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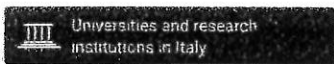
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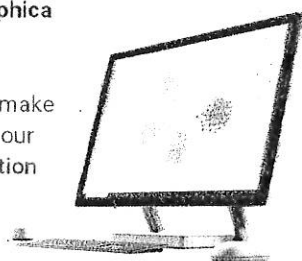
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
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



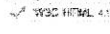

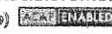
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Diagnostic problems and management of pituitary gigantism leading to ischemic stroke and atrial myxoma in young adult patient: a case report



Nabilah¹, Sony Wibisono^{1*}, Libriansyah², Joni Wahyuhadi³, Muhammad Reza Arifianto³

ABSTRACT

Background: Gigantism is the excessive secretion of growth hormones (GH) during childhood and is mostly caused by benign pituitary adenomas. The signs and symptoms are not specific in early childhood due to growth spurt. An ischemic stroke is rarely present in pituitary adenoma, and here we present a case of ischemic stroke and atrial myxoma associated with pituitary gigantism.

Case Presentation: The patient was an 18-year-old male who complained of continuous growth. In June 2016, the patient suffered from an embolic stroke, and in January 2017 he complained of fatigue and shortness of breath. The echocardiography showed a mass in the left atrium that was removed in March 2017 through open-heart surgery; the pathological histology confirmed a myxoma. The brain magnetic resonance imaging (MRI) showed a pituitary macroadenoma, and the growth hormone (GH) level was 20.6 ng/mL. In October 2019, the patient was referred to Dr. Soetomo Hospital. The height increased from 185 cm in 2017 to 205 cm in 2019. The height was 205cm, weight 85kg, body mass index 20.2 kg/m², GH level >40 ng/mL, cortisol 11.24 ug/dL, prolactin 1.21 ng/mL, testosterone 425.6 ng/dL, free thyroxine (FT4) 1.03 ng/dL, and insulin-like growth factor I (IGF-I) 688 ng/mL. The patient was administered oral cabergoline 0.25 mg twice a week and had endoscopic endonasal transsphenoidal hypophysectomy (EETH). The patient developed postoperative polyuria after surgery which indicated diabetes insipidus, and the patient was administered desmopressin 0.05mg/12 h with fluid restriction. One week later, the morning cortisol level was low, and hydrocortisone therapy was administered and was tap-off. One month-post surgery, the level of morning serum cortisol was 0.86 µg/dL.

Conclusion: This case is extremely rare and we demonstrated that the EETH surgery the stability of GH could be achieved.

Keywords: Gigantism, pituitary macroadenoma, growth hormone, ischemic stroke, atrial myxoma.

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INTRODUCTION

Ischemic stroke in people aged 17 to 22 are estimated to be infrequent, affecting between 10% and 15% of stroke patients.¹ The etiology of the ischemic stroke in people at age 17 to 22 are varied and relatively uncommon, leading to diagnostic uncertainty and necessitating specific management.² However, it is understood that cardioembolic stroke is responsible for roughly one-third of all ischemic strokes in those aged 17 to 22 and is primarily caused by atrial myxoma.^{1,3} Cardioembolic stroke associated with a primary cardiac tumor is extremely rare, occurring at a rate of less than 0.03 percent. Most of them are benign tumors called primary myxomas, with over 75% occurring in the left atrium. Nevertheless,

most cases of atrial myxoma are sporadic, and the exact etiology is unknown.⁴

Currently, there is increasing evidence that growth hormone (GH) and/or insulin-like growth factor-I (IGF-I) are present in the intricate cascade of events related to the regulation of heart development and hypertrophy.⁵ The GH level reflects neurosecretory dysfunction, a characteristic of GH-cell adenomas that cause gigantism. Gigantism is a syndrome that arises when the epiphyseal growth plates remain open during the teenage years. Additionally, it refers to various non-hormonally mediated growth issues in minors and is frequently used to refer to an excess of growth hormone (GH), which is quite rare in childhood and teenager, with known occurrences numbering in the hundreds.⁶

Here, we reported the patient with gigantism and a pituitary adenoma, developing into ischemic stroke and atrial myxoma. The purpose of this report is to describe diagnostic difficulty and treatment options of the patient.

CASE PRESENTATION

An 18-years-old male complained of a narrow body, thinness, and taller height than his parents, indicating an atypical linear growth pattern. In the meantime, the height has risen at a rate of 10 cm each year for the past two years. The patient also complained of a narrowed visual field in his right eye, but no other symptoms such as fatigue, dizziness, palpitation, hair loss, sweating, excessive defecation, nausea, or tremor were reported. In June 2016, the patient was referred to

the emergency unit after experiencing sudden weakness in his arm and leg and difficulty to speak and walking. However, there were no headaches, vomiting, fever, photophobia, diplopia, recent traumas, or seizures reported. The magnetic resonance imaging (MRI) of the left hemisphere revealed a severe cerebral infarction involving hemorrhagic alteration extending from the internal capsule and basal ganglia towards the corona radiata. Magnetic resonance angiography (MRA) indicated no aneurysm or arteriovenous abnormality in the left internal carotid artery. Following that, it was determined that the patient had an embolic stroke. Nine months later, in March 2017, the patient complained of shortness of breath and chest heaviness, especially during exertion. The patient was examined for echocardiography, and a mass was found in the left atrium. Therefore, open-heart surgery was performed to remove the mass, and the pathological histology obtained a myxoma. Since there was a feeling of continuous growth in the body, a brain MRI was performed with normal results, and the growth hormone level was 20.60 ng/mL.

The patient was referred to Dr. Soetomo Hospital in October 2019. The subject weighed 85 kg, 205 cm tall, and had a body mass index (BMI) 20.2 kg/m² (Figure 1). The patient was found to be in good general health, *compos mentis*, with a blood pressure of 110/70 mmHg, a pulse rate of 94 bpm, a respiration rate of 18 bpm, and an axillary temperature of 36.8°C. Additionally, no evidence of jaundice or cyanosis, no abnormality on lymph nodes and jugular venous pressure was normal. Thoracic examination revealed symmetrical chest movement, absence of retraction, vesicular breathing, absence of rhonchi and wheezing. The heart sound was normal, and no additional heart or gallop noises were detected. The abdominal examination revealed a pliable stomach, bowel sounds within normal limits, no palpable mass, and enlargement of the liver and spleen.

The laboratory results were as follows, Hb 14.2 g/dL, white blood cell (WBC) 6600/mm³, neutrophils 68.7%, platelet count (PLT) 233000/mm³, sodium 141.8 mmol/L, potassium 3.53 mmol/L,

albumin 5.39 g/dL, creatinine serum 0.9 mg/dL, estimated glomerular filtration rate (e-GFR) 158.72 ml/min, free T4 (fT4) 1.03 pmol/L, thyroid-stimulating hormone (TSH) 1.53 uIU/mL, growth hormone (GH) >40 ng/mL, cortisol 11.24 µg/dL, prolactin 1.21 ng/mL, testosterone 425.60 ng/dL, and IGF-1 688 ng/mL. The urinalysis revealed pH 6.0 and no nitrite, crystal, glucose or protein were identified. There was no abnormality in the chest X-ray in which heart and lung were both within normal limits, and the electrocardiography (ECG) value was 80x/min sinus rhythm with the normal axis. The brain MRI showed a slight enhancing intrasellar mass approximately 1.6x1.1x1 cm, suggesting a pituitary macroadenoma (Figure 2). The patient was diagnosed with pituitary gigantism and scheduled for visual field examination by an ophthalmologist and consultation with a neurosurgeon. The patient was administered with a cabergoline of 0.25 mg per oral twice a week.

In November 21, 2019, the ophthalmology examination revealed a homonym hemianopsia dextra that was associated with pituitary macroadenoma and was scheduled for endoscopic endonasal transsphenoidal (EETH) surgery by a neurosurgeon. On the subsequent visit, January 24, 2020, the

patient was hospitalized in preparation for surgery. He was in good overall health; his GCS score was 456, with 120/80 mmHg blood pressure, 90 bpm pace of heart beat, and 18 bpm respiration rate.

The patient had the surgery on February 13, 2020. The pathological analysis of the tumor revealed that it was a pituitary adenoma (Figure 3). There were no complaints of increased appetite



Figure 1. A 18-years-old man with a height of 205 cm with a 165 cm physician as comparison.



Figure 2. A contrast-enhanced brain MRI shows a slight enhancing intrasellar mass approximately 1.6x1.1x1 cm, suggesting a pituitary macroadenoma.

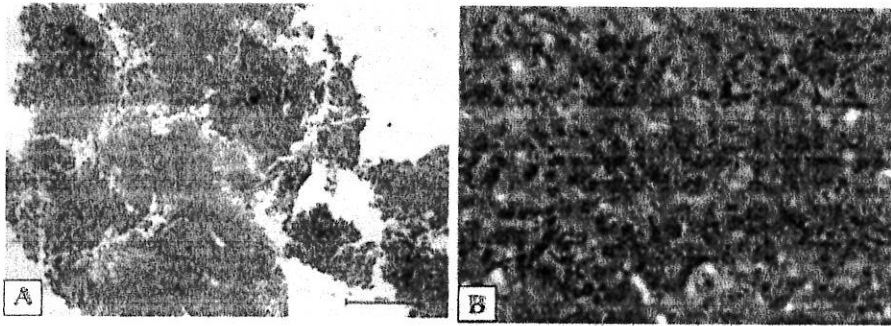


Figure 3. Pathological anatomy examination of pituitary adenoma. (A) 40-folds magnification and (B) showed 400-folds magnification.

or dizziness following surgery, but there was an abnormally high urine output of roughly 8000 ml/24hr. Desmopressin 0.05mg/12hr was administered with water intake restriction. Urine production returned to normal in four days following surgery, and GH level remained within the normal range (1.48 ng/mL). The patient was discharged and monitored at the Endocrinology Polyclinic without complaint one week later. Also, the patient had hydrocortisone tap-off therapy and one month later the morning serum cortisol was 0.86 µg/dL with sodium 138 mmol/L, potassium 4.2 mmol/L, and chloride 102 mmol/L suggesting that the EETH surgery could achieved the stability of growth hormone level.

DISCUSSION

In this case, the patient suffered an embolic stroke without any risk factor and it was suggested that it was caused by cardioembolic disease, a myxoma in the left atrium. In this patient the IGF-1 level was very high, 688 ng/mL and this stimulated the growth of organ tissue. There is growing evidence that GH and/or IGF-I are part of the intricate chain of events that govern heart development and hypertrophy.⁵ In addition, a previous study showed that both GH and IGF-1 increase the risk for certain cancers.⁷ GH and/or IGF-1 could facilitate new tumor formation or growth and therefore these hormones promote neoplastic growth of various cell types.⁸ After two years, the patient was diagnosed as a pituitary macroadenoma with abnormal growth with excessive GH due to pituitary macroadenoma. This case is extremely rare.

The gold standard for imaging of pituitary disease is MRI of the pituitary region employing thin sections, sagittal and coronal reconstruction. Visual field loss is frequently used as the key neurological criteria to decide the surgical management in the patient. Humphrey computed visual fields using a Humphrey field analyser (HFA) is beneficial even when there is no interaction between the optic pathways and the pituitary tumor. This is because field irregularities may occur due to pre-decompression impingement, vascular shunting, or chiasm displacement.⁹ The patient was managed with an EETH surgery where the pathological anatomy examination of the tumor revealed a pituitary adenoma. Soon after, GH level restored to be normal.

CONCLUSION

In pituitary tumors, attempts are made to reduce tumor mass, restore hormone function, and restore normal vision with medications, surgery, and radiation. Hence, medical treatment reduces tumor size, controls excess hormones, or corrects hormonal deficiencies. In this rare case, the pituitary gigantism caused ischemic stroke and atrial myxoma in young adult patient and EETH surgery could normalize the level of the hormones of the patient.

PATIENT CONSENT

The patient agreed and signed informed consent prior to the study and agreed that the case will be published in an academic journal without revealing the patient identity.

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DISCLOSURE OF CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTION

All authors contributed significantly to the study from the conceptual, data acquisition, data analysis and during manuscript preparation.

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