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Ultra-Low Anti-Müllerian Hormone Levels in Recurrent Cystic Ovarian Neoplasm: A Case Report

Merci Monica br Pasaribu[1], Naufal Arkan Abiyyu Ibrahim[2], Dayu Satriani[2]

[1] Department of Clinical Pathology, Faculty of Medicine, Universitas Indonesia/Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
E-mail: mercipasaribu@gmail.com
[2] Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

ABSTRACT

Fertility has been a major issue in the management of cystic ovarian neoplasm. This case report presents an extreme case of ultra-low AMH levels in a young female with recurrent cystic ovarian neoplasm and analyzes the potential causes. A twenty-two-year-old female presented with stomach discomfort. The patient had undergone two surgeries for ovarian neoplasm within the last six years. The patient had another abdominal lump suspected to be a residual tumor mass. After further examination, the patient was diagnosed with cystic ovarian neoplasm. The laboratory findings showed low T4 levels, increased TSH levels, and ultra-low AMH levels (0.023 ng/mL). Management of cystic ovarian neoplasm should concern the effect on fertility. The AMH level can be used for pre-treatment counseling in these patients.

Keywords: Anti-Müllerian hormone, ovarian neoplasm, ovarian cysts, fertility, case report

INTRODUCTION

The ovarian cyst has become an essential topic in reproductive medicine. The prevalence of ovarian cysts remains unclear because many cases are asymptomatic and undiagnosed. Ovarian cysts can occur at any age but are more common in reproductive years.[1] Global Cancer Observatory (GLOBOCAN) reported an increasing trend for females aged <40 in Asia.[2] Although most cases are benign, ovarian cysts could present as malignant neoplasms.[3] Post-menopausal and older females are associated with a higher risk for malignancy.[1]

Cystic ovarian neoplasm is usually treated with surgery. One of the significant concerns regarding surgical management is the preservation of fertility. Fertility-sparing surgery has been the preferred treatment, especially in benign cases and in younger patients.[4] However, the extent to which this procedure truly affects fertility remains unclear. Several studies have shown that surgery hurts the ovarian reserve.[5,6]

Anti-Müllerian Hormone (AMH) is a glycoprotein hormone that belongs to the Transforming Growth Factor-β (TGF-β) group. The physiological role of AMH is to inhibit the recruitment of primordial follicles, thereby preventing premature depletion of the ovarian reserve. In clinical settings, the AMH has been known for its role as a marker of ovarian reserve. The function of AMH has extended, from predicting the response of ovarium to stimulation to predicting the result of the Assisted Reproduction Techniques (ART). The AMH also has an essential role in evaluating the ovary function before and after a surgical procedure.[7]

In this case report, present a case of ultra-low serum AMH in a young female with recurrent cystic ovarian neoplasm who had undergone two surgeries. This case report analyze the potential causes of the low AMH levels and how the treatment for the cystic ovarian neoplasm affected the ovarian reserve.

CASE

A twenty-two-year-old female patient went to our hospital with stomach discomfort, which had been coming and going for the past month. The patient also experienced frequent urination without dysuria or bloody urine. The patient had a history of irregular menstruation and had a normal Body Mass Index (BMI). Six years ago, the patient was diagnosed with ovarian endometrioma and underwent surgery in the same year. Four years after the surgery, the patient underwent a laparotomy, omentectomy, and appendectomy. A pathology examination was carried out with a conclusion of ovarian mucinous cystadenoma. The patient had another lump in the abdomen a year ago and was suspected to have a residual tumor mass.

No abnormality was found during the physical examination except for pale conjunctiva. Abdominal Multi-slice Computed Tomography (MSCT) with

Table 1. Patient's laboratory findings

Laboratory Test	Findings on Admission	Findings after One Month	Reference Value
Hematology			
Hemoglobin (g/dL)	**10.8**	**9.8**	12.0-15.0
Hematocrit (%)	**32.6**	**29.4**	36.0-46.0
Erythrocyte (10^6/µL)	**5.74**	**5.07**	3.80-4.80
MCV (fL)	**56.8**	**58.0**	83.0-101.0
MCH (Pg)	**18.8**	**19.3**	27.0-32.0
MCHC (g/dl)	33.1	33.3	31.5-34.5
Thrombocyte (10^3/ µL)	**434**	**415**	150-410
Leukocyte (10^3/ µL)	8.90	6.91	4.00-10.00
Basophil (%)	0.8	12	0-2
Eosinophil (%)	3.8	3.8	1-6
Neutrophil (%)	47.6	44.5	40.0-80.0
Lymphocyte (%)	**42.0**	**43.7**	20-40
Monocyte (%)	5.8	6.8	2-10
Immunology			
TSH (µIU/mL)	-	**39.177**	0.35-4.94
Free T4 (ng/dL)	-	**0.68**	0.70-1.48
CEA (ng/mL)	0.7	0.7	≤ 5
CA 19-9 (U/mL)	**145.7**	**145.7**	≤ 37
CA-125 (U/mL)	15.8	15.8	0.0-35.0
B-HCG (mIU/mL)	-	< 1.20	
AFP (ng/mL)	-	2.01	0.89-8.78
AMH (ng/mL)	**< 0.023**	**< 0.023**	0-14.8

AFP=Alpha-Fetoprotein, AMH=Anti-Mullerian Hormone, CA=Carbohydrate Antigen, CEA=Carcinoembryonic Antigen, HCG= Human Chorionic Gonadotropin, MCH=Mean Corpuscular Hemoglobin, MCHC=Mean Corpuscular Hemoglobin Concentration, MCV=Mean Corpuscular Volume, TSH=Thyroid-Stimulating Hormone

contrast showed a well-demarcated hypodense multilocular cystic lesion. There was also a solid component in the adnexa's pelvic cavity, which extended to the right and left upper abdomen. The patient was diagnosed with cystic ovarian neoplasm. The laboratory findings showed hypochromic microcytic anemia and increased tumor marker CA 19-9 (Table 1). The AMH was ultra-low. Another laboratory examination was performed next month, and similar results, including the AMH, were found. Additional immunology examination found that the patient had a high Thyroid Stimulating Hormone (TSH) and low free T4 levels. There was no further pathology examination performed. The patient underwent salpingo-oophorectomy. No chemotherapy, radiotherapy, or hormonal therapy was prescribed for the patient.

DISCUSSION

The AMH levels in circulation change during several phases of life. In females, the ovarian granulosa cells begin to secrete the AMH from 36 weeks of gestation and continue until menopause. The AMH level peaks around the age of 25 years and then constantly declines until menopause. In females of reproductive age, the AMH levels are relatively stable because they are influenced mainly by the early recruitment rate of the follicular pool rather than the menstrual cycle.[7] Patient was 22 years old, and the AMH levels were supposedly near the peak; however, the AMH level was as low as <0.023.

AMH has been speculated to have an inhibitory role in the development of ovarian cancer since the early 80s. The hypothesis was based on the effect of AMH on the regression of Müllerian ducts during sex differentiation.[8,9] However, this effect remained inconclusive. There is still a knowledge gap between in-vitro or in-vivo and human studies. Several in-vitro and in-vivo studies suggest that AMH suppresses the development of ovarian tumors.[10,11] AMH initiates intracellular cascades that modify regulator protein and transcription factors related to cell proliferation and differentiation. These studies showed that AMH decreases tumor growth and cell proliferation and increases the apoptosis of cancerous cells.[8] These findings were inconsistent with the human studies, which found no association between AMH and

ovarian cancer development.[8,12] Further prospective study with a larger sample is needed to answer the remaining questions.

Several factors are associated with lower AMH levels, including genetic mutations, hormonal contraception, and obesity.[7] Although the genetic mutation in the patients remained unclear, the patient had no history of using hormonal contraception and had a normal BMI. High TSH levels also influence the reduction of AMH levels. Recent studies showed that TSH levels were inversely correlated with AMH levels in infertile females of reproductive age.[13] Although the diagnosis of infertility had not yet been established in the patient, the high TSH levels might influence the reduction in AMH levels. In an in-vivo study, TSH had a role in the failure of follicle development and affected the cal/interstitial and luteal cell steroidogenesis.[14]

The patient had recurrent cystic ovarian neoplasm and had undergone two surgeries within the last six years. Several studies have shown that AMH levels were significantly reduced after surgery. A meta-analysis showed that patients with benign non-endometriotic cysts had a 38% reduction in AMH level after cystectomy. The underlying mechanism was that the healthy ovarian tissues were removed during the surgery or damaged by the excessive use of diathermy for hemostasis.[5] The reduction is even higher and long-lasting in patients with endometriomas than in patients with a dermoid cyst or other benign ovarian cysts. A study by Lind *et al*. showed that patients with endometrioma had a 51% reduction in AMH level 6 months after surgery.[6] In the patients, the baseline AMH level was unknown; therefore, the timing of when the reduction happened cannot be identified. However, surgery might play a vital role in the reduction of AMH levels.

Low AMH levels have been associated with lower pregnancy and live birth rates. A study showed that patients with deficient AMH levels (<0.5 ng/mL) had an 18% clinical pregnancy rate per patient.[15] The cancellation rate for patients with deficient AMH levels was around 37.5%, as reported by Reichman *et al*.[16] For patients with ultra-low AMH levels (<0.16 ng/mL), Seifer *et al*. reported a clinical pregnancy rate of 13% and a cancellation rate of 54%.[17] As the AMH level in our patient was even lower, the clinical pregnancy rate and cancellation rate might resemble the rate reported by these studies.

Several studies have shown that the AMH level could recover in time if the rearrangement of follicle cohorts from the healthy primordial pool occurs. The AMH levels recovered after three months to nine months after surgery.[18] However, a trial showed that the AMH levels were still significantly lower than the basal level even three months post-surgery.[19] Another study investigating the effects of laparoscopic excision of endometrioma on AML level also showed that the AML decreased significantly to around 61% six months after surgery.[20] The AMH measurement in the patient was performed two years after the last surgery. The results of two consecutive examinations showed that the AMH level remained ultra-low.

CONCLUSION

Ovarian reserve has been a crucial point of view in females's reproductive health. Several factors and ovarian neoplasm surgery have been shown to reduce AMH levels. Our patient is one of the extreme cases where the AMH levels were ultra-low and remained so two years after the last surgery. Therefore, it is essential to identify the most appropriate surgical method regarding its effect on the AMH level. The AMH level is also helpful for pre-treatment counseling in patients with cystic ovarian neoplasm who desire fertility after surgery.

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