Diagnostic challenges and management a patient with micropenis and pituitary microadenoma

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INTRODUCTION

Micropenis is a condition where the penis length is less than 2.5 standard deviations without structural abnormalities.¹ This abnormality can arise from systemic disorders or from the penis, usually caused by congenital.¹ In the United States, the incidence of micropenis is 1.5:10,000 in males born in 1997-2000.³ The development of the penis occurs since the embryonic period, begins with beta-human chorionic gonadotropin (hCG), which will affect the Leydig cells to produce testosterone, resulting in the penis development until it reaches about 20 mm in size at about 38 weeks of gestation. Congenital abnormalities and hormonal disturbances from birth potentially cause micropenis.¹,³

A pituitary adenoma is the most common intracranial tumor; the prevalence is 22% from magnetic resonance imaging (MRI) and 14% from autopsies performed on brain tumors.³ This disease is generally silent and was discovered by accident.⁴,⁵ Pituitary adenomas are commonly benign and rarely develop into malignant.³ Symptoms that appear frequently are the result of suppression due to tumor mass or hormonal disturbances.⁴ According to the World Health Organization (WHO), pituitary tumors are classified based on size and ability to produce hormones.⁶ Based on the size, they are divided into microadenoma, if the size is smaller than 10 mm; and macroadenoma, if the adenoma size is larger than 10 mm. Pituitary microadenoma is more prevalent than pituitary macroadenoma (57.4%: 42.6%).⁶

In general, pituitary microadenoma is asymptomatic. In this case-report we present a patient with pituitary microadenoma with symptoms due to hormonal disturbances including a micropenis. This case-report could provide information to better detect and manage the pituitary microadenoma to improve the quality of life.

CASE PRESENTATION

A 40-year-old male patient, came to the Endocrine Polyclinic of Dr Soetomo Hospital with a chief complaint of having a small penis that did not match the proportions of the body but could still erect and ejaculate. The patient experienced fatigue for about two months before the admission and struggled to concentrate while walking for the last six months. The laboratory results were hyperprolactinemia, hypoalbumin, and dyslipidemia. From the MRI examination with contrast, a mass was found in the left pituitary. The patient was diagnosed with pituitary microadenoma, hypogonadotropic hypogonadism, micropenis, hypotestosterone, hypocortisolism, and hypothyroidism. The patient was assigned for monthly monitoring. Consultation with a neurosurgeon suggested there were no indications for surgery. The patient was treated with testosterone intramuscular injection 250 mg every month, methylprednisolone 4 mg every 8 h, simvastatin 20 mg every 24 h, and levothyroxine sodium 50 mg every 24 h. One month follow up, fatigue was disappeared and nine months follow up found improvements in hormone levels and balance during walking.

Conclusion: Pituitary microadenoma can manifest as micropenis, hypocortisolism, and shift hormone levels. The main therapy for pituitary microadenoma is hormone therapy as presented this present case report.

Keywords: Micropenis, pituitary microadenoma, hypogonadotropic hypogonadism, hypophysis.


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ABSTRACT

Background: Micropenis is a condition where the penis size is smaller than 2.5 standard deviation on average without any anatomical malformations. Hypogonadotropic hypogonadism is one of the causes of micropenis and one of the structural disorders that could lead to hypogonadotropic hypogonadism is a pituitary microadenoma that alters the levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH) and testosterone. In this case-report we present a patient with micropenis caused by pituitary adenoma.

Case presentation: A 40-year-old male patient, presented to Dr Soetomo Hospital with a chief complaint of having a small penis that did not match the proportions of the body but could still erect and ejaculate. The patient experienced fatigue for about two months before the admission and struggled to concentrate while walking for the last six months. The laboratory results were hyperprolactinemia, hypoalbumin, and dyslipidemia. From the MRI examination with contrast, a mass was found in the left pituitary. The patient was diagnosed with pituitary microadenoma, hypogonadotropic hypogonadism, micropenis, hypotestosterone, hypocortisolism, and hypothyroidism. The patient was assigned for monthly monitoring. Consultation with a neurosurgeon suggested there were no indications for surgery. The patient was treated with testosterone intramuscular injection 250 mg every month, methylprednisolone 4 mg every 8 h, simvastatin 20 mg every 24 h, and levothyroxine sodium 50 mg every 24 h. One month follow up, fatigue was disappeared and nine months follow up found improvements in hormone levels and balance during walking.

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transaminase (SGOT) 45 mg/dL, serum glutamic pyruvic transaminase (SGPT) 40 mg/dL, albumin 3.2 mg/dL, blood glucose level 185 mg/dL, prolactin 30 ng/mL (normal value: 2–18 ng/mL), testosterone 2.0 ng/dL (normal value: 2.2–10.5 ng/dL), growth hormone: 0.085 ng/dL (normal value: 0.4–10 ng/dL). Hepatitis B surface antigen (HbsAg) and antibody to hepatitis C virus (anti-HCV) test results were non-reactive.

The radiological examination of posterior-anterior (PA) thorax X-ray showed the heart and lungs were within normal limits. Results of the head magnetic resonance imaging (MRI) examination suggested a lesion on the left side of the pituitary subcentimeter, which showed slight contrast enhancement (Figure 2A). There is an arachnoid cyst in the left anterior medial temporal lobe measuring 8.3 mm x 1.4 mm and in the left cerebellopontine angle (CPA) measuring 2.7 mm x 1.17 mm (Figure 2B and C). There was no compression of the cranial nerve VII and VIII left or inner ear. MRI results concluded left pituitary microadenoma without infundibulum shifting, chiasmal compression or left cavernous sinus. The patient was diagnosed with pituitary microadenoma with micropenis and hyperprolactinemia, hypogonadotropic hypogonadism, hypotestosterone and hypoalbumin. The patient was recommended with a high-calorie, high-protein diet, methylprednisolone 4 mg every 8 h, bromocriptine 2.5 mg every 12 h, and testosterone intramuscular injection 250 mg each month.

The patient was asked to follow-up to the endocrine policlinic a month later by examining levels of free thyroxine (FT4), thyroid stimulating hormone (TSH), follicle stimulating hormone (FSH), luteinizing hormone (LH), and lipid profile. The patient was consulted to a neurosurgeon specialist regarding the management of a pituitary microadenoma.

One month later, the patient still felt unbalanced when starting to walk. The small testicles and penis were still present. Other complaints were absent. From the physical examination showed no signs of anemia. Heart, lungs and abdomen were within normal limits. The results of laboratory examination were: Hb 13...
g/dL, leukocytes 11,750/mm³, platelets 210,000/mm³, prolactin 27 ng/mL, growth hormone 0.083 ng/dL, FT4 0.64 ng/dL, TSH 5.7 IU/mL, FSH 1.2 IU/mL (normal range: 1.5-12.4), LH 1.5 IU/mL (normal range: 1.7-8.6), cortisol 2.52 μg/dL (normal range: 10-20 μg/dL), triglyceride 256 mg/dL, LDL 192 mg/dL, HDL 45 mg/dL, total cholesterol 200 mg/dL. The patient was diagnosed with pituitary microadenoma with micropenis and hypocortisolism, hypothyroidism, hyperprolactinemia, dyslipidemia and hypogonadism. The presence of a pituitary microadenoma, especially in cases of hypogonadotropic hypogonadism, can affect the occurrence of micropenis, especially in patients with small penises. Micropenis therapy generally aims to make the patient have a penis size that suits the patient's body image and can perform normal urination and sexual functions. Hormonal therapy can be achieved by giving 250 mg of testosterone intramuscularly. This therapy has been recommended by urologists, especially in patients with small penises. However, surgery is an alternative if hormonal therapy does not work. In this patient, 250 mg of testosterone was administered intramuscularly. The effect of giving testosterone is still being evaluated because the penis size in the patient is still around 4 cm after eight months of administration.

In micropenis case, the cause should be explored. Related hormones should be examined, including growth hormone, prolactin, testosterone, TSH, FSH, LH, ACTH; since these hormones play a role in the formation and development of male genital organs from infancy. In addition, a head MRI scan can also be performed to identify for anatomical disorders that can affect the occurrence of micropenis, especially in cases of hypogonadotropic hypogonadism. In addition, some experts also use karyotype examination using Y-fluorescence, to determine gender. The patient's penis erection size was 4 cm (less than 2.5 standard deviations), without any anatomical abnormalities. The patient had FSH levels of 1.2 mIU/mL (normal: 1.5-12.4 IU/mL), LH: 1.5 IU/mL (normal: 1.7-8.6 IU/mL), testosterone: 220 ng/dL. The patient also had a pituitary microadenoma. Therefore, the patient was diagnosed with micropenis due to decreased secretion of FSH, LH, and testosterone hormones due to hypogonadotropic hypogonadism. Pituitary microadenoma in the patient can affect these hormones to decrease.

Seven months after the first visit, patient's balance when walking was gradually improving. The patient complained that the penis size was still small, and could not produce sperm. A wound was found on the patient's left ankle, the patient claimed that it was since a week ago due to scratching. From the physical examination, blood pressure: 130/90 mmHg, pulse: 99 x/min. The head and neck were within normal limits. The results of laboratory examination were: prolactin 25 ng/dL, cortisol 1.5 μg/dL, TSH 2.0 IU/mL, FT4 1.5 ng/dL. The patient was treated with testosterone intramuscular injection 250 mg every month, methylprednisolone 4 mg every 8 h, simvastatin 20 mg every 24 h, and levothyroxine sodium 50 mg every 24 h. The patient was planned to follow up every month to evaluate hormonal levels.

Nine months follow-up, the balance was improving much better. The penis size was still small, and could not produce sperm. A wound was found on the patient's left ankle, the patient claimed that it was since a week ago due to scratching. From the physical examination, blood pressure: 130/90 mmHg, pulse: 99 x/min. The head and neck were within normal limits. The results of laboratory examination were: prolactin 25 ng/dL, cortisol 1.5 μg/dL, TSH 2.0 IU/mL, FT4 1.5 ng/dL. The patient was treated with testosterone intramuscular injection 250 mg every month, methylprednisolone 4 mg every 8 h, simvastatin 20 mg every 24 h, and levothyroxine sodium 50 mg every 24 h. The patient was planned to follow up every month to evaluate hormonal levels.

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Our patient complained of protruding nipples, accompanied by a small penis with erection difficulties. From laboratory examination, there was an increase in prolactin production (27ng/dL), low FT4 and TSH values, low cortisol, low testosterone, and low growth hormone values. From the MRI examination with contrast, a mass was found in the left pituitary with a size of 8.3 x 1.4 mm. The patient was diagnosed with pituitary microadenoma with increased prolactin production, micropenis, hypotestosterone, hypocortisolism, and hypothyroidism. The anterior pituitary produces growth hormone (GH). The decrease in GH in adults occurs in 1:100,000 of the population and can be caused by damage to the pituitary, mainly caused by tumors in the pituitary. In this patient, there was a decrease in growth hormone, namely 0.085 ng/mL, and the presence of a microadenoma in the patient's pituitary. The presence of a pituitary microadenoma causes a decrease in growth hormone. Treatment in adult patients with growth hormone deficiency is the administration...
of recombinant growth hormone. Recombinant growth hormone can be given at a dose of 0.2-0.3 mg daily at 30-60 years old.11

The patient stated that body tremors accompanied complaints of frequent weakness. Patients also feel a decrease in sexual ability. The patient had low cortisol levels, with pituitary microadenoma. Thus, hypocortisolism in patients occurs due to pituitary microadenoma. The patient was treated with methylprednisolone 3 x 4 mg equivalent to 20 mg hydrocortisone. Then the patient underwent routine follow-up to the endocrine policlinic to monitor cortisol levels.

Hyperprolactinemia in pituitary microadenomas is often found and accounts for 30-40% of the causes that occur in pituitary adenomas.12 The administration of bromocriptine is a drug that is widely used in cases of hyperprolactinemia due to pituitary adenoma. Administration of bromocriptine can reduce tumor size by inhibiting the synthesis and secretion of the hormone prolactin and inhibiting angiogenesis around the tumor.12 Giving bromocriptine can reduce levels of the hormone prolactin up to 7.5-10 mg/day. Giving bromocriptine to male patients can restore sexual function in approximately one year. However, the use of bromocriptine has several disadvantages, namely, it can cause fibrosis and hardening of the tumor and thickening of the tumor capsule, making surgical strategies difficult.12

In this case, bromocriptine was given 2 x 2.5 mg/day. The purpose of giving bromocriptine is to reduce the production of the prolactin hormone by decreasing the secretion of the prolactin hormone. The results showed a decrease in the hormone prolactin from 30 to 20 ng/dL. In addition to giving bromocriptine to inhibit the secretion of the hormone prolactin, the patient was also given levothyroxine sodium, methylprednisolone, and testosterone injection to overcome the decrease in hormones.

Treatment for decrease in testosterone levels can use testosterone replacement therapy, namely testosterone injection.13 Our patient had decreased testosterone levels (2.0 ng/mL), along with low FSH and LH followed by the presence of a pituitary microadenoma in the patient. This patient was male and unmarried so the patient was given 250 mg of testosterone replacement injection every month. Testosterone hormone monitoring is needed to determine the evaluation of treatment results.

This patient had complaints of tiredness and dry skin, constipation or weight gain was absent. The patient also had low FT4 (0.64ng/mL), low TSH (5.7 IU/mL) accompanied by a pituitary microadenoma. We therefore diagnosed the patient with hypothyroidism caused by a pituitary microadenoma. Our patient was treated with levothyroxine sodium and the patient's FT4 level improved.

The prognosis in microenines patients with pituitary microadenoma with hormonal disturbances varies widely. It needs adequate hormone regulation and control of tumor size in patients to live better. In addition, it is also necessary to pay attention to the side effects of medical therapy given to patients, for example, related to the use of corticosteroids and regarding blood sugar control in patients. Education about other symptoms that arise, for example, double vision, headaches, tiredness, and is needed to be mentioned to patients so that the seek for medical attention is immediate and reduce complications caused by pituitary microadenoma or hormonal disturbances caused.14 If medical management is unsuccessful and the tumor size continues to increase to more than 10mm, surgery and radiotherapy may be considered.15

This patient is still being monitored regularly every month to evaluate the success of hormonal treatment and the size of the tumor in the patient. So far, fatigue complaints are reduced and there is no double vision experienced in the patient.

CONCLUSION

It has been reported that a male patient had a pituitary microadenoma with complications of microenines, hypocortisolism, decreased testosterone levels, hyperprolactinemia and decreased TSH. The patient was treated with bromocriptine, methylprednisolone, and testosterone injection therapy. The patient improved prolactin levels, but persistent low cortisol levels and testosterone levels show that evaluation is needed for further therapy. Patient complaints, such as fatigue, were still present but improving. Monitoring is needed for evaluation of therapy for patients. Pituitary microadenomas as experienced by the patient could be managed by hormone therapy.

PATIENT CONSENT

The patient provided written informed consent to include the case as case-report.

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DISCLOSURE OF CONFLICTS OF INTEREST

We do not have conflict of interest.

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AUTHOR CONTRIBUTION

All authors contributed significantly to the case-report.

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