JAMBI MEDICAL JOURNAL
Jurnal Kedokteran dan Kesehatan

p-Issn : 2339-269x
e-Issn : 2580-6874

Vol. 11, No. 4, November 2023
DOI: 10.22437/jmj.v11i4.27776
Journal homepage: https://online-journal.unja.ac.id/kedokteran

Case Report

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

Michael Johan[1], Handry Pangestu[2]

[1]General Practitioner, Mitra Keluarga Kemayoran Hospital, Jakarta
[2]Internal Medicine Department, Mitra Keluarga Kemayoran Hospital, Jakarta
E-mail Corresponding: michael.johan1211@gmail.com

Article History:

Received Aug 13, 2023
Accepted Nov 24, 2023

Keyword:

Apoplexy
Pituitary Tumor
Anticoagulant

ABSTRACT

Pituitary apoplexy, defined as bleeding or infarct on pituitary gland which often occurs in undiagnosed pituitary tumour. Some of the mechanisms thought to trigger pituitary apoplexy are fluctuations in blood pressure, hormonal stimulation of the pituitary gland, coagulation disorders or vascular disorders.

We reported the case of a male patient, aged 73 years from India who came to the emergency department 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 are given blood thinners in the form of 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 an apoplexy of a pituitary tumour. Hormone function tests show a non-functioning pituitary tumour. The blood thinners were discontinued, then vitamin K and dexamethasone were given to reduce the patient's symptoms. After a few days, the headaches and double vision began to improve. Another MRI of the head was done and the result shoed that the mass remained the same and the bleeding did not expand.

It is known that patients with pituitary tumors are at risk of experiencing bleeding after administration of blood thinners. The presence of a pituitary tumour may be a relative contraindication to the use of dual antiplatelets and anticoagulants in acute coronary syndromes especially in group with renal or liver comorbidities.

INTRODUCTION

Pituitary apoplexy is an endocrine emergency in which bleeding or ischemic occurs in the pituitary gland, commonly occurring in pituitary tumour. Most often pituitary apoplexy occurs in previously undiagnosed pituitary tumour. This case was first described in 1950 by Brougham in which there is a sudden onset of combined clinical manifestations (headache, visual disturbances, and eye movement disturbances) with signs of bleeding in a pituitary mass that is radiologically detectable.[1,2]

The epidemiology of pituitary apoplexy is difficult to assess because of the scanty data, but there are studies which state that there are 6.2 cases in every 100,000 population. Generally, 3 out of 4 cases of pituitary apoplexy occur in undiagnosed pituitary tumours at the time of the incident. Pituitary apoplexy may occur in 2% - 12% of patients with various types of pituitary adenomas.[3] Most cases of pituitary apoplexy occur in the 5th to 6th decades of age, and slightly more dominant in males.[2]

The main factors that can trigger pituitary apoplexy are: (1) Fluctuations in blood pressure; (2) Hormonal stimulation of the pituitary gland; (3) Coagulation; and (4) Vascular disorders.[1]

We report a case of pituitary apoplexy that occurred after administration of anticoagulants for acute coronary syndrome. This article should be a reminder for all of us to be more aware of the various side effects of anticoagulants, including those that are very rare.

CASE ILUSTRATION

We report a male patient, aged 73 years from India who came to the emergency department with complaints of chest pain for the last four hours. The patient has a history of stent placement since 20 years ago in India. In addition, the patient also has a history of diabetes mellitus (DM) and glaucoma. Physical examination showed the patient had normal blood pressure, 95% O2 saturation without oxygen, 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 limit <50 ng/L). The patient's kidney function has decreased with an estimated glomerular filtration rate of 41.5 mL/minute/1.73m2 based on the CKD-EPI formula. Echocardiography was examined in the patient and the results were normal with a left ventricular ejection fraction of 64%. Meanwhile, chest X-ray in the patient were suggestive of bilateral bronchopneumonia. Therefore, our medical team diagnosed the patient as acute coronary syndrome accompanied by bronchopneumonia and renal insufficiency, so he was treated in the intensive care unit.

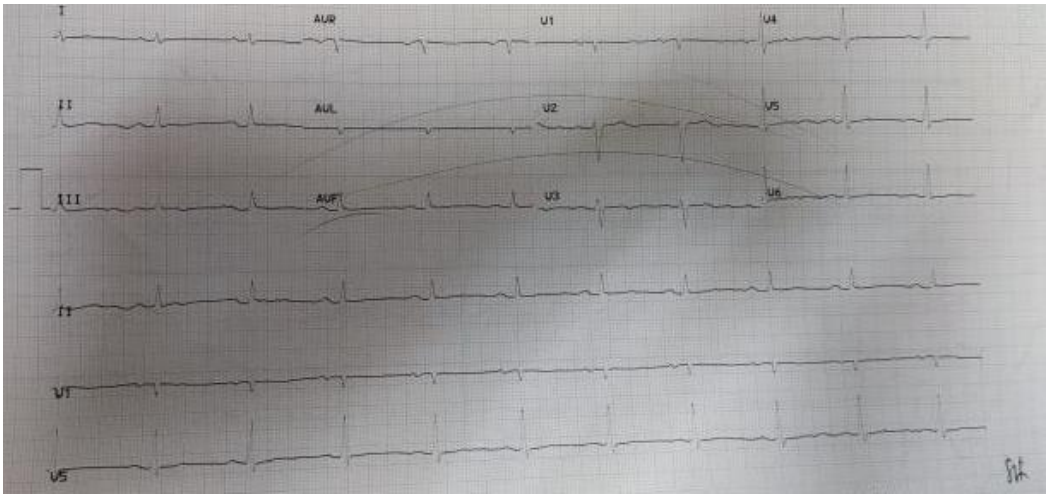

Figure 1. Patient's Electrocardiography (ECG)

The therapy given for acute coronary syndrome in patients are anticoagulants in the form of fondaparinux 1x2.5 mg, dual antiplatelets (clopidogrel and aspirin), and isosorbide dinitrate (ISDN) for chest pain. As for bronchopneumonia, the patient was given intravenous antibiotics in the form of ceftriaxone two gram once a day and levofloxacin 750 mg once a day. However, on the fourth day of treatment, the patient suddenly experienced a severe headache, projectile vomiting, and double vision.

The patient was re-evaluated, where there was an increase in blood pressure to 140/80 mmHg, decreased vision, impressions of exotropia and hypertropia in the right eyeball, and disturbed movement of the right eyeball when looking left and down (right VI nerve paresis). Campimetry examination could not be performed because the patient complained of severe headaches during the campimetry examination. Magnetic resonance imaging (MRI) examination of the head showed a pituitary macroadenoma with signs of diffuse bleeding, indicating pituitary tumour apoplexy. In addition, there is a narrowed suprasellar cistern and compression of the optic chiasma, without vascular invasion to the parasellar or cavernous areas. The patient was then diagnosed as having pituitary apoplexy, then given therapy in the form of dexamethasone 3x10 mg IV, vitamin K 3x10 mg IV, paracetamol 3x1 g IV, gabapentin 3x100 mg PO, and tramadol 37.5 mg/paracetamol 325 mg tablet if the headache had not been resolved. The patient was also examined for the prolactin hormone, growth hormone, thyroid and found normal results. The cortisol hormone was not examined because the patient received steroids immediately after being diagnosed as pituitary apoplexy.

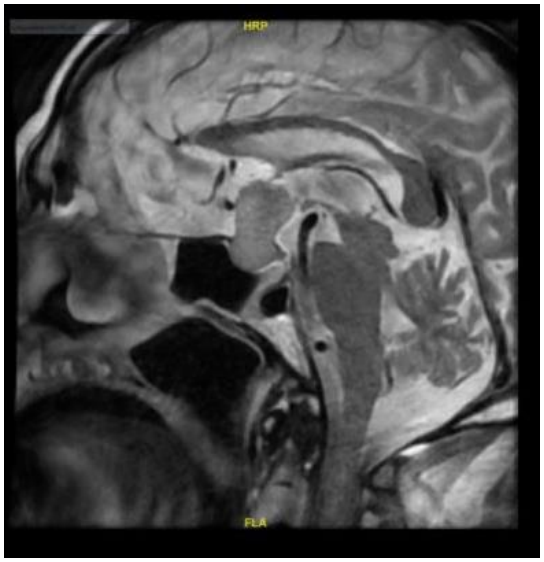

Figure 2. Magnetic Resonance Imaging (MRI) Showing Diffuse Haemorrhages to the pituitary gland

After a few days, headache and double vision of the patient improved. Thus, the patient was re-evaluated with MRI again on day 10 from the onset of apoplexy and the MRI showed no sign of increased bleeding. The patient was then discharged and continued his treatment in India.

DISCUSSION

The above case describes a patient with pituitary apoplexy in a patient who was not previously known to have a pituitary tumour. This incident is in accordance with epidemiological studies which state that

most cases of pituitary apoplexy occur in patients with undiagnosed pituitary tumour.[3]

The pathophysiology of pituitary apoplexy is not fully understood and most cases occur in pituitary macroadenomas (≥ 10 mm).[3] In contrast to the normal pituitary, the vascularization of a pituitary adenoma is supplied by the arteries directly, not by the portal system as in the pituitary organs. Contrast imaging study showed less blood flow in a pituitary tumour than a normal pituitary, contributing to the infarction. In addition, pituitary tumour bleed easily because of their unique and fragile vascularization. The blood vessels of the pituitary tumour also show signs of incomplete maturation, poor fenestration, and have basement membrane that tears easily.[4]

Pituitary apoplexy in the case we reported was triggered by blood thinners (aspirin, clopidogrel, and fondaparinux) given as an indication for acute coronary syndrome (ACS). Actually, various blood thinners are known to be useful in treating vascular thrombosis. Various clinical trials confirmed that aspirin, an antiplatelet, reduced morbidity and mortality by up to 50% in patients with ACS. Another antiplatelet, clopidogrel, was associated with a 20% reduction in cardiovascular-related death, myocardial infarction, or stroke in both low and high-risk patients.[5]

Another blood thinner that we gave to patients is fondaparinux, an anticoagulant that works by inhibiting Xa factor indirectly and is one of the drugs of choice in non-ST elevation ACS. The OASIS-5 clinical trial compared fondaparinux with enoxaparin in 20,078 non-ST elevation ACS patients. The results OASIS-5 study found that the mortality, myocardial infarction, and refractory ischemia rates were not much different between both anticoagulants, but fondaparinux had a lower bleeding rate (almost 50%) on the 30th day of therapy indicating lower risk of bleeding. Nonetheless, ACS patients who received fondaparinux and underwent percutaneous coronary intervention (PCI) had a catheterization-related thrombosis rate three times higher than those with enoxaparin.[6]

Basically, treatment of ACS with blood thinners can restore perfusion to the heart muscle by overcoming thrombus and inhibiting platelet aggregation. However, administration of blood thinners is always accompanied by a significant risk of bleeding.[7] In addition, patient's renal also insufficient so this condition increase the half-life of drugs that are excreted through the kidneys. According to its pharmacokinetics, fondaparinux is almost completely excreted via the urine in its intact form (64-77% of the drug dose is found in the urine after 72 hours of administration in healthy individuals).[8]

Early diagnosis is a key aspect in our case so that 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 support compared to CT-Scan because it can detect ischemia and bleeding, while CT-Scan can only detect bleeding in the acute phase. Early diagnosis is also important because in its most severe form, pituitary apoplexy can require emergency intervention.[9] Death, permanent visual impairment, and hormonal insufficiency are complications that can occur when a pituitary apoplexy is diagnosed too late.[10]

Conservative management applied to patients with corticosteroids seems to give a good outcome. According to Vicente et al., empirical corticosteroid therapy is mandatory in pituitary apoplexy patients with hemodynamic instability, impaired consciousness, reduced visual acuity, and visual field defects.[10] Surgical decompression is indicated in patients with

a pituitary apoplexy score (PAS) ≥ 3. This scoring includes an assessment of: (1) patient awareness (assessed by the Glasgow Coma Scale (GCS)); (2) visual acuity test; (3) visual field defects; (4) ocular paresis. The full PAS scoring table can be seen in table 1.[11]

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Table 1. Pituitary apoplexy score (PAS)[11]

Level of consciousness: Glasgow coma scale (GCS)	**Score**
GCS: 15	0
GCS: 8-14	2
GCS: <8	4
Visual acuity:	
Normal (6/6):	0
Low: Unilateral	1
Low: Bilateral	2
Visual field defect	
Normal	0
Unilateral	1
Bilateral	2
Ocular paresis	
No	0
Yes (unilateral)	1
Bilateral	2

Although in the past, treatment for pituitary apoplexy was almost always surgical, conservative treatment has gained popularity in the last decade. A recent retrospective study found no significant difference in endocrine and visual outcomes between the conservative management group and the initial surgical intervention group. Study also show resolution of apoplexy pituitary tumors without surgery, so surgery does not guarantee better results considering the risks of cerebrospinal fluid rhinorrhea, permanent diabetes insipidus, and removal of anterior pituitary after surgery.[12]

CONCLUSION

Through this case, we know that patients with pituitary tumours are at risk for bleeding after taking blood thinners. The presence of a 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. In addition, conservative therapy with steroids may provide good outcome in pituitary apoplexy.

REFERENCES

1. *Capatina C, Inder W, Karavitaki N, Wass JAH. Management of endocrine disease: pituitary tumour apoplexy. Eur J Endocrinol. Mei 2015;172(5):R179-90.*
2. *Ranabir S, Baruah MP. Pituitary apoplexy. Indian J Endocrinol Metab. September 2011;15 Suppl 3(Suppl3):S188-96.*

3. *Briet C, Salenave S, Bonneville J-F, Laws ER, Chanson P. Pituitary Apoplexy. Endocr Rev. Desember 2015;36(6):622–45.*
4. *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. September 2013;89:7–14.*
5. *Singh D, Gupta K, Vacek JL. Anticoagulation and antiplatelet therapy in acute coronary syndromes. Cleve Clin J Med. Februari 2014;81(2):103–14.*
6. *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. April 2006;354(14):1464–76.*
7. *Tersalvi G, Biasco L, Cioffi GM, Pedrazzini G. Acute Coronary Syndrome, Antiplatelet Therapy, and Bleeding: A Clinical Perspective. J Clin Med. Juli 2020;9(7).*
8. *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.*
9. *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. 1254.*
10. *Vicente A, Lecumberri B, Gálvez MÁ. [Clinical practice guideline for the diagnosis and treatment of pituitary apoplexy]. Endocrinol y Nutr organo la Soc Esp Endocrinol y Nutr. Desember 2013;60(10):582.e1-582.e12.*
11. *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. S37.*
12. *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). Januari 2011;74(1):9–20..*