



Pituitary Apoplexy Induced by Anticoagulant Therapy in Patient with Acute Coronary Syndrome

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ABSTRACT

Pituitary apoplexy defined as bleeding or infarct on pituitary gland often occurs in undiagnosed pituitary tumour. Mechanisms thought to trigger pituitary apoplexy are fluctuations in blood pressure, hormonal stimulation of the pituitary gland, coagulation disorders, or vascular disorders. The case is a male, aged 73 years, from India, with complaints of chest pain in the last four hours. Electrocardiography (ECG) and laboratory examination results lead to an acute coronary syndrome (ACS) event. Patients are given fondaparinux, aspirin, and clopidogrel. On the 4th day of hospitalization, the patient experienced a severe headache, projectile vomiting, and double vision. Radiological examination reveals a pituitary tumour with signs of diffuse haemorrhage compressing the optic chiasma, suggesting a pituitary tumour apoplexy. Hormone function tests show a non-functioning pituitary tumour. The blood thinners were discontinued, vitamin K and dexamethasone were given to reduce the patient's symptoms. After a few days, the headaches and double vision began to improve. Head MRI showed stable mass of bleeding. Pituitary tumour may be a relative contraindication to dual antiplatelets and anticoagulants in acute coronary syndromes especially in group with renal or liver comorbidities.

Keywords: Anticoagulant, apoplexy, pituitary tumour.

ABSTRAK

Apopleksi hipofisis didefinisikan sebagai perdarahan atau infark kelenjar hipofisis, dapat terjadi pada tumor hipofisis yang belum terdiagnosis. Beberapa mekanisme yang diduga memicu apopleksi hipofisis adalah fluktuasi tekanan darah, stimulasi hormonal pada kelenjar hipofisis, gangguan koagulasi, atau gangguan vaskular. Kasus laki-laki, berusia 73 tahun, warga negara India, dengan keluhan nyeri dada sejak 4 jam yang lalu. Pemeriksaan elektrokardiografi (EKG) dan laboratorium mengarah pada sindrom koroner akut (SKA). Pasien diberi *fondaparinux*, *aspirin*, dan *clopidogrel*. Pada hari ke-4 perawatan pasien nyeri kepala berat, muntah menyembur, dan pandangan ganda. Pemeriksaan radiologis menunjukkan tumor hipofisis dengan tanda-tanda perdarahan tersebar yang mengkompresi kiasma optik, menunjukkan apopleksi tumor hipofisis. Pemeriksaan fungsi hormon menunjukkan tumor hipofisis yang tidak mensekresi hormon. Pengencer darah dihentikan kemudian diberi vitamin K dan *dexamethasone*. Setelah beberapa hari, nyeri kepala dan pandangan ganda membaik. Pemeriksaan MRI kepala ulang mendapatkan massa tetap dan perdarahan tidak bertambah. Tumor hipofisis bisa menjadi kontraindikasi relatif penggunaan *antiplatelet* ganda dan antikoagulan pada sindrom koroner akut, terutama pada kelompok komorbiditas penyakit ginjal atau hati. **Michael Johan, Handry Pangestu. Apopleksi Hipofisis Diinduksi Terapi Antikoagulan pada Pasien Sindrom Koroner Akut.**

Kata Kunci: Antikoagulan, apopleksi, tumor hipofisis.



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INTRODUCTION

Pituitary apoplexy is bleeding or ischemia in the pituitary gland, commonly in pituitary tumour; it is an endocrine emergency. Pituitary apoplexy often occurs in previously undiagnosed pituitary tumour. This condition was first described in 1950 by Brougham in a case of sudden onset of combined clinical manifestations (headache, visual disturbances, and eye movement disturbances) with radiologically detectable signs of bleeding in a pituitary mass.^{1,2}

There are 6.2 cases in every 100,000 population.³ Pituitary apoplexy may occur in 2% - 12% of patients with various types of pituitary adenomas; 3 of 4 cases of pituitary apoplexy occur in undiagnosed pituitary tumours.⁴ Most pituitary apoplexy occurs in the 5th to 6th decades of age, slightly more dominant in males.²

The main trigger factors are: (1) Fluctuations in blood pressure;⁵ (2) Hormonal stimulation of the pituitary gland;⁶ (3) Coagulation disorders;⁷

and (4) Vascular disorders.⁸

We report a case of pituitary apoplexy after administration of anticoagulants for acute coronary syndrome. This article should be a reminder to various, including very rare, side effects of anticoagulants.

CASE

An Indian male, aged 73 years, came to the emergency department with chest pain for the last four hours. The patient has a history

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of stent placement 20 years ago in India. He also has a history of diabetes mellitus (DM) and glaucoma. Physical examination showed normal blood pressure, 95% oxygen saturation in room air, and crackles at the bases of both lung fields. Electrocardiography (ECG) examination showed inverted T in V3 lead and pathological Q in aVL lead, while laboratory tests showed elevated Troponin T at 377 ng/L (normal <50 ng/L). The patient's kidney function decreased with an estimated glomerular filtration rate of 41.5 mL/minute/1.73m² based on the CKD-EPI formula. Echocardiography results were normal with a left ventricular ejection fraction of 64%. Chest x-ray was suggestive of bilateral bronchopneumonia. He was diagnosed with acute coronary syndrome accompanied by bronchopneumonia and renal insufficiency, and treated in the intensive care unit.

The therapy given were anticoagulants fondaparinux 1x2.5 mg subcutaneous (s.c.), clopidogrel loading dose 300 mg and 75 mg/day afterwards per oral (p.o.), aspirin loading dose 320 mg and 80 mg/day afterwards (p.o.), and isosorbide dinitrate (ISDN) 2.5 mg sublingually (s.l.) for chest pain if needed. Intravenous ceftriaxone 2 grams/day and intravenous levofloxacin 750 mg/day were given for bronchopneumonia.

On the fourth day, the patient experienced a sudden severe headache, projectile vomiting, and double vision. His blood pressure was 140/80 mmHg with decreased vision, exotropia, hypertropia and downward movement of the right eye (right VI cranial nerve paresis). Campimetry could not be performed because of severe headache. Magnetic resonance imaging (MRI) of the head showed a pituitary macroadenoma with signs of diffuse bleeding, indicating pituitary tumour apoplexy; with narrowed suprasellar cistern and optic chiasma compression without vascular invasion to the parasellar or cavernous areas (**Figure**).

The patient was diagnosed as pituitary apoplexy, and treated with dexamethasone 10 mg i.v. thrice a day, vitamin K i.v. 10 mg thrice a day, paracetamol i.v. 1 g thrice a day, gabapentin tablet 100 mg thrice a day, and tramadol 37.5 mg/paracetamol 325 mg tablet if needed. Prolactin hormone, growth hormone, thyroid examinations were normal.

Cortisol was not examined because the patient had received steroids earlier.

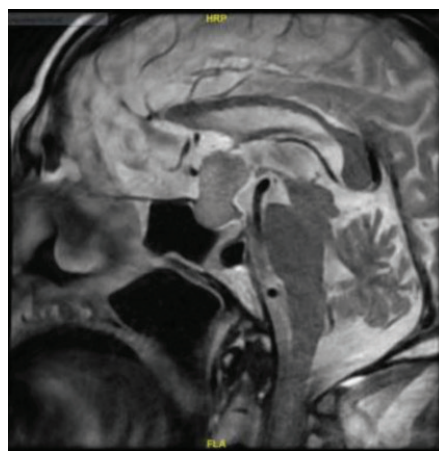


Figure. Magnetic resonance imaging (MRI) showing diffuse haemorrhages to the pituitary gland.

Headache and double vision were improved. MRI re-evaluation on day 10 showed no sign of increased bleeding. The patient was then discharged and continued his treatment in India.

DISCUSSION

The case describes a pituitary apoplexy in a patient not previously known to have a pituitary tumour. This incident is in accordance with epidemiological studies that most pituitary apoplexy cases occur in patients with undiagnosed pituitary tumour.⁴

The pathophysiology of pituitary apoplexy is not fully understood; most cases occur in pituitary macroadenomas (≥ 10 mm).⁴ In contrast to the normal pituitary, pituitary tumour is supplied by direct arteries, not by the portal system as in the normal pituitary gland. Contrast imaging study also showed reduced blood flow in a pituitary tumour compared to a normal pituitary gland, which also a contributing factor to the infarction. It also bleed easily because of their unique and fragile vascularization; its blood vessels show signs of incomplete maturation, poor fenestration, and fragile basement membrane.⁹

Pituitary apoplexy in the case was triggered by medications (aspirin, clopidogrel, and fondaparinux) given for acute coronary syndrome (ACS). Aspirin, an antiplatelet,

has reduced morbidity and mortality by up to 50% in patients with ACS.¹⁰ Another antiplatelet, clopidogrel, was associated with a 20% reduction in cardiovascular-related death, myocardial infarction, or stroke in both low and high-risk patients.¹¹ Fondaparinux, an anticoagulant by indirect Xa factor inhibition is one of the drugs of choice in non-ST elevation ACS.¹² The OASIS-5 compared fondaparinux with enoxaparin in 20,078 non-ST elevation ACS patients. The results found that the mortality, myocardial infarction, and refractory ischemia rates were not different between both anticoagulants, but fondaparinux had a lower bleeding rate (almost 50%) on the 30th day of therapy indicating lower risk of bleeding. On the other hand, ACS patients who received fondaparinux and underwent percutaneous coronary intervention (PCI) had a catheterization-related thrombosis rate three times higher than those with enoxaparin.¹³

Basically, treatment of ACS with blood thinners can restore perfusion to the heart muscle by overcoming thrombus and inhibiting platelet aggregation. However, it is always accompanied by a significant risk of bleeding.¹⁴ The patient's insufficient renal function can increase the half-life of drugs excreted through kidneys; while fondaparinux is almost completely excreted via urine in its intact form 64%-77% drug doses were found in the urine after 72 hours of administration in healthy individuals).¹⁵

Early diagnosis is a key aspect so anticoagulants can be stopped immediately. A high index of suspicion is necessary for diagnosis because the symptoms can be very variable, and are often subclinical. Head MRI is preferred as the main diagnostic because it can detect ischemia and bleeding, while CT scan can only detect bleeding in the acute phase.¹⁶ Early diagnosis is also important because pituitary apoplexy can require emergency intervention.¹⁷ Death, permanent visual impairment, and hormonal insufficiency are potential complications.¹⁶

Conservative management with corticosteroids seems to give a good outcome; empirical corticosteroid therapy is mandatory in pituitary apoplexy patients with hemodynamic instability, impaired consciousness, reduced visual acuity, and visual field defects.¹⁶ Surgical decompression is indicated in patients with a pituitary apoplexy





Table. Pituitary apoplexy score (PAS).¹⁸

Level of Consciousness: Glasgow Coma Scale (GCS)		Score
1.	GCS: 15	0
	GCS: 8-14	2
	GCS: <8	4
2.	Visual Acuity:	
	Normal (6/6):	0
	Low: Unilateral	1
	Low: Bilateral	2
3.	Visual Field Defect	
	Normal	0
	Unilateral	1
	Bilateral	2
4.	Ocular Paresis	
	No	0
	Yes (unilateral)	1
	Bilateral	2

score (PAS) \geq 3. This scoring includes an assessment of: (1) patient awareness (Glasgow Coma Scale (GCS)); (2) visual acuity; (3) visual field defects; (4) ocular paresis. (Table).¹⁸

Treatment for pituitary apoplexy was previously almost always surgical, but conservative treatment has gained popularity in the last decade.¹⁹ A recent retrospective study found no significant difference in

endocrine and visual outcomes between the conservative management group and the initial surgical intervention group.²⁰ Since current evidence showed resolution of apoplexy pituitary tumors without surgery and surgery does not guarantee better results, international guideline have recommended conservative management as initial approach considering the risks of cerebrospinal fluid rhinorrhea, permanent diabetes insipidus, and accidental removal of anterior pituitary caused by pituitary surgery.¹⁹

CONCLUSION

Patients with pituitary tumours are at risk for bleeding after taking blood thinners. Pituitary tumour may be a relative contraindication to the use of dual antiplatelets and anticoagulants in acute coronary syndromes, especially in patients with comorbidities such as renal or hepatic impairment. Conservative management with steroid therapy may provide good outcome in pituitary apoplexy.

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