Case report

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

Michael Johan[1], Handry Pangestu[2]

From, [1]General Practitioner, [2]Internal Medicine Department, Mitra Keluarga Kemayoran Hospital, Jakarta, Indonesia

ABSTRACT

Pituitary apoplexy, defined as bleeding or infarct on the pituitary gland often occurs in undiagnosed pituitary tumors. The patient presented to the emergency room with complaints of chest pain in the last four hours. Electrocardiographic (ECG) and laboratory examination results lead to an acute coronary syndrome (ACS) event. Patients were given fondaparinux, aspirin, and clopidogrel. On the fourth day of hospitalization, the patient experienced a severe headache, projectile vomiting, and double vision. Radiological examination reveals a pituitary tumors apoplexy. The patient improved after a conservative approach by the surgeon. In conclusion, pituitary tumors may be a relative contraindication to dual antiplatelets and anticoagulants in acute coronary syndromes especially in patients with renal or liver comorbidities.

Key words: Apoplexy, Pituitary tumors, Anticoagulant

Pituitary apoplexy is bleeding or ischemia in the pituitary gland, commonly in pituitary tumors; it is an endocrine emergency. Pituitary apoplexy often occurs in previously undiagnosed pituitary tumors. 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 tumors.[4] Most pituitary apoplexy occurs in the 5th to 6th decades of age, slightly more dominant in males.[2]

The main trigger factors are: fluctuations in blood pressure[5]; hormonal stimulation of the pituitary gland[6]; coagulation disorders[7]; and vascular disorders.[8] We report a case of pituitary apoplexy after administration of anticoagulants for acute coronary syndrome. This article should be a reminder of various, including very rare, side effects of anticoagulants.

Access this article online	
Received – 18th July 2024 Initial Review – 21st July 2024 Accepted – 12th August 2024	Quick Response code
DOI: 10.32677/ijcr.v10i10.4685	

CASE REPORT

An Indian male, aged 73 years came to the emergency department with chest pain for the last four hours. The patient has a history of stent placement 20 years ago in India. He also has a history of diabetes mellitus for five years and glaucoma for three years. Physical examination upon admission showed that the patient was alert, had blood pressure of 130/80 mmHg, heart rate of 92x/minute, respiratory rate of 24x/minute, body temperature of 36.5 ^{O}C, oxygen saturation of 95% 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.

Correspondence to: Dr Michael Johan, Internal Medicine Department, Mitra Keluarga Kemayoran Hospital, Jakarta, Indonesia. **E-mail:** michael.johan1211@gmail.com

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

On the fourth day, the patient suddenly experienced a severe headache, projectile vomiting, and double vision. His blood pressure was 140/80 mmHg with decreased vision, exotropia, hypertropia and disturbed left and downward movement of the right eye (right VI nerve paresis). Campimetry could not be performed because of a severe headache. Magnetic resonance imaging (MRI) of the head showed a pituitary macroadenoma with signs of diffuse bleeding, indicating pituitary tumors apoplexy; with narrowed suprasellar cistern and optic chiasma compression without vascular invasion to the parasellar or cavernous areas (Figure 1).

The patient was diagnosed with pituitary apoplexy, and treated with dexamethasone 10 mg intravenously (i.v.) thrice a day, vitamin K 10 mg thrice a day (i.v.), paracetamol 1 g thrice a day (i.v.), gabapentin 100 mg thrice a day per os (p.o.), and tramadol 37.5 mg/paracetamol 325 mg tablet (p.o.) if needed. Prolactin hormone, growth hormone, and thyroid examinations were normal. Cortisol was not examined because the patient had received steroids earlier.

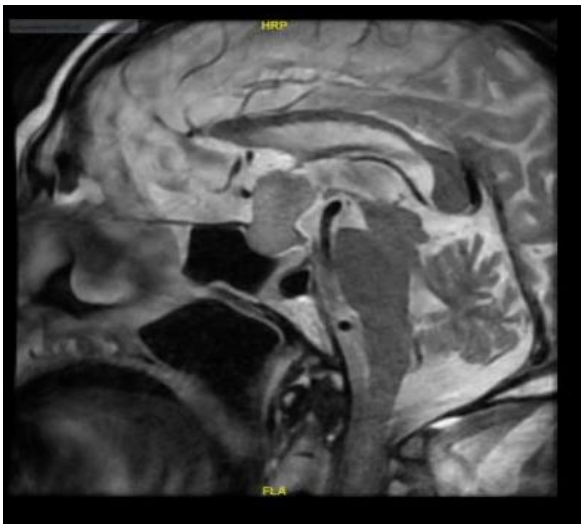

Figure 1: Magnetic Resonance Imaging (MRI) showing Diffuse Haemorrhages to the Pituitary Gland

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 tumors. This incident is in accordance with epidemiological studies that most pituitary apoplexy cases occur in patients with undiagnosed pituitary tumors.[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, the pituitary tumors 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 tumors compared to a normal pituitary gland, which is also a contributing factor to the infarction. It also bleeds easily because of its 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 a 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% of 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 score (PAS) ≥ 3. This scoring includes an assessment of: (1) patient awareness (Glasgow Coma Scale -GCS); (2) visual acuity; (3) visual field defects; and (4) ocular paresis. (Table 1).[18]

Table 1: Pituitary apoplexy score (PAS)[18]

1.	Level of consciousness: Glasgow coma scale (GCS)	Score
	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

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 shows resolution of apoplexy pituitary tumors without surgery and surgery does not guarantee better results, international guidelines have recommended conservative management as the 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 tumors are at risk for bleeding after taking blood thinners. Pituitary tumors 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 a good outcome in pituitary apoplexy.

REFERENCE

1. Capatina C, Inder W, Karavitaki N, Wass JAH. Management of endocrine disease: pituitary tumour apoplexy. Eur J Endocrinol. 2015 May;172(5):R179-90.
2. Ranabir S, Baruah MP. Pituitary apoplexy. Indian J Endocrinol Metab. 2011 Sep;15 Suppl 3(Suppl3):S188-96.
3. Fernandez A, Karavitaki N, Wass JAH. Prevalence of pituitary adenomas: a community-based, cross-sectional study in Banbury (Oxfordshire, UK). Clin Endocrinol (Oxf). 2010 Mar 1;72(3):377–82.
4. Briet C, Salenave S, Bonneville JF, Laws ER, Chanson P. Pituitary Apoplexy. Endocr Rev. 2015 Dec;36(6):622–45.
5. Tansel T, Ugurlucan M, Onursal E. Pituitary Apoplexy Following Coronary Artery Bypass Grafting Report of a Case. Acta Chir Belg. 2010 Jan 1;110(4):484–6.
6. Kılıçlı F, Dökmetaş H, Gürelik M. Development of pituitary apoplexy during TRH/GnRH test in a patient with pituitary macroadenoma. Singapore Med J. 2010 Nov 1;51:e179-81.
7. Uemura M, Miyashita F, Shimomura R, Fujinami J, Toyoda K. Pituitary apoplexy during treatment with dabigatran. Neurol Clin Neurosci. 2013 Mar 1;1(2):82–3.
8. Kumar V, Kataria R, Mehta V. Dengue hemorrhagic fever: a rare cause of pituitary tumor hemorrhage and reversible vision loss. Indian Journal of Ophtalmology. 2011;59:311–2.
9. Di Ieva A, Weckman A, Di Michele J, Rotondo F, Grizzi F, Kovacs K, et al. Microvascular morphometrics of the hypophysis and pituitary tumors: from bench to operating theatre. Microvasc Res. 2013 Sep;89:7–14.
10. Lewis HD, Davis JW, Archibald DG, Steinke WE, Smitherman TC, Doherty JE, et al. Protective Effects of Aspirin against Acute Myocardial Infarction and Death in Men with Unstable Angina. New England Journal of Medicine. 1983 Aug 18;309(7):396–403.
11. Singh D, Gupta K, Vacek JL. Anticoagulation and antiplatelet therapy in acute coronary syndromes. Cleve Clin J Med. 2014 Feb;81(2):103–14.
12. Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Ganiats TG, Holmes DR, et al. 2014 AHA/ACC Guideline for the Management of Patients with Non–ST-Elevation Acute Coronary Syndromes. Circulation. 2014 Dec 1;130(25):e344–426.
13. Yusuf S, Mehta SR, Chrolavicius S, Afzal R, Pogue J, Granger CB, et al. Comparison of fondaparinux and enoxaparin in acute coronary syndromes. N Engl J Med. 2006 Apr;354(14):1464–76.
14. Tersalvi G, Biasco L, Cioffi GM, Pedrazzini G. Acute Coronary Syndrome, Antiplatelet Therapy, and Bleeding: A Clinical Perspective. J Clin Med. 2020 Jul;9(7):2064-83.
15. Donat F, Duret JP, Santoni A, Cariou R, Necciari J, Magnani H, et al. The Pharmacokinetics of Fondaparinux Sodium in Healthy Volunteers. Clin Pharmacokinet. 2002;41(2):1–9.
16. Vicente A, Lecumberri B, Gálvez MÁ. Clinical practice guideline for the diagnosis and treatment of pituitary apoplexy. Endocrinol Nutr. 2013 Dec;60(10):582.e1-582.e12.
17. Santos AR, Bello CT, Sousa A, Duarte JS, Campos L. Pituitary Apoplexy Following Systemic Anticoagulation. Vol. 6, European journal of case reports in internal medicine. Italy; 2019. p. 1254.

18. Mudalagiri M, Ayyar V, Bantwal G, George B, Appaiah S. Abstract 103: The pituitary apoplexy score (PAS) in the evaluation and management of pituitary apoplexy: A single centre experience. Vol. 26, Indian Journal of Endocrinology and Metabolism. 2022. p. S37.
19. Rajasekaran S, Vanderpump M, Baldeweg S, Drake W, Reddy N, Lanyon M, et al. UK guidelines for the management of pituitary apoplexy. Clin Endocrinol (Oxf). 2011 Jan;74(1):9–20.
20. Fan Y, Bao X, Wang R. Conservative treatment cures an elderly pituitary apoplexy patient with oculomotor paralysis and optic nerve compression: A case report and systematic review of the literature. Clin Interv Aging. 2018;13:1981–5.

Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Johan M, Pangestu H. Pituitary Apoplexy Induced by Anticoagulant Therapy in Patient with Acute Coronary Syndrome. Indian J Case Reports. 2024; 10(10):1-4.