje rzadko, ale jest stanem zagrożenia życia. Wskazywano na kilka mechanizmów wystąpienia tego powikłania, ale dotąd nie określono jednoznacznej przyczyny.

Przedstawiono przypadek udaru przysadki, który wystąpił u 74-letniego mężczyzny po 6 godz. od operacji serca. U chorego zaobserwowano zmęczenie, jednostronne opadnięcie powieki i zaburzenia gałkoruchowe. W badaniu neurologicznym stwierdzono porażenie prawego nerwu okoruchowego i zaburzenia przytomności. W badaniu za pomocą rezonansu magnetycznego uwidoczniło gruczolaka przysadki ze zmianami krwotocznymi i martwiczymi. Zaburzenia świadomości ustąpiły po niezwłocznym leczeniu hydrokortyzonem i lewotyroksyną. Usunięcie nieczynnego wydzielniczo gruczolaka z dużymi obszarami martwicy spowodowało powrót do zdrowia.

Należy pamiętać o zawale w obrębie gruczolaka przysadki jako powikłaniu operacji na otwartym sercu. Nieleczona, choroba ta może doprowadzić do zgonu lub trwałych następstw neurologicznych bądź endokrynologicznych. Leczenie chirurgiczne i endokrynologiczne może być w tej sytuacji działaniem ratującym życie.

Słowa kluczowe: udar przysadki, zespół Sheehana, operacja serca, gruczolak przysadki.

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Introduction

Most cases of pituitary apoplexy (60-80%) occur spontaneously in asymptomatic patients.

Common predisposing factors include head trauma, hypotension, hypertension, pituitary irradiation history, cardiac surgery, anticoagulant therapy, treatment with dopamine agonists, pituitary stimulation tests and pregnancy [1,2].

Hypopituitarism developing after coronary bypass surgery, however, is a rare but known phenomenon [3]. One of the plausible pathophysiological mechanisms suggests that the fall of arterial blood pressure induces ischaemia followed by infarction of the pituitary gland [4]. A variety of clinical symptoms associated with pituitary apoplexy have been described including headache, lethargy, confusion, obtundation, Addisonian crisis, unilateral ptosis, myosis, hemiparesis, visual field deficits and ophthalmoplegia [5,6]. Prevalence of the disorder is 10 times greater in men [6].

It should be kept in mind that pituitary apoplexy can mimic tumour apoplexy, ischaemic changes or normal pituitary gland pathology such as Sheehan syndrome or Rathke cleft cyst haemorrhage [1,7].

Pituitary apoplexy occurs in less than 5% of all surgically resected adenomas (range 0.6-10%; mean 2%) [1]. For unknown reasons, macroadenomas carry a higher risk for clinically evident apoplexy than microadenomas [7].

Mattke *et al.* reviewed reports of all 15 cases of pituitary apoplexy after cardiac surgery in 2002 [8]. Pituitary infarction may present in many different ways, ranging from the entirely silent to florid neuro-ophthalmological features of apoplexy. It may occur in a normal or adenomatous pituitary gland [9]. The acute neuro-ophthalmological complications present within 48 hours of coronary artery bypass grafting (CABG). This is presumably secondary to necrosis, haemorrhage or acute swelling into a pre-existing pituitary tumour [10].

Hypogonadism after a few months of CABG is typically the delayed presentation of pituitary infarction. Microemboli during bypass, non-pulsatile flow and haemodynamic changes in the brain during bypass are mechanisms blamed for pituitary infarction after CABG [10,11]. Decreased tissue perfusion pressure results in ischaemic necrosis of the anterior part of the pituitary gland, and consequently low prolactin levels. Patients with normal or elevated serum prolactin levels at presentation tend to have less severe hypopituitarism;

the ones without hypopituitarism have greater chance for a full recovery of pituitary functions after decompressive surgery [1,7]. The most common symptom appears to be headache, followed by visual deficits, ophthalmoplegia or ptosis, anisocoria, nausea, alteration in mental status, meningismus, hemiparesis and fever in order of decreasing frequency [8,12].

We present a case of pituitary apoplexy that developed insidiously as a result of pre-existing pituitary adenoma infarction which occurred after CABG.

Case report

A 74-year-old man was referred to our department 6 hours after open cardiac surgery due to debility and visual problems. Three-vessel CABG was performed for extensive coronary artery disease. A saphenous vein graft was also inserted. The procedure was uneventful but after 6 hours the patient was still confused and woke up too late after general anaesthesia. The plasma sodium concentration was 125 mmol/L (normal range [NR]: 135-142 mmol/L). His body temperature was 37.8°C and blood pressure was 80/50 mm Hg.

Neurological examination revealed right ophthalmoplegia with ptosis and mydriasis on the same side. The patient was confused. Immediate computed tomography (CT) of the head was performed and showed a mass effect in the area of the pituitary gland (Fig. 1). Magnetic resonance imaging (MRI) of the pituitary gland confirmed the diagnosis of pituitary macroadenoma with areas of haemorrhage and infarction (Fig. 2). The evaluation of serum concentration of hormones brought the following results: cortisol was 2.94 µg/dL (NR: 6.2-19.4 µg/dL), prolactin 0.4 µg/L (NR: 2.6-27.8 µg/L), luteinizing hormone 1.7 IU/L (NR: 2.3-14.9 IU/L), follicle stimulating hormone 1.6 IU/L (NR: 1-14.7 IU/L), free T3 was 1.01 µg/L (NR: 1.9-5.1 µg/L), free T4 was 0.604 µg/L (NR: 0.8-3.4 µg/L) and TSH was 0.322 IU/L (NR: 0.27-4.2 IU/L). After replacement therapy with intravenous hydrocortisone (50 mg daily) and oral levothyroxine (0.2 mg daily), the patient regained consciousness and urgent transcranial adenoma excision was performed the next morning, i.e. after 18 hours. Endoscopic transnasal transsphenoidal adenoma excision was preferred as a treatment modality because of our clinical experiences (Fig. 3).

Pathological investigation confirmed pituitary adenoma with bleeding and necrosis (Fig. 4). The patient

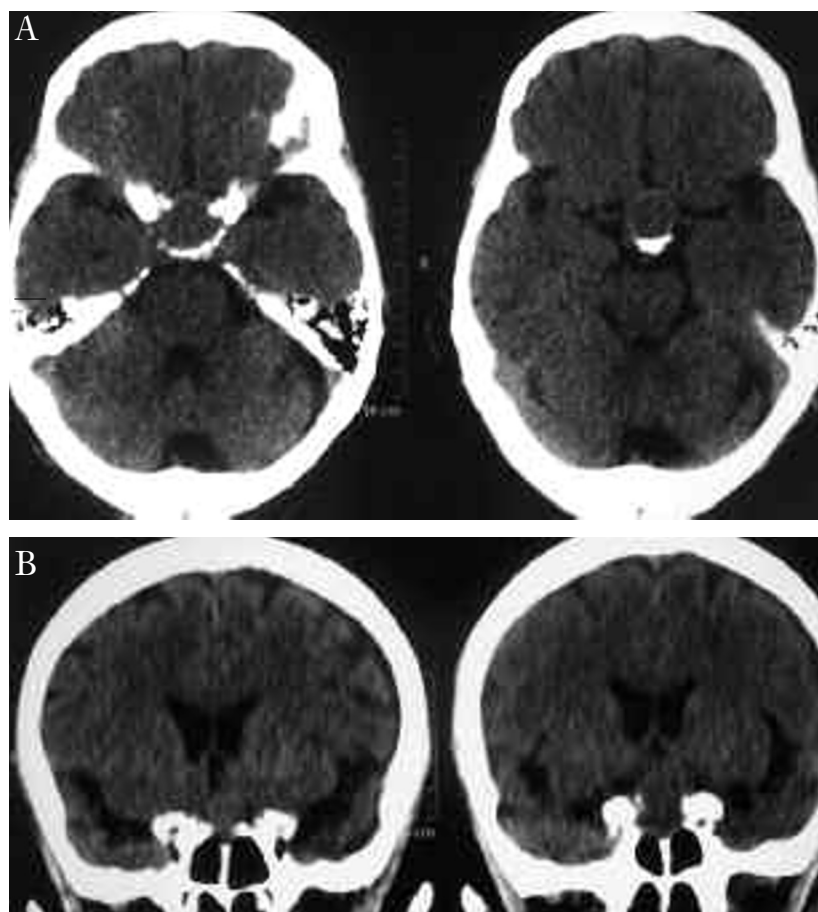


Fig. 1. Computed tomography images in axial (A) and coronal (B) plane show a mass lesion in the sellar area

experienced almost full recovery of ptosis, visual field deficits and mental changes within 2 weeks of surgery. The patient stayed in the intensive care unit (ICU) for 7 days after surgery and was discharged from hospital on the tenth postoperative day. The dose of dexamethasone treatment, which started within the preoperative period, was 4 mg intravenously every 6 hours. The therapy was tapered slowly within 2 weeks. Currently, he receives replacement treatment with low dose levothyroxine (0.1 mg daily) and his extraocular movements are normal. Blood levels of cortisol and pituitary hormones were within normal ranges after one month.

Discussion

There are many theories about pituitary apoplexy but the pathogenesis still remains unclear. Pituitary tumours are known to bleed 5.4 times more than other intracranial tumours. According to one theory, the enlarged pituitary tumour compresses the vascular

supply, causing ischaemia and necrosis both of the gland and the tumour. Others suggest that the critical perfusion pressure of the adenomas is below normal gland arterial pressure, so instantaneous changes in perfusion pressure cause the adenoma infarction. Yet another explanation suggests that the increase of the blood supply because of the tumour enlargement results in the ischaemic necrosis and secondary haemorrhage [1,7].

Sheehan described pituitary apoplexy during gestation which results in hypopituitarism similar to our case. Careful perioperative hormone supplementation is necessary for patients with Sheehan's syndrome [13].

Radiation therapy, trauma, anticoagulation, pregnancy after induction of ovulation with clomiphene, prolonged coughing, positive-end pressure ventilation and others have been cited as causes of apoplexy [14]. Anticoagulation is known as a precipitating factor but Levy *et al.* argued that despite the large number of patients treated with anticoagulation, pituitary apoplexy remained a rare finding [15]. We all agree that the number of non-surgical patients who received anticoagulation

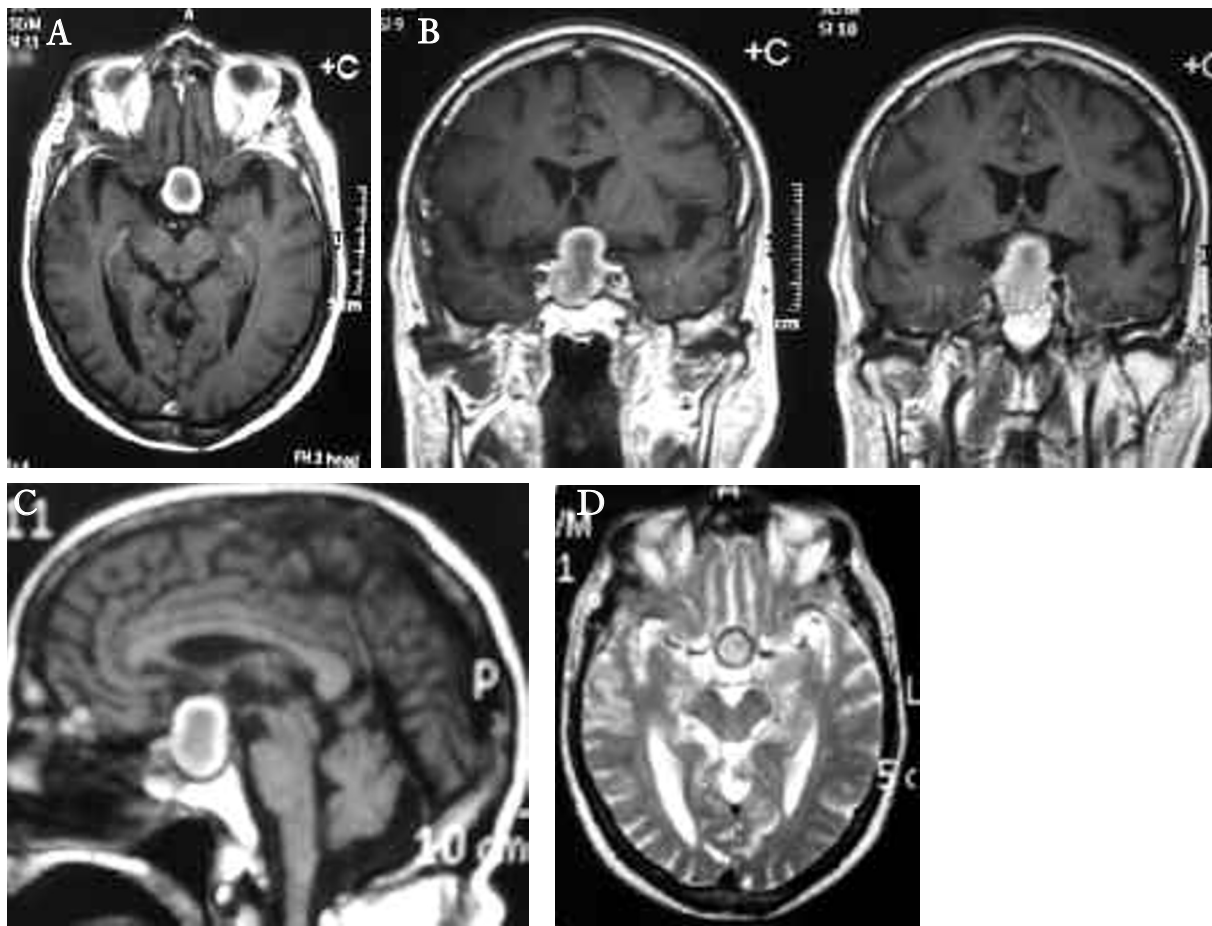


Fig. 2. T1-weighted MR images in axial (A) and coronal (B) plane after gadolinium injection reveal necrotic area surrounded by contrast agent; T1-weighted image in sagittal plane (C) after gadolinium injection shows the suprasellar dumbbell-shaped lesion encircled with contrast agent; (D) T2-weighted MR image shows the supra-sellar lesion

is much larger than that of patients who had CABG with CPB (cardiopulmonary bypass).

Nowadays, the frequency of CABG surgery is increasing. The number of operations performed in the United Kingdom has risen steadily from 16 000 in 1990 to 22 000 in 1995; mortality fell from 3.7% to 2.7% at the same time [9]. Pituitary apoplexy after CABG is a very rare perioperative complication but it has been reported since the 1960s [9]. Kovacs and Yao reported their study on necropsy. They found pituitary necrosis in 15% of patients who died 10 days within bypass surgery [9,16]. During cardiac surgery, cardiopulmonary bypass-induced cerebral oedema may contribute to the critical enlargement of silent pituitary adenomas. Cardiopulmonary bypass may also cause infarction or haemorrhage in pituitary adenomas. The main reason behind this condition may be increased

susceptibility to hypoperfusion or ischaemia of the abnormal pituitary tissue or an increased risk of bleeding as a result of anticoagulation.

Levy *et al.* reported that non-pulsatile flow, low perfusion pressure during CABG surgery, coagulation problems and haemodilution increase the risk for pituitary apoplexy events. They suggested that off-pump technique during CABG surgery can decrease the apoplexy risk by maintaining pulsatile flow [15].

Mou *et al.* reported a study about immuno-histochemical analysis of the different hormone types of pituitary tumours and their immunological target expressions. They found out that proliferating cell nuclear antigen (PCNA) was trustworthy as a cell proliferation marker, and its expression was significantly higher in patients with apoplexy than in those without apoplexy for all hormone types of tumours except for prolactin-



Fig. 3. Postoperative coronal T1-weighted MR image

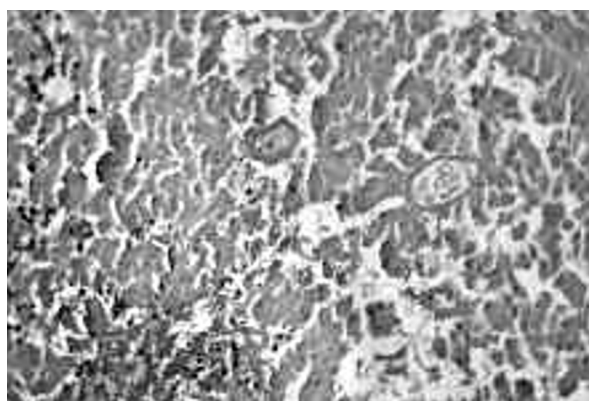


Fig. 4. Pathology shows necrotic neoplasm with high vascularity and papillary pattern. Collapsed reticulin roof monotonous cells with spherical or oval nucleus in addition to focal calcification are present. This specimen demonstrates the cell characteristics of a pituitary adenoma with areas of necrosis and haemorrhage

secreting tumours. They concluded that increased PCNA expression was an important immunological factor for apoplexy of pituitary tumours [7,17].

Pituitary apoplexy occurs in 2-10% of all pituitary adenomas. It is reported that apoplexy in non-secreting pituitary adenomas may be seen in 45% of all pituitary tumours; Mou *et al.*, however, concluded that secreting adenomas are more risky [1,7,17].

The manifestations of pituitary apoplexy range from visual changes to headache, ophthalmoplegia, endocrine failure, and decreasing level of consciousness [5,10,18]. Headache is the most common complaint at presentation. Reid *et al.* reported that visual impairment was present in 62% of the patients. Ophthalmoplegia, most often third nerve palsy, occurs in 40% of cases [19].

In the current case, pituitary infarction of our patient occurred during CABG and signs such as hyponatraemia, fever and hypotension were secondary to hypopituitarism. Haemodynamic changes during CABG surgery are probably the major cause of pituitary infarction. Cardioplegia, non-pulsatile blood flow, hypotension and embolism or haemorrhage can be the cause of infarct in the pituitary [9]. It is plausible that fragile pituitary adenoma tissue is more susceptible to ischaemic challenge during surgery or the perioperative period [5].

Hyponatraemia, as seen in our patient, is an important indicator of pituitary infarction occurrence [9]. Identification of hyponatraemia is very important, as it helps to diagnose hypoadrenalism in which treatment with corticosteroids can be life-saving. Also low grade fever is another indicator for hypoadrenalism when infection is excluded, as reported by Davies *et al.* [9]. Hydrocortisone (50 mg intravenously every 6 hours) is recommended as initial therapy. Neurologically unstable patients require emergency surgical decompression [17].

Pituitary adenomas invading the cavernous sinus present with third nerve palsy in absence of apoplexy. Demere *et al.* reported six cases of third nerve palsy patients after coronary artery bypass surgery [20]. Our patient had third nerve palsy due to an existing and previously unrecognized pituitary tumour in the immediate postoperative period after cardiac surgery. Similar cases of ophthalmoplegia have been reported but unilateral third cranial nerve palsy with ptosis and mydriasis is very rare.

MRI is the best modality to show the pituitary infarction and haemorrhage and also the compression to the parasellar area, but early decompression is important in apoplexy with severe visual problems. It is suggested, therefore, that in cases diagnosed with CT, treatment with corticosteroids and urgent surgical decompression without MRI can be another choice [21].

The imaging studies of our patient revealed a suprasellar mass consistent with pituitary apoplexy. Surgical intervention is the most common choice of treatment in pituitary apoplexy, especially for sudden impairment of the visual field and unconsciousness [5]. Surgery within the first week was associated with better visual outcome when compared with delayed surgery [7]. It is reported that approximately 80% of patients will require at least one form of hormone replacement therapy after surgery [1].

Previous studies have shown that the outcome of medical treatment in pituitary apoplexy in stable patients without neuro-ophthalmic deficits is similar to the

outcome in those undergoing surgery, but if progressive visual loss exists, emergent decompression should be considered after medical stabilization to prevent fatal rebleeding [22].

In conclusion, pituitary apoplexy after CABG is a rare complication but the physician should be aware of hyponatraemia, altered mental status, visual changes, ophthalmoplegia or even coma, as presenting features. The tumour and/or pituitary tissue after apoplexy may compress the surrounding structures. The outcome depends on early diagnosis and proper intervention. We stress that pituitary apoplexy can be fatal or cause permanent neurological or endocrine damage in absence of proper treatment.

Disclosure

Authors report no conflict of interest.

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