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Impact of Serum CA19-9 Level in Clinico- Pathological and Radiologic Feature of Mature Cystic Teratoma: A Case Series

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ABSTRACT

Background & Objective: Ovarian mature cystic teratomas (OMCTS) are one of the most common benign ovarian tumors. Most MCTs can be diagnosed by ultrasonography (us). Due to heterogeneous composition and a variety of appearance, in some non-diagnostic imaging reports it is suggested that we evaluate some tumor markers (CA125 and CA19-9) to complement imaging modalities. According to previous investigation, a single elevated CA 19-9 is in association with specific radio-pathologic features, such as size, torsion, bronchial glands, fat and teeth components. Here we are presenting three different cases of OMCT with different characteristics.

Case Presentation: Case 1: asymptomatic, non-diagnostic US, single- elevated CA19-9, smaller than in 10 cm with bronchial glands and fat component. Case 2: symptomatic, non-diagnostic U.S. normal CA19-9, larger than 10 cm with torsion and necrosis. Case 3: symptomatic, diagnostic US, single- elevated CA19-9, smaller than 10 cm, full of hair and sebaceous material. Computer tomography (CT), in all of our cases was diagnostic based on OMCT. Apologia of pathologic pathway of elevated CA19-9 in both cases 1 and 3 were in agreement with the result of previous investigations. In case 2, despite its large size and torsion, CA 19-9 level was low.

Conclusion: Single- elevated CA 19-9 level in OMCTs could impact benign characteristics of this kind of tumor.

Keywords: Teratoma, CA19-9, CA125, Tumor

Introduction

Ovarian mature cystic teratoma (OMCT) is one of the most common ovarian tumors and 95% of all ovarian germ cell neoplasms with most presenting in the second and third decades of life. The clinical manifestation of this tumor is related to its size (including asymptomatic), acute abdomen due to torsion, hemorrhage, and chemical peritonitis. The majority of these tumors are cystic and contain mature tissue of ectodermal, mesodermal or endodermal origin. Perhaps the elevation of some tumor marker such as CA19-9 or CA125 is due to this kind of heterogeneous elements. Most OMCT can be diagnosed by sonography with echogenic sebaceous material and calcifications. Due to fat components in these tumors, diagnosis of OMCT by computed tomography (CT) and magnetic resonance imaging (MRI) is easier **(1-3)**. We provide three cases of OMCT with different characteristics to increase awareness of the importance of serum tumor markers in OMCT.

Case Presentation

Case 1

A 36-year-old woman (gravida: 2 live: 1, abortion: 1) was referred to our oncology clinic for evaluation of ovarian mass, suspected to be mucinous carcinoma that was accidentally reported on sonography for her recent abortion due to an embryonic pregnancy (Blighted ovum). Her previous medical history included normal vaginal delivery, curettage and appendectomy. Physical examination revealed fullness in the posterior cul-de-sac. Pelvic transvaginal ultrasound revealed 50 ×60 mm left adnexal cyst with a hyper-echogenic area and thick septum. An abdomino- pelvic computed

tomography (CT) showed a well-defined solid mass of 7×5 cm in the left adnexal region with fat component and central soft tissue mass that included central nodular calcification without cystic component (Figure 1). Serum tumor markers were (A125: 21 u/ml and CA19-9 > 1000 u/ml. The patient underwent laparotomy, 60×70 mm cystic mass in the left adnexa that is trapped in the posterior cul-de-sac with loose adhesion to the rectum and cervix.

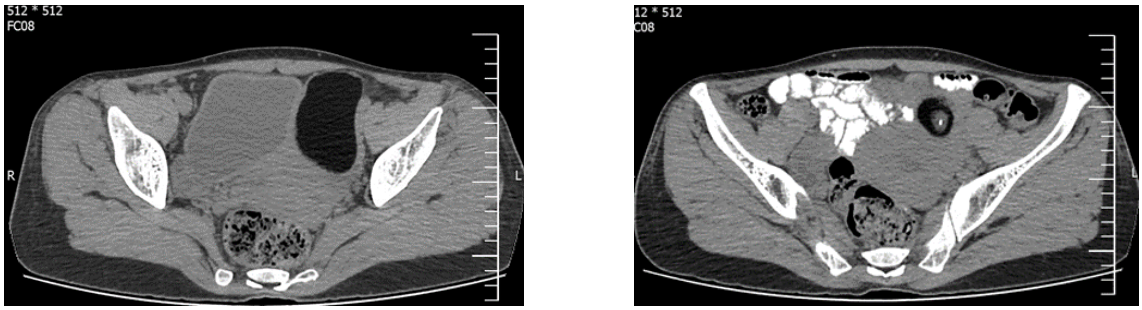

Figure 1. In axial noncontract computed tomography, there is a well-defined solid mass of 7×5 cm in left adnexal region. Note the fat component (figure A) and central soft tissue mass including central nodular calcification without cystic component (figure B)

After enough dissection, the ovarian cyst was removed. This tumor was a smooth lined cyst and on opening it was unilocular cystic lesion containing oily liquid, scant white hair and a small solid protuberance projecting from cyst wall or dermoid plug (Figure 2).

In permanent pathology, it was reported that mature teratoma included squamous epithelium, sebaceous gland, adipose tissue and respiratory epithelium (Figure 3).

Figure 2. A cyst containing clear oily fluid and few hair strands with raised protuberance in cyst wall

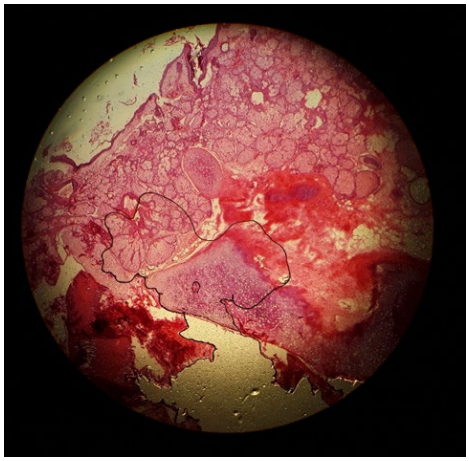

Figure 3. Sections show squamous epithelium, sebaceous gland, adipose tissue and respiratory epithelium.

Case 2

A 46-year-old woman (gravida: 6, live: 6) was admitted to our gynecology department (Urmia, Iran) with compliant of abdominal pain, nausea and weakness. Her past medical history included depression with a drug history of Nortriptylin, Risperidone and Citalopram. Physical examination demonstrated tachycardia (heart rate 116 bpm), pale features and a bulged abdomen with a huge tender pelvic mass extending up to the umbilical part. On a bimanual pelvic examination, there is a huge mass in midline of the abdomen so it was difficult to distinguish other pelvic organs. The sonographic finding suggested a multiseptated huge cyst with a solid component in the left adnexa. In axial post contrast pelvic computed tomography, there was a large 12×15cm mixed density solid cystic mass including the soft tissue, fat, calcified nodule and cystic component in the right adnexal region, suggestive of teratoma (Figure 4). Laboratory investigations reported a hemoglobin value of 6 g/dl and serum tumor markers were CA-125:29u/mL and CA19-9: 15 u/ml. Four units of blood were transfused before surgery and the patient underwent laparotomy. Intra-operatively, a 15×15 cm congested mid-lined mass with adhesions to surrounding tissues, was dissected from omentum, bladder, uterus and bowel adhesions.

Figure 4. In axial post contrast pelvic computed tomography, there is a lager 12×15cm mixed density solid cystic mass including soft tissue, fat, calcified nodule and cystic component in right adnexal region

This mass, in right adnexa had torsed 3 times and there were some necrotic areas with scant spillage. After enough dissection, the right salpingo-oophorectomy was carried out. The surgical specimen cut-section showed multilocular cysts, filled with extensive blood clots, sebaceous material, and hair with necrotic and congestive parenchyma, that was grossly complicated teratoma (Figure 5). Total hysterectomy, bilateral salpingo-oophorectomy and appendectomy were done due to adhesion and disrupted anatomy. Permanent pathology reported the hemorrhagic infarction of the ovary without special histology due to ischemic necrosis of ovary (Figure 6).

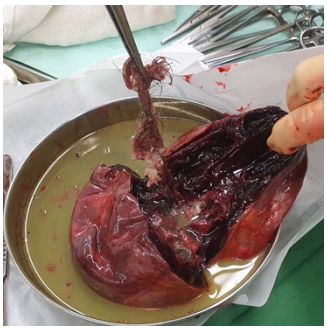

Figure 5. A smooth hemorrhagic cyst containing blood clots, amorphous sebaceous material and hair tuft.

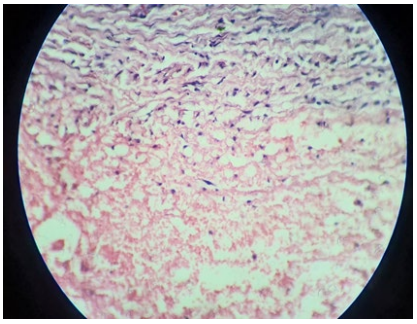

Figure 6. Sections show infarction hemorrhagic area.

Case 3

A 48-year-old woman (gravida: 4, Live: 3, abortion: 1) without a previous medical history was admitted to our oncology department with abdominal pain, and nausea. Pelvic transvaginal sonography revealed a normal uterus and left ovary but there was a heterogenic mass of 7 × 5 cm in the right adnexa. The pelvic computed tomography (CT) findings showed a well-defined 5×5 cm right adnexal mixed density solid mass including fat and soft tissue component without cystic component or calcification (Figure 7). Serum tumor markers were CA 125: 9 g/ml and CA19-9: 944 u/ml.

Intra- operatively, a 6×5 cm cystic mass in the right adnexa without torsion, adhesion, and spillage was found. After removing this cyst, on opening, the bulk of the cyst cavity was filled with hair and the Rokitansky nodule, which had the yellowish appearance of fat and sebaceous components (Figure 8).

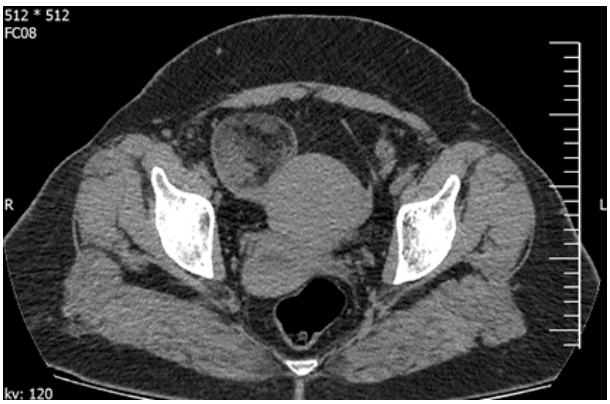

Figure 7. There is a well-defined 5×5cm right adnexal mixed density solid mass including fat and soft tissue component without cystic component or calcification

Figure 8. Gray colored smooth cyst containing amorphous sebaceous material, adipose tissue, hair tuft with raised protuberance in cyst wall.

In permanent pathology, it was reported that mature cystic teratoma included squamous epithelium, sebaceous gland, adipose tissue and hair follicle without calcification (Figure 9).

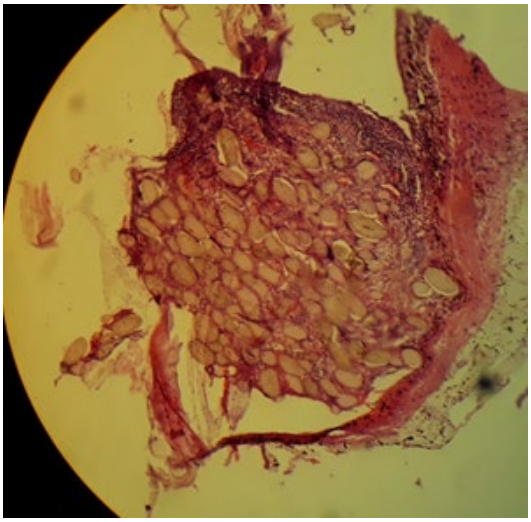

Figure 9. Sections show squamous epithelia site and sebaceous gland, adipose tissue hair follicle without calcification

Table1. Patients' characteristics

Variable	Age	Torsion	Adhesion	CA125	CA19-9
Case1	36	-	+	21	>1000
Case2	46	+	+++	2.9	15
Case3	48	-	-	9	944

Table2. Radiopathological characteristic

Variable	Size	Fat	Calcification	Hair	Sebum	Respiratory epithelium
Case1	7×5 cm	+	+	+	+	+
Case2	15×12 cm	+	+	++	-	-
Case3	5×5 cm	++	-	+++	++	-

Discussion

Ovarian mature cystic teratoma (OMCT) is one of the most common benign ovarian germ cell tumors, typically contains mature tissues of ectodermal (skin, neural tissue), mesodermal (muscle, fat, bone) and endodermal (mucinous or ciliated epithelium) origin **(4)**. This heterogeneous tissues in MCTs, are responsible for various radio-pathologic feature. The diagnosis of MCTs is not difficult and most of MCTs can be diagnosed at sonography. Three common manifestation of MCTs in ultrasound is firstly, a cystic lesion with a densely echogenic tubercle projecting into the cyst lumen (Rokitansky nodule), secondly is diffuse or partial echogenic mass owing to sebaceous material and hair within the cyst cavity, and the third is multiple thin, echogenic bands caused by hair in cyst cavity and other rare features. Pure sebum within the cyst may be hypoechoic or anechoic **(5, 6)**. The diagnosis of MCTs at CT and MR imaging is straightforward because of more sensitivity for fat and calcification in this kind of modalities **(7)**. Despite the specific features of MCTs in imaging studies in some pitfalls due to some pelvic pathology such as fibroma, endometrioma, chronic torsion of MCTs in hemorrhagic masses, has been suggested to evaluate some tumor markers such as cancer antigen (CA) 125 and CA19-9 **(3, 7)**. It has been reported that CA 125 elevation may be related to peritoneal inflammation and CA19-9 is produced in the respiratory glands and mucosa of MCTs. Elevated CA19-9 levels due to leakage from the cystic cavity into bloodstream or

direct secretion to the bloodstream **(7-9)**. Cho et al. showed that simultaneous elevation of CA19-9 and CA125 was more prevalent in patients with ovarian malignancy, but single elevation of CA19-9 was more detected in MCTs **(7, 10)**. Prodromidon et al. showed the associations of elevated CA19-9 levels with larger MCTs and with components such as fat and tooth. Based on suggested mechanism of secretion of CA19-9 from bronchial mucosa and glands, endodermal component has been reported as the most frequent in high CA19-9 levels, resembling mesodermal component **(8, 11)**. Elevated serum CA19-9 levels correlated with larger tumor diameters and higher torsion rate has been reported **(12)**. The rise in serum CA19-9 levels may be related to ovarian torsion and the extent of the necrosis of the ovary **(2, 6, 13)**.

Malignant transformation of mature cystic teratoma is rare and occurs in less than 2% of the cases. Predictive information for malignant transformation is patient's age, tumor size, CEA concentration and squamous-cell carcinoma antigen. Isolated high level of CA19-9 is not associated with malignant transformation **(3, 9, 14)**.

In our patients, in the first case without symptoms, pelvic mass accidentally was reported at sonography based on mucinous tumor but mature cystic teratoma was confirmed with CT. In the second and third cases with symptom of abdominal pain, both of the sonography and computer tomography had reported MCTs. Thus, there are some pitfalls in sonography in diagnosis of MCT and in some cases it needs CT or MRI with high accuracy. Both of our cases with high level of CA19-9 were less than 10 cm, despite the previous studies based on association of high level of CA19-9 with MCT size. In the second case, surrounding tissues of MCT were inflammatory with severe adhesion but CA125 was normal. In this case, huge size, torsion with congestion, scant spillage and fat component could not lead to elevated level of CA 19-9, despite of reported investigations. Indeed, grossly, it was multiseptated mass similar to a hemorrhagic cyst full of hair and oily liquid and pathologically it was disseminated necrosis. It seems that early detection and prediction value of high level of CA19-9 for torsion according to investigation was limited to only acute phase of torsion and in delayed necrotic phase, it may be decreased in bloodstream, such as our second case. Despite the huge size, fat component, and torsion of second case, it did not have high level of CA19-9. In many studies, association of CA19-9 level with fat and bronchial glands was reported, so as our first case, despite small size, markedly high level of CA19-9 in this case may be due to bronchial glands and fat component, but in third case was not accounted for high level CA19-9 except fat component. According to the previous studies, it seems that the combination of definitive report of sonography based on MCT with isolated high level of CA19-9 wouldn't increase risk of ovarian malignancy. It is not cost-effective nor is useful, therefore it is not recommended and we suggest other diagnostic modalities such as CT or MRI.

Furthermore, in these kinds of MCTs with isolated elevated CA19-9, it is not recommended that we limit minimally invasive surgery. The exact role of CA19-9 and pathophysiologic pathway of this biomarker elevation in MCT is obscure. Attention to previous investigations, in definitive diagnosis of MCT by imaging modalities, it doesn't need to evaluate serum levels of CA19-9 in routine clinical practice and high level of CA19-9, doesn't impact malignant transformation.

Conclusion

It is recommended that in referral centers of oncology it is better to perform multi-diagnostic modalities for making better our knowledge in the field of biologic behavior of MCTs and it is suggested that we do increase pathologically our investigation for more clarifying of production pathway of CA19-9.

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Conflict of Interest

There is no conflict of interest.

Funding/ Support

There is no funding / support.

Informed Consent

Written informed consent was obtained from the patient.

Ethics Committee Approval

This study was approved by the Ethics Committee of Urmia University Medical Sciences.

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