

CASE REPORT**MANAGEMENT OF HYPERPROLACTINEMIA CAUSED BY PITUITARY MICROADENOMA**

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Abstract

Hyperprolactinemia is an increase in fasting levels of the hormone prolactin above 20 ng/ml in men and above 25 ng/ml in women. Hyperprolactinemia occurs more often in women of reproductive age, with a percentage of 9 – 17%. The etiology of hyperprolactinemia can occur due to abnormal pituitary secretions, systemic disease, use of drugs, damage to the hypothalamus-pituitary axis. A 33-year old female patient came to the FER Polyclinic at M. Djamil Hospital with complaints of not menstruating for the past 2 months. Irregular menstruation since 15 years ago, menstruation 2-3 times in 6 months, irregular cycle for 7-8 days. The patient also complained of a fluid like breast milk coming out of the breast for 5 years, initially the fluid came out in a trickle and then gradually reduced and now the fluid comes out occasionally if the breast is squeezed. From the supporting examinations carried out, it was found that the prolactin hormone level in this patient was 134.53, and the results of the MRI examination showed a mass measuring 1.05x1.12x0.5 mm, which was diagnosed as secondary amenorrhea, hyperprolactinemia, and suspected pituitary microadenoma. The patient will be monitored for general condition and vital signs, as well as consultations with colleagues involved, such as consultations to the Internal Medicine section, Endocrinology, Metabolic and Diabetes Subdivision.

Keyword: Hyperprolactinemia; Pituitary microadenoma; Secondary amenorrhea

Introduction

Prolactin (PRL) plays a central role in various reproductive functions. Initially, although this hormone related to lactation in women, more recent research has focused on prolactin in relation to its effects on reproduction. Hyperprolactinemia is a condition of increased levels of prolactin in the blood, which can be physiological, pathological or idiopathic. Unlike other tropic hormones secreted by the anterior pituitary gland, prolactin secretion is controlled primarily by inhibition from the hypothalamus and does not follow a negative feedback loop directly or indirectly by peripheral hormones.¹ Hyperprolactinoma is a common endocrine disorder of the hypothalamo-hypophyseal axis. Hyperprolactinoma happens more often in women. The prevalence of hyperprolactinemia ranges from 0.4% in the adult population to as high as 9–17% in women with reproductive disease. The prevalence was found to be 5% in family planning clinics, 9% in women with adult-onset amenorrhea, and 17% in women with polycystic ovary syndrome.¹

Prolactinomas comprise nearly 40% of all pituitary tumors. Patients with prolactinoma usually present to healthcare facilities as a result of symptoms caused by elevated prolactin levels, such as hypogonadism, menstrual irregularities, infertility, galactorrhea, or due to mass effect. Sometimes, patients are present in an emergency, either because of vision loss or because of an acute severe headache associated with hypopituitarism. Most patients with hyperprolactinemia do not have prolactinoma.² Physiological hyperprolactinemia is usually mild or moderate. During normal pregnancy, serum prolactin increases progressively to approximately 200-500 ng/mL. Many common medications cause hyperprolactinemia usually with prolactin levels less than 100 ng/mL. Prolactinoma accounts for 25-30% of functioning pituitary tumors and is the most common cause of chronic hyperprolactinemia.³ Prolactinomas are divided into two groups: (1) microadenomas (smaller than 10 mm), which are more common in premenopausal women, and (2) macroadenomas (10 mm or larger), which are more common in men and postmenopausal women.

Management of hyperprolactinemia secondary to pituitary macroadenoma is accepted as needed. Drugs in the form of dopamine agonists are the first line of treatment, with surgery and radiotherapy being options for patients who are refractory and intolerant to drugs. The primary goal of treatment in patients with pituitary macroadenoma is to control the compressive effects of the tumor, including compression of the optic chiasm, with a secondary goal of restoring gonadal function. However, the indications and treatment modalities for hyperprolactinemia due to pituitary microadenomas are less clearly different from macroadenomas.⁴ Not all patients with hyperprolactinemia require treatment.

The primary goal of treatment in patients with pituitary macroadenoma is to control the compression effects of the tumor, including compression of the optic chiasm, with a secondary goal of restoring gonadal function.⁴ Cabergoline and bromocriptine have been the treatment of choice for more than 15 years in many countries, as they allow normalization of prolactin blood levels in 90% of patients with microadenomas and 80% with macroadenomas at a weekly dose of ~1.0 mg, but from several studies conducted most used bromocriptine as

first-line medical therapy.⁵

Case Report

A 33-year old female patient came to the FER Polyclinic at M DJAMIL Hospital with complaints of not menstruating for the past 2 months. Irregular menstruation since 15 years ago, menstruation 2-3 times in 6 months, irregular cycle, for 7-8 days, 2-3 changes of sanitary napkins per day, menstrual pain (-), First day of last menstruation May 17 2023. The patient also complained of a fluid like breast milk coming out of the breast for 5 years, initially the fluid came out in a trickle and then gradually reduced and now the fluid comes out occasionally if the breast is squeezed. Changes in the shape of the breast skin are denied. The patient did not experience smell disorders, fever, trauma, vaginal discharge, drastic weight loss, pain during intercourse, bleeding during intercourse, or bowel and urination disorders. The results of the physical examination were within normal limits. The patient underwent laboratory tests for prolactin, TSH, FT4, ultrasound, and intracranial MRI.

Laboratory examination results showed that there were increased levels of prolactin (134.53; N= 5.18-26.53) and FT4 (1.24; N=0.82-1.21). Laboratory results can be seen in table 1. Intracranial MRI results show that there is a pathological lesion is hypointense on T2W1 and hyperintense on STIR filling the intrasellar area with firm borders, regular edges measuring 1.05x1.12x0.56 mm, the lesion is not accompanied by calcification, and the lesion is still limited inside sella (Figure 1). Meanwhile, the ultrasound results showed that the uterus and adnexa were within normal limits. From all the examinations that had been carried out, the patient was diagnosed with secondary amenorrhea, hyperprolactinemia, and suspected pituitary microadenoma. The patient is planned to be consulted at the Department of Internal Medicine, Endocrine Subdivision.

Table 1. Laboratory Results.

	Hasil	Nilai normal
Prolaktin	134.53	5.18-26.53
TSH	1.07	0.25-5.0
FT4	1.24	0.82-1.21

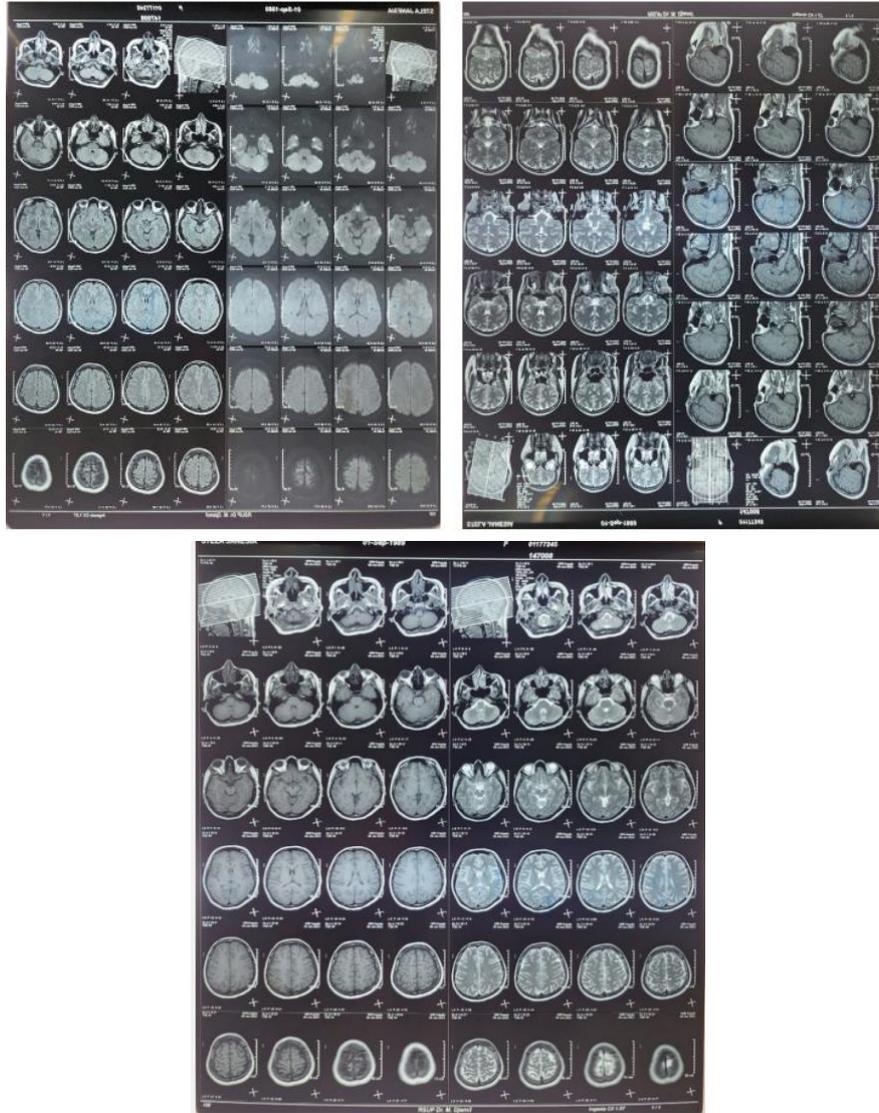


Figure 1. Intracranial MRI results.

Discussion

Hyperprolactinemia is a condition of increased levels of prolactin in the blood which can be physiological, pathological or idiopathic.¹ Prolactin is a 198 amino acid protein (23-kd) produced in the lactotroph cells of the anterior pituitary gland. Its main function is to promote breast development during pregnancy and to induce lactation. However, prolactin also binds to specific receptors in the gonads, lymphoid cells, and liver.⁶ Hyperprolactinemia can be assessed through laboratory and imaging tests.

Hyperprolactinemia can be physiological or pathological. During normal pregnancy, serum prolactin increases progressively to approximately 200-500 ng/mL. Many common medications cause hyperprolactinemia usually with prolactin levels less than 100 ng/mL. Prolactinoma accounts for 25–30% of functioning pituitary tumors and is the most frequent cause of chronic hyperprolactinemia.³ Prolactinomas are divided into two groups: (1) microadenomas (smaller than 10 mm) which are more common in premenopausal women,

and (2) macroadenomas (10 mm or larger) which are more common in men and postmenopausal women.

The case of a 33-year-old woman came with complaints of not menstruating for the past two months. A fluid like breast milk coming out of her breasts for five years. The fluid initially came out in a trickle, gradually decreasing, and now the fluid comes out occasionally if the breast is squeezed. Irregular menstruation since 15 years ago. The patient complained of headaches 16 years ago. Then, the patient underwent a laboratory examination of prolactin and found that the levels had increased. MRI examination was carried out and diagnosed with suspected pituitary microadenoma. The next problem for this patient is how to provide appropriate follow-up treatment for this patient.

Based on the management algorithm included in the research of Majumdar et al., after a patient is diagnosed with a microadenoma, the first treatment that can be carried out is by administering medical therapy.¹ As a first-line therapy, dopamine agonists, namely bromocriptine, can be given at a dose of 1.25 mg at bedtime or after dinner every day for one week. After that, the dose is increased to 1.25mg 2 times a day taken after breakfast and dinner. The dose can be increased every four weeks if prolactin hormone levels have not reached normal by administering a maximum dose of 5 mg 2 times a day. Following the literature, the drug bromocriptine, a class of dopamine agonists, is the first choice for conditions of hyperprolactinemia. Dopamine agonists work by suppressing the synthesis and release of the hormone prolactin and the proliferation of lactotroph cells so that they can reduce tumor size.^{2,6}

Prolactin hormone level evaluation is carried out four weeks after administering the drug. If the levels are normal, there is no need to carry out repeat or serial examinations however, if the symptoms that the patient complains of still exist, the examination can be repeated after 3 - 6 months. If after administering the drug it is found that the prolactin hormone levels have returned to normal, further evaluations are carried out every 3 - 6 months in the first year, then every 6 - 12 months in the following year.

Based on the literature, surgery is performed if the patient cannot tolerate medication, women with prolactinomas measuring more than 3 cm. The surgical procedure that could be an option is transnasal transsphenoidal microsurgery (ETTA) which is indicated for large tumor sizes, tumors that extend to the suprasellar, and persistent visual impairment.¹ However, in this case, there is no indication for surgery because of the size of the tumor is still under 3cm. So, the patient will be tried with medical therapy first after that, a further evaluation will be carried out on the patient's clinical condition and prolactin hormone levels.

Conclusion

1. Hyperprolactinemia is an increase in fasting levels of the hormone prolactin above 20 ng/ml in men and above 25 ng/ml in women. Hyperprolactinemia occurs more often in women of reproductive age, with a percentage of 9 – 17%



2. The etiology of hyperprolactinemia can occur due to abnormal pituitary secretions, systemic disease, use of drugs, damage to the hypothalamus-pituitary axis. Of the various etiologies, increased levels of the hormone prolactin often caused by abnormal secretions from the pituitary and 40% are due to pituitary adenoma.
3. Clinical conditions due to increased secretion of the hormone prolactin, ranging from reproductive disorders, suppression due to mass effects and other accompanying symptoms. In this patient, secondary amenorrhea had been clinically evident for eight months, and there had been visual disturbances for three months.
4. From the supporting examinations carried out, it was found that the prolactin hormone level in this patient was 134.53, and the results of the MRI examination showed a mass measuring 1.05x1.12x0.5 mm, which was diagnosed as pituitary microadenoma based on its size.
5. The patient will be monitored for general condition and vital signs, as well as consultations with colleagues involved, such as consultations to the Internal Medicine section, Endocrinology, Metabolic and Diabetes Subdivision.

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