Case Report
Cholesterol granuloma mimicking ovarian cancer

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Abstract: Cholesterol granuloma is a consequence of a chronic inflammatory reaction with accumulation of cholesterol crystals in the tissue. Ovarian cholesterol granuloma is rarely reported in the literature and can be misdiagnosed as ovarian cancer during surgery due to pelvic fibrosis and adhesion secondary to chronic inflammation, especially in postmenopausal women. We present a patient who had been referred to our gynecologic oncology clinic. The patient was a 65-year-old overweight female. She was referred to our tertiary hospital due to suspicion of ovarian cancer since she had CA 125 level above 3000 U/ml with a pelvic mass. To date, no cases of cholesterol granuloma causing CA 125 level above 3000 U/ml have been reported in the literature. We performed an elective diagnostic laparotomy to rule out occult malignancy. After removing the mass, it was sent for frozen section intraoperative consultation. Grossly the mass had irregular surface with yellow-brown appearance. The final diagnosis of cholesterol granuloma with serous cystadenofibroma was made. No evidence of malignancy was found. Symptoms, clinical and intraoperative findings of ovarian cholesterol granuloma can be misdiagnosed as cancer. Since the final diagnosis of a pelvic mass depends on histologic analysis, cholesterol granuloma should be kept in mind as a differential diagnosis of pelvic mass.

Keywords: Cholesterol granuloma, ovarian cancer, cholesterol crystals, female genital system

Introduction

Cholesterol granuloma is a consequence of chronic inflammatory reaction due to accumulation of cholesterol crystals in the tissue. Although it occurs in several parts of the body, its most common site is ear [1]. It is a benign tumor-like lesion. It is very rare in humans. To the best of our knowledge there are a few cases of cholesterol granulomas affecting the female genital tract [2]. Especially when it occurs in postmenopausal women, it can be difficult to diagnose because it resembles malignant ovarian cyst due to a solid appearance. It is not always easy to distinguish benign and malignant adnexal masses in gynecological practice. Therefore, some patients may have to be operated unnecessarily despite having a benign mass. Today, no serum biomarker, physical examination finding, or radiological finding is both highly sensitive and specific for the diagnosis of ovarian cancer. Thus, it is necessary to combine examination findings, serum markers, and radiologic images to improve the detection of malignancy. Although CA 125 is increased in many benign conditions, it is the most widely used serum biomarker for the evaluation of an adnexal mass. The diagnostic reliability of CA 125 is beneficial mainly in postmenopausal patients. Although CA 125 sensitivity and specificity are higher in postmenopausal women than premenopausal women, it still has a false positive rate.

In this paper, we present a patient who had been referred to our gynecologic oncology clinic with the pre-diagnosis of ovarian cancer; however, she was diagnosed with cholesterol granuloma of ovary.

Case presentation

Our patient was a 65-year-old overweight female. She was referred to our tertiary hospital due to suspicion of ovarian cancer since she had CA 125 level above 3000 U/ml with a pelvic mass. Our study was done with patient consent. She was para three with three live births.
delivered by vaginal delivery. She had a medical history of hypertension and diabetes mellitus for 10 years. On examination an immobile solid mass, approximately 10 cm in diameter, was palpated in the right pelvic region.

Blood examination tests showed her haemoglobin level was 10.6 g/dL, WBC count 9,480 cells/mm³ with 56.6% neutrophils, blood sugar level was 93 mg/dL, and HbA1c concentration was 6.8%. Other biochemical values were within normal limits including total cholesterol, LDL cholesterol and triglyceride level. Her CA 125 level was above 1500 U/ml.

On the trans-vaginal ultrasonography, the endometrium was 3.2 mm in thickness. The left ovary was normal, in the right adnexal region there was 10 cm solid cyst with irregular surface. There was no ascites. She had undergone an abdominal CT scan in another hospital.

These scans underwent the consultation of our Radiology Division. A 97 × 10⁶ mm cystic lesion consisting of nodular extensions was observed (Figure 1). The patient’s CA 125 level was within the normal range [7.0 U/mL; RR <35 IU/ml], PAP smear showed no evidence of cervical intraepithelial lesion.

We performed an elective diagnostic laparotomy to rule out occult malignancy. Intraoperatively, the omentum was firmly adherent to the anterior abdominal wall and pelvic region. Adhesions were released. Approximately a 10 cm immobile mass enclosing the appendix and densely adherent to intestinal mesentery was noted. During dissection glassy-yellow fluid was drained from the ruptured area of the mass. Frozen section intraoperative consultation was done. Grossly the mass had irregular surface with yellow-brown appearance (Figure 2).

The uterus was normal, while left-sided ovary and tube were adherent to the sigmoid colon. Right ovary was also adherent to the right side of the pelvic wall. Total hysterectomy with bilateral salpingo-oopherectomy was done and sent for histopathologic examination. There were small multiple yellowish-white nodular lesions on the omentum and intestines that were dissected also. Frozen section evaluation of the specimen reported a benign granulomatous reaction.

Microscopic examination showed aggregates of longitudinal clefts of cholesterol crystals surrounded by lymphocytes, foamy histiocytes, neutrophils, and many multinucleated giant cells comprising a cholesterol granuloma in adipose tissue (Figures 3, 4). Histologic examination of parametrium, omental and intestinal lesions revealed cholesterol granuloma. Lymphocytes and hemolyzed erythrocytes were noted in the peritoneal fluid. A final diagnosis of cholesterol granuloma with serous cystadenofibroma was made. No evidence of malignancy was seen in any of the sections processed. The patient was discharged from hospital on the 5th day after surgery.

Discussion

Cholesterol granuloma was first described in 1917 by Manase. According to literature it
Cholesterol granuloma of ovary

Figure 3. Adipose tissue showing aggregates of longitudinal clefts of cholesterol crystals surrounded by multinucleated giant cells, epithelioid histiocytes, and chronic inflammatory cells [H&E × 40].

Figure 4. Adipose tissue showing aggregates of longitudinal clefts of cholesterol crystals surrounded by multinucleated giant cells, epithelioid histiocytes, and chronic inflammatory cells [H&E × 200].

Ovarian cholesterol granuloma is a rare entity and demonstrates a benign ovarian cyst, but it can mimic ovarian cancer clinically and radiographically. Exact diagnosis depends on histopathologic findings.

Although histological examination shows a foreign body reaction to cholesterol crystals, no clear consensus exists on the accurate etiopathogenesis. Moreover, the molecular mechanism for cholesterol granuloma formation in the cyst wall is still unidentified [8]. It has non-specific characteristics of chronic inflammation. Since the inflammation occurs against cholesterol crystals, a foreign body reaction is revealed by the accumulation of histiocytes, multinucleated giant cells, foamy macrophages, neutrophils, hemosiderin-laden macrophages, and cholesterol clefts [9]. The breakdown products of blood and inflammatory tissue affect foreign body giant cells, resulting in fibrosis. The cholesterol crystals may be derived from disintegrated erythrocyte cell membranes, plasma lipids, or fatty degeneration of connective tissue in a cyst blocked by inflammation. In our case histopathologic examination showed similar characteristics.

Since cholesterol granuloma formation is associated with inflammation and fibrosis, adhesions between granuloma and adjacent organs can be observed during surgery as in our case. Our patient had a conglomerated mass of ovarian cyst and intestines that was yellow-brown.

Impairment of drainage, hemorrhage with hemolysis, and hyperlipidemia [10] are thought to be causes of cholesterol granuloma formation [1]. Although our patient had the compo-
Cholesterol granuloma of ovary

Cholesterol granuloma of ovary

Components of metabolic syndrome, serum lipid levels were within normal limits. In animal studies it’s suggested that diabetes mellitus-induced hyperlipidemia may be a predisposing factor for development of cholesterol granuloma [2].

Presence of cholesterol granulomas has been rarely reported in female genitals. Sumathi represented a 65-year-old woman with endometrial cholesterol granuloma suffering from dribbling of urine and constipation [11] and Pounder reported another case of endometrial cholesterol granuloma which had strong suspicion of carcinoma clinically as in our case [12]. In imaging studies of the breast, it is stated that cholesterol granuloma can mimic breast cancer [13]. In addition, there are cases in which breast cancer was detected with cholesterol granuloma concurrently [14]. A single case of ovarian cholesterol granuloma was reported in a 37-year-old female in a journal and it was associated with torsion [4]. Our case is the first reported case with a suspected ovarian cancer in the literature.

Epithelial ovarian cancer [EOC] presents several diagnostic challenges. There are many difficulties in differentiating benign and malignant adnexal masses, so they can result in many surgical procedures for masses that are ultimately determined to be benign. Currently, no serum biomarker is both highly sensitive and specific for the diagnosis of EOC. Thus, we combined examination findings, serum markers, and radiologic images to improve the detection of malignancy. CA 125 is the most widely used serum biomarker for evaluation of an adnexal mass although it is increased in many benign conditions such as myoma, mesos, fibroids, endometriosis, liver, or peritoneal diseases. The diagnostic reliability of CA 125 is beneficial mainly in postmenopausal patients. Although the sensitivity and specificity of CA 125 is higher in postmenopausal women compared to premenopausal women, it has still a false positive rate. It has been shown that factors other than ovarian cancer may cause an increase in CA 125 value. In a study, the CA 125 value was higher in women over 60 years old when compared to women aged 55-59. But it was also shown as decreased in obese patients in the same study [15]. Our patient was a 65-year-old obese woman. There are many CA 125 tests currently used to increase the accuracy of ovarian cancer diagnosis, each with different test performance. We think that they all have equal accuracy in our daily practice. When evaluating the CA 125 value, serial tests should be done with the same test, which usually means using the same laboratory. The CA 125 level studied in the external center was higher than the one studied in our hospital. He4 could be studied in addition to CA 125, but in our hospital but there was no He4 assay. We did not intend to take a biopsy by diagnostic laparoscopy or pre-operative interventional radiology in order to avoid seeding cancer. In our case, it might have been more accurate to perform an MRI in the pre-operative study of the patient. Because cholesterol granuloma mainly contains lipid and our patient is a postmenopausal woman, the radiology department could report the mass as cholesterol granuloma with a low probability of teratoma. Since definitive diagnosis of ovarian cancer requires histopathologic examination of excised tissue, we decided to perform a surgical intervention for the diagnosis of our postmenopausal patient by evaluating her examination findings, radiologic findings, and blood test results together.

Conclusion

This case is presented because of its suspicion for cancer and rarity of site. Symptoms, clinical, and intraoperative findings of cholesterol granuloma can be misdiagnosed as ovarian cancer. Since the final diagnosis of a pelvic mass depends on histologic analysis, cholesterol granuloma should be kept in mind as a differential diagnosis of pelvic mass.

Disclosure of conflict of interest

None.

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References

Cholesterol granuloma of ovary


