

Case Report of Premature Ovarian Insufficiency in a 22 - Year - Old Woman with Low AMH Levels

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Abstract: *Premature Ovarian Insufficiency or POI is a diagnosis that is rarely found, this occurs due to the ovaries function failure to perform its main task and occurs at the age of <40 years so it is often referred to as early menopause, the prevalence is only 1%. POI can cause infertility in patients, examination of Anti - Müllerian hormone or AMH levels is often used to estimate the number and quality of the patient's oocytes. POI can also cause various complications and can also reduce the quality of life in patients with POI. We report the case of a young patient with a diagnosis of POI and low AMH levels.*

Keywords: Premature Ovarian Insufficiency, POI, AMH

1. Introduction

Premature Ovarian Insufficiency or also known as Premature ovarian failure is a condition where the ovaries are unable to function properly before reaching the age of 40 years. POI is usually characterized by the presence of hypoestrogen in the patient, this causes menstrual disorders, infertility and psychological problems, causing disturbances in the patient's quality of life.¹ The rate of occurrence of POI is 1% of all women. The risk of POI in patients before the age of 40 years is about 1%. At the age of 18 - 25 years, the prevalence of the incidence of POI is 1: 10, 000, and 1: 1000 in patients aged 25 - 30 years. In patients with primary amenorrhea it is 10 - 28%, whereas in patients with secondary amenorrhea it is 4 - 18%.¹ In a study conducted by Golizar S et al using the meta - analysis method, the global POI was 3.7%.² Meanwhile, in another study conducted in Sweden, the incidence rate was 1.8%.³ POI will cause lifelong problems in patients with this diagnosis, the incidence of infertility caused by POI is absolute, and the therapy given does not have much effect on this problem. Long - term effects of POI include cardiovascular disorders, osteoporosis, cognitive impairment and psychological disorders.⁴ The average age of menopausal patients is 51 years, experiencing menopause at the age of under 45 years occurs in 5% of women. The number of ovarian follicles is reduced so that only about 1000 follicles per 1 ovary remain during perimenopause. Symptoms of POI are amenorrhea that has occurred for at least 4 months with characteristics on examination of hormonal levels, an increase in FSH levels and a decrease in AMH levels can be found in patients. The most common cause of POI is idiopathic, other causes include autoimmune, genetic, iatrogenic, and environmental factors where idiopathic events are most often found with an incidence rate of 74 - 90% of POI patients.¹ Previous studies have suggested a recognizable cause of POI can be found in 10 - 15% of POI patients.⁵

In patients with POI, FSH and AMH levels are often abnormal, these two tests are also used to assess the fertility status of a woman with POI. AMH is better known as a serum marker to assess the function of the ovaries, AMH is a polypeptide, which is a family of Transforming Growth

Factor - β (TGF β). The AMH gene is located on chromosome 13 and its receptor on chromosome 12 is called AMHR2.6 AMH levels will increase at the time after puberty and reach its peak at the age of 24 years, after that, the number will begin to decrease and reach its lowest point at the age of menopause. The number and quality of oocytes has a strong relationship with AMH levels in women.⁷ So that AMH can be used as a measuring tool to assess fertility status in women because it can estimate the number and quality of oocytes.

2. Case Report

A 22 - year - old woman came to the Obstetrics & Gynecology polyclinic with complaints of amenorrhea, the initial complaint was said when the patient was 16 years old, amenorrhea lasted for approximately 15 months. The patient experienced menarche at the age of 15 years and had menstruation for 3 days, but for no known reason, her menstruation stopped for approximately 15 months before the patient finally decided to go to the ob - gyn polyclinic. Previously, the patient did not have a history of any disease, there was no history of using any contraception in this patient or the use of drugs and also a history of surgery and radiotherapy was denied. The history of development from birth was found that the patient was born at term, and was born with a normal delivery. History of growth and development within normal limits. The patient has 1 brother. On physical examination, there were no signs of hirsutism, goitre, or galactorrhea. Vital signs were obtained, blood pressure 110/70, pulse 78x/minute, respiration 18x/minute, body temperature 36.7 degrees Celsius, body weight 55 kg, height 155cm, examination of the thorax and abdomen found no abnormalities. The appearance of the vulva was normal, with tanner II breast growth and tanner I growth for pubic hair. On investigation, the FSH level was 137.00mIU/mL (normal value 1.48 - 11.70), LH 70.50mIU/mL (normal level 0.6 - 21.0), Prolactin level was obtained 7.70ng/mL (normal level 3.10 - 17.90ng/mL), estradiol level <20.00 pg/mL (normal level <=111pg/mL), AMH level <0.01 ng/mL (normal level 1.66 - 9.49 ng/mL), DHEA 148.8 ug/dL (normal level 134.2 - 407.4 ug/ dL), ACTH levels 9pg/mL (normal levels 6 - 50). The patient

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was also checked for thyroid hormone levels TSHs: 0.609 uIU/mL (normal level 0.350 - 4.940uL/mL) from the results of laboratory tests, the results were hypogonadotropic and hypogonadism due to premature ovarian failure. After getting the results. The patient was given HRT therapy using Combination of contraceptive pill therapy, and the patient finally returned to menstruating for 5 days with a 28 - day menstrual cycle. However, when therapy is discontinued, amenorrhea returns to this patient.

3. Discussion

POI is a very rare condition found in young female patients. The incidence of idiopathic POI in early to middle adolescence is extremely rare and rarely recognized, with an extremely rare incidence of 10/100, 000 cases in patients under 20 years of age reported annually.⁸

In this case, we report the case of a 22 - year - old woman who had secondary amenorrhea since she was 15 years old. The new patient came for a check - up when she was 16 years old, which is 1 year after the first amenorrhea occurred, on her appearance it was found that this patient looked like a woman in general according to his age, and after the examination, the FSH and LH levels increased quite high. This patient has experienced amenorrhea for approximately 1 year since she had her first menstruation, this is in accordance with the criteria for the diagnosis of POI where the patient has not had menstruation for at least 4 - 6 months, besides that the patient also experienced an increase in gonadotropin levels and also experienced a decrease in gonadotropin levels. on estradiol levels. Examination of FSH levels is referred to as the gold standard examination in cases of POI, in a study conducted, the results obtained were no follicles were found in the ovaries on ovarian biopsy examination in secondary amenorrhea patients with FSH levels > 40 mIU/mL. Patients with POI due to idiopathic causes had higher rates than patients with POI due to other causes. Examination of FSH levels is usually done by checking FSH levels twice with a time difference of 4 - 6 weeks.⁹ The limit level that is widely used is more than >40IU/L, a lower cut - off level is recommended by the European Society of Human Reproduction and Embryology suggesting an FSH level of >25IU/L.⁹ In general, the diagnosis of POI is made on amenorrhea caused by malfunction of the ovaries as indicated by the presence of hypergonadotropic hypogonadism, which can occur before menarche or as secondary amenorrhea. One of the known causes of hypergonadotropic hypogonadism in POI patients is a genetic abnormality that causes mutations in the gonadotropin receptor. Variants of LH gene inactivation and defects in steroidogenic enzymes (StAR mutation, CYP17, and aromatase) lead to impaired estradiol production which ultimately leads to low estrogen levels and high FSH levels.⁸ Symptoms that usually occur in patients with POI include a feeling of heat, night sweats, dyspareunia and vaginal dryness, sleep disturbances, mood disorders that these patients sometimes experience. This is caused by an abnormality in low levels of the hormone estrogen, but these symptoms do not always occur in all POI patients, symptoms can occur and come and go because they are influenced by changing ovarian function, so this cannot rule

out the diagnosis of POI in these patients. patient. Patients may also experience these symptoms when the contraceptive pill is discontinued.⁹

In this patient, the level of anti - Müllerian hormone (AMH) was also checked, which decreased in the result <0.01 ng/mL. AMH is also used as a marker to estimate the amount of ovarian reserve and one of the problems with POI is infertility, so AMH examinations are often performed on POI patients. The AMH test is currently the most frequently performed measure of ovarian reserve and is usually very low or even undetectable in patients with POI.¹⁰ Serum AMH levels will decrease along with the number of follicles that continue to decrease over time and reach their lowest levels at the time of physiological menopause. A study examining AMH levels found that AMH levels were lower in patients with POI.⁹ Examination of AMH levels in this patient was carried out when the patient stopped HRT therapy with the contraceptive pill because the use of contraceptive pills could affect the results of assessing AMH serum levels in patients.¹¹ Research conducted by Landersoe et al in a retrospective study showed that AMH levels were 30% to 40% lower in women using oral contraceptives and in women using intrauterine devices, AMH levels decreased by 17%.¹²

Research conducted by Alipour F et al showed that the sensitivity of AMH examination in the incidence of POI was higher than FSH examination but both had the same specificity, a significant difference was obtained with p value < 0.05 with AMH accuracy more than FSH so that AMH examination was more reliable. than FSH examination in POI cases.⁶ Another researcher also said that AMH examination was more reliable in detecting ovarian reserve than FSH, inhibin, and antral follicle count examinations.¹⁰ Nyström et al stated that AMH is the most accurate serum marker for determining POI, antral follicle count examination requires the use of transvaginal ultrasound which is often not approved by young patients because it causes discomfort, therefore transvaginal ultrasound examination for Antral follicular count assessment was not performed in these patients.¹³ In addition, AMH is a hormone that is considered stable and not too influenced by the cycle of ovarian activity so that its assessment is considered to be better than FSH levels, whose values are usually influenced by the activity of the ovarian cycle.⁷ One of the advantages of assessing AMH levels is that it can be used to identify patients who are at risk of developing POI such as in patients with a family history of POI, patients with a history of chemotherapy in the pelvic region, and in patients with a history of autoimmune disease. for early detection of POI.⁶

The most important treatment in cases of POI is Hormonal Replacement Therapy (HRT). HRT therapy should not be delayed in POI patients, unless there is a contraindication to HRT. Several studies have shown that HRT therapy can reduce the risk of complications that often occur in POI such as cardiovascular disorders and osteoporosis. Patients with POI should be informed that HRT before the normal age of menopause is necessary if there are no contraindications.⁴ The goal of POI treatment is to replace hormones that cannot be produced because of abnormalities in the ovaries

that occur at the age before menopause. Regardless of the cause of POI, patients with POI have low levels of the hormone estrogen. Young women require higher doses of estrogen than women who have gone through menopause to ensure that patients receive adequate hormonal replacement. Hormonal replacement therapy should be continued until the patient reaches menopause. Hormonal therapy in POI patients is very important for various aspects, hormonal therapy serves to help the formation of secondary sexual characters in prepubertal women with primary amenorrhea, hormone therapy also helps to reduce symptoms such as burning sensation and urogenital problems that are often complained of in patients with POI, and also hormonal therapy can help improve the patient's quality of life by improving mood, and cognitive problems that often occur in patients with POI, hormonal therapy can also increase the likelihood of spontaneous pregnancy in POI patients, spontaneous pregnancy in POI cases occurs in 5 - 10% of cases patients with a diagnosis of POI.¹⁴ And lastly, hormonal therapy can also reduce the risk of long - term side effects such as osteoporosis and cardiovascular disease in patients.⁸ Research conducted by Zhu D et al said that POI patients with hormonal therapy for a long time, especially use of more than 10 years, could reduce the risk of cardiovascular disease compared to patients who did not use hormonal therapy.¹⁵ Routine monitoring needs to be carried out in patients at risk of cardiovascular disease, monitoring blood pressure, weight and smoking habits can be routinely carried out on patients. In addition to cardiovascular disease, osteoporosis is also one of the serious problems that are often faced by patients with POI. With a prevalence of about 8% - 27% cases of osteoporosis at POI.¹⁶ Women with POI tend to have lower BMD levels than women with menopausal age usually. This osteoporosis problem can be handled with regular bone health screening. In addition, patients are also advised to live a healthy life, exercise using weights to avoid smoking, patients are also advised to add calcium and vitamin D supplements as additional vitamins and control body weight to optimize health the bones.

Another problem that can occur in patients with POI is the problem of psychological problems and the patient's quality of life is declining. The decreased quality of life is thought to be caused by sleep disorders that are often experienced by POI patients which ultimately affect the patient's mood, social activities, and affect performance at work. And many patients with POI also experience depression and psychological disorders. Several studies have revealed that the combination of conventional medical therapy and psychological therapy can increase the cure rate in POI patients, which in turn can improve the quality of life of these patients.¹⁷ Mood disorders that occur in POI patients are usually caused by the patient's worry about his health problems and also due to reproductive problems that occur in patients who want to have offspring. This causes depression and decreased self - confidence in POI patients.¹⁸ Intervention from a psychiatrist and support from the family is needed for this problem. Sexual problems and genitourinary function should also be considered for patients with POI. The problems most frequently complained of by patients with estrogen disorders are vaginal dryness, vaginal irritation and itching in the genital area.¹⁹ One study said that patients with POI experienced serious sexual problems

where the patient felt more pain and problems with lubrication during sexual intercourse.¹⁸ This can be overcome by adding lubricant gel before starting sexual intercourse.

Infertility is frightening for patients with POI who wish to have children. Although the possibility of spontaneous pregnancy can occur in patients with POI, the probability is small, namely 5 - 10% of patients with POI are found to have spontaneous pregnancies. Therapy that can be used to treat infertility problems in POI patients is oocyte donation. The percentage of successful pregnancy with the oocyte donation method is quite high, namely 40% after 1 cycle of oocyte donation and the percentage increases after 4 cycles of oocyte donation until it reaches 70 - 80% success.²⁰ However, such therapy is not available in all countries, and not all patients are willing to use this type of therapy.¹

Hormonal replacement therapy in POI patients is a long - term use. POI patients often complain about feeling tired and bored to take medication every day and also complain about the side effects of HRT therapy, some of the side effects of HRT are weight gain, weight that often fluctuates, decreased stamina, nausea, migraine, excessive acne and hair loss.²² Socio - economic issues should also be considered in POI patients. A study conducted in Korea by Lim YM et al concluded that low socioeconomic status was strongly associated with an increased risk for POI and early menopause.²³ Considering that HRT therapy in this patient is carried out for a long time so that the costs needed for therapy are quite high so that the socio - economic status of the patient must also be considered in the selection of therapy.

4. Conclusion

This patient had low FSH and AMH levels. This is the basis for the diagnosis of POI in this patient. From previous research, it was found that AMH levels were more reliable in detecting POI. Of the many causes that can cause patients to experience POF, until now the most common cause is idiopathic, in this case a clear etiology has not been found as the main cause of the occurrence of POI but maybe in another time, we can do further examination to seek the cause of poi in this patient such as chromosomal analysis, and Fragile - X premutation testing⁹. POI in adolescents is very rare and requires more attention considering the complications that can occur in POI patients are a serious problem. Therefore, in addition to HRT therapy, monitoring of complications that can occur needs to get more attention.

5. Author Contribution

All authors contributed equally.

6. Conflict of Interests

There is no conflict of interests in this case report.

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