Mature cystic ovarian teratoma. A case report.

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Case Report

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ABSTRACT:

Introduction: The teratoma (from the Greek teras, meaning monster and onkoma meaning swelling) is a tumour characterized by multiple tissue types derived from all three primitive germ layers (endo- meso- and ectoderm), such as hair, teeth, bone, rudiments of thyroid gland, etc.

Case Report: We present the case of a young patient 6 years of evolution with chronic constipation, diagnosed and treated as chronic colitis, with subsequent development of increased volume and abdominal pain. USG and CT revealed data compatible with teratoma, requiring surgical management.

Conclusion: Teratomas are slow-growing benign lesions, they are usually asymptomatic until they reach large dimensions, causing compressive symptoms, requiring surgical management

Keywords: Ovarian teratoma, Mature cystic teratomas, Rokitansky's node

Introduction

Mature cystic teratoma is the most common germ cell ovarian tumour, which accounts for 15-20% of all ovarian neoplasms[8,16,21]. The frequency of MCT cases undergoing malignant transformation ranges from 0.17% to 2% [11,16]. In 60% of cases, patients are asymptomatic [8]. The most common symptoms of ovarian teratomas are pressure, pelvic pain and irregular bleeding, but the symptoms can also result from complications such as torsion, rupture, peritonitis and autoimmune hemolytic anemia [7].

Ultrasonography and tumor markers, such as CA19-9, are common tools used for early detection and characterization of ovarian masses, such as mature or immature teratomas [21]. A common finding is a cystic lesion with a densely echogenic tubercle ('Rokitansky's node') projecting into the lumen of the cyst. Rokitansky's nodule, also commonly known as a dermoid plug, contains hair, teeth, and fat and can cause acoustic shadowing [5,8].

Complete surgical excision is the standard of care for any teratomatous tumor, whether mature or immature [14].Total abdominal hysterectomy in conjunction with opposite salpingo-oophorectomy is considered the most appropriate surgical option for postmenopausal women or women who do not intend to have more children if specimens from these women reveal MCT by frozen section examination. In women desiring fertility, a unilateral oophorectomy is performed if there is no capsular invasion or metastasis [22].

Case report

We present the case of a young patient 6 years of evolution with chronic constipation, diagnosed and treated as chronic colitis, with subsequent development of increased volume and abdominal pain. USG and CT revealed data compatible with teratoma, requiring surgical management.

Discussion

Definition

Teratoma (from the Greek teras, meaning monster and onkoma meaning swelling) is a tumour characterized by multiple tissue types derived from all three primitive germ layers (endo- meso- and ectoderm), such as hair, teeth, bone, rudiments of thyroid gland, etc. [1,8]. Teratoma is a germ cell tumor originate from a parthenogenetically activated oocyte after first meiosis15 derived from stem cells of the early embryo and the germ line [5].

They usually contain disorganized, tridermal, mature components, in which ectodermal tissue predominates. The cystic portion of the tumor is usually filled with fat and hair. Solid nodules are often observed within the tumor capsule, and these may contain cartilage or calcified tissues, such as teeth[15].

Etiology

The origin of these tumors appeals to several theories. The work of Linder et al. initially showed

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Figure 1. Left. Ovarian teratoma. Right. Macroscopic appearance of tumor with regular borders, multilobed,

that teratomas originated from a single isolated germ cell whose abnormality occurs from the first meiotic division. Based on karyotype analysis of immature ovarian teratoma, Ohama et al. confirmed this first hypothesis, but also showed that for a number of tumors, the abnormality occurred later during the second meiotic division, or even from a mature oocyte[12].

The most accepted theory to explain the existence of ovarian teratomas is the parthenogenetic activation of oocytes. The fact that the 46,XX karyotype is found in almost all mature teratomas strengthens this theory. Even though embryonic development without the male gamete, named parthenogenesis, can be found in some lower organisms, this sort of reproduction seems to be completely unsuccesful in mammals[24]. The increasing levels of estrogen and progesterone may explain the increase in size of mature cystic teratomas after puberty, and their arrested growth after menopause[21].

Classification

Ovarian teratomas (OT) may be subdivided into mature teratomas, immature teratomas and monodermal teratomas[6]. Ninety-nine percent of cases of OT are mature cystic teratomas (MCTs), also known as dermoids or dermoid cysts.

MT comprise about 20% of all ovarian neoplasms in adults[1,8,16,21] and almost 50% of the tumours in children[14], most are unilateral, approximately 10% of cases are bilateral[20,21]. The most frequent size of a teratoma ranges between 5 and 15 cm but some reach 45 cm [8]. These tumors are usually slow-growingwith an estimated growth rate of 1.8 mm/year [14,21.]

The tissues in teratomas are usually well differentiated (i.e. mature), up to 75% of these contain bony tissue [17], but they can also remain at the fetal stage of development (i.e. immature). The most common immature tissue found is neuroectodermal tissue, and such tumors are considered malignant[7]. MT tend to be diagnosed in young women around the age of 30 years [20]. These often bizarre tumours are usually located at the midline and paraxial regions of the body. One of the most common locations is the ovary[24].

Mature Cystic Teratoma

Mature cystic teratoma (MCT) is a benign tumor, typically contains mature tissues derived from at least two germ cell layers[1,5], is characterized by a thick, well-formed capsule lined by stratified squamous epithelium, with a variety of skin appendages including sweat, apocrine, and sebaceous glands[13]. Over 80% of cases present in reproductive periods, especially in women under the age of 40 [4]. Unilateral cases involve the right side more frequently, and are asymptomatic unless a complication develops[5]. They tend to be diploid, have a normal 46 XX karyotype, and lack i12p[10].

Immature teratomas

They are much less common, account for <1% of the ovarian teratomas[5], often occur in adolescence, never occur after menopause, are usually solid, and are almost never bilateral. The immature elements are almost always predominantly neuroectoderm, consisting mainly of primitive neuroectodermal tubules and sheets of small, round, malignant cells, which may be associated with glial formation[17]. On imagings, immature teratomas tend to be larger than MTs at the time of diagnosis, and irregular solid components containing coarse calcifcations, small foci of fat, and hemorrhagic foci are often observed unlike typical MTs[5]. Its malignant potential depends directly on the degree of immaturity and the presence of

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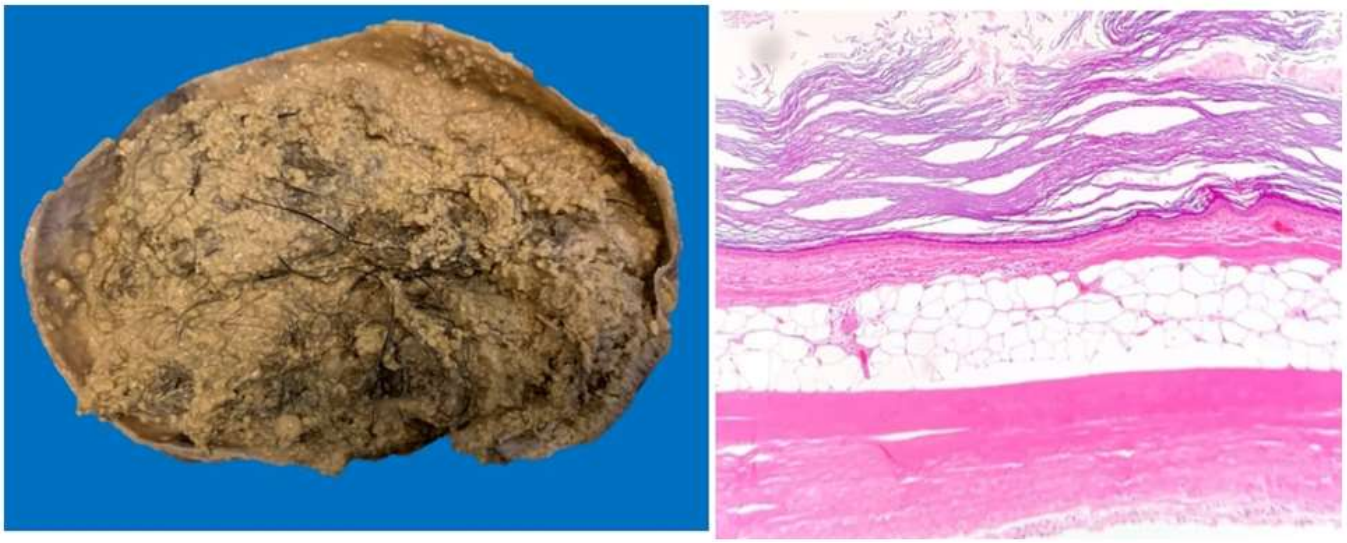

Figure 2. Left. Ovoid specimen of 27.8 x 18.9 x 17 cm, with a shiny surface, with hairs and bait inside. Right. Germinal tumor consisting of stratified squamous epithelium, with keratin sheets and annexes, mature adipose tissue, respiratory epithelium and congestive vessels.

neuroectoderm, which allows establishing a classification in three degrees of increasing malignancy according to the Norris classification, this classification was initially proposed by Thurlbeck and Scully and modified in 1976 by Norris and O'Connor to better define therapeutic indications. The evolution of immature teratomas is marked by very rapid tumor growth. The extension is then mainly locoregional, responsible for peritoneal invasion, which requires a capsular rupture[12]. Treatment involves unilateral salpingo-oophorectomy and staging procedures, including peritoneal washing, omentectomy, pelvic and para-aortic lymphadenectomy, and multiple peritoneal biopsie Immature teratomas beyond stage I require postoperative chemotherapy. Current combination therapy is BEP (bleomycin, etoposide, platinum), which has proved to have less recurrence and less toxicity than VAC (vincristine, dactinomycin, cyclophosphamide)[17].

Monodermal Mature Teratomas

They have a predominance of 1 particular tissue type, the most common of which are thyroid and carcinoid, although a variety of tissues may be recognized, including sebaceous, melanotic, and pituitary. If thyroid tissue has overgrown all other tissues, the teratoma is termed struma ovarii. This tumour comprises 2.7% of OTs. Malignant transformation may occur in 5% of these struma ovari[17].

Clincal Presentation

The clinical course of teratomas depends on age of the patient, histological type, and anatomical site. For example, majority of the teratomas occur in the ovaries in adults and usually are mature teratomas (MTs). On the other hand, the sacrococcygeal region is the most common site in pediatric patients, and the frequency of immature teratomas is relatively high[5].

In 60% of cases, patients are asymptomatic[8]. The most common symptoms of ovarian teratomas are pressure, pelvic pain and irregular bleeding, but the symptoms can also result from complications such as torsion, rupture, peritonitis and autoimmune hemolytic anemia[7].

Radiological diagnosis

Ultrasonography and tumor markers, such as CA125, CA19-9, and alphafetoprotein, are common tools used for the early detection and characterization of ovarian masses, such as mature or immature teratomas. Ultrasonography is an excellent, non-invasive, investigative procedure that can be used for women of any age[21]. Sometimes, there is a solid protuberance projecting into the cyst cavity. It is known as the Rokitansky nodule or dermoid plug. Most of the hair arise from this nodule and bone and teeth can be present in it[5,8]. "Dermoid mesh" is also considered a specific diagnostic sign and refers to multiple linear echogenic bands floating within the cyst, which have been shown to be hair fibers. A lesion containing primarily hair or a mass of hair floating on sebum results in an acoustic shadow distal to the echogenic hairball. This appearance has been called the "tip of the iceberg sign". Another described appearance typically reported in mature teratomas >10 cm in diameter on ultrasound is multiple echogenic globules floating in hypoechoic fluid. On CT, a large amount of fat attenuation within an ovarian lesion, with or without wall calcification, is diagnostic. On MRI, the sebaceous component of the dermoid cyst parallels the signal intensity of fat in all sequences[14]. The diagnostic value of computed tomography and magnetic resonance imaging examinations is important when identifying malignant manifestations, such as

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bleeding, necrosis, cyst wall growth, invasion of surrounding structures, or the occurrence of pelvic abdominal metastases[11].

Biomarkers

Serum CA19-9 is the most reliable biomarker of ovarian mature cystic teratomas; higher levels of serum CA19-9 are correlated with larger tumor sizes. However, the diagnostic value of CA19-9 in patients with mature cystic tumors is low when used alone [13]. Clinically, serum CA125 is still used to distinguish between benign and malignant pelvic masses[21]. Alpha-fetoprotein can be increased in 18 to 45% of cases. A serum level greater than 400 ng is considered a risk factor for a pejorative evolution[12].

Risk of malignancy

When the tumor's diameter is greater than 9.9 cm, its sensitivity to forming cancer is 86%[11], the presence of an enhancing soft tissue component and an obtuse angle between the soft tissue and the inner wall of the cyst, as well as extracapsular tumor growth with extension into adjacent structures or disseminated diseases are common imaging findings of malignant transformed teratomas. They also observed in patients older than 45 years, elevated tumor markers of these patients[23]. Previous studies have reported that imaging characteristics most suggestive of malignancy are the presence of solid components and involvement of adjacent organs[4]. Malignant transformation usually occurs in a Rokitansky nodule. Contrast enhancement of a Rokitansky nodule should raise the possibility of malignant transformation, but enhancement of a Rokitansky nodule always does not necessarily indicate malignancy in the same sense that imaging findings in benign and malignant ovarian tumors overlap[23].

Treatment

The laparoscopic approach should replace laparotomy for benign adnexal masses without complex features and less than 8 cm in maximum diameter. Laparotomy should be considered the standard of care in suspected malignancy, as surgical staging is mandatory. Larger masses are often associated with a higher likelihood of malignancy, and are usually treated with a laparotomy approach to prevent rupture or intraperitoneal spread of the tumor[26]. Total abdominal hysterectomy together with opposite salpingooophorectomy is considered to be the most appropriate surgical option for postmenopausal women or for women, who have no intention for further childbirth if the specimens of these women reveal MCT by frozen section examination. In fertility-sparing surgery, unilateral oophorectomy is performed if there is no capsular invasion or metastasis[22].

The use of ovarian-sparing surgery (OSS) as the gold standard treatment for benign masses is also supported by evidence that, for these neoplasms, the risk of ipsilateral recurrence is less than the risk of contralateral metachronous malignancy. Additionally, it is important to note that women with only one ovary have decreased ovarian reserve and lower levels of anti-Müllerian hormone, and the resulting early menopause can affect their overall health by increasing the risk of cardiovascular disease and osteoporosis. According to Chabaud-Williamson et al. and Oue et al., OSS should always be considered when technically feasible in the case of a 'mature localized teratoma', meeting the following criteria: no evidence of lymphadenopathy or liver/lung metastases, normal levels of tumor markers, absence of calcifications or specific radiological findings. Oophorectomy should be preferred only in the following cases: mature teratoma that does not meet the criteria for a localized mature teratoma, preoperative diagnosis of immature teratoma, high intraoperative suspicion of malignancy, or malignancy diagnosed on postoperative histopathological examination. Spinelli et al. showed that OSS could be challenging because the lesion often involves the entire ovary, making it very difficult to find a clear dissection plane between neoplastic tissue and normal ovary. Also, large ovarian masses can stretch the surrounding tissue enough that no functional ovarian tissue is found after resection. However, although at surgery the ovarian tissue appears as a thin streak, subsequent histological examination demonstrated that functional ovarian tissue is still present [25].

Therapeutically and according to the French Cancer Society 2013, the treatment of immature teratomas is divided into two parts, surgical treatment followed by chemotherapy according to histological grade. Surgical treatment is always conservative and has 3 objectives: diagnosis (histology), therapeutic (ablation of the tumor), and determination of the extension stage, so we recommend an initial surgery during which we perform at least one unilateral adnexectomy, complete exploration. of the pelvis and the entire abdominal cavity, peritoneal lavage and/or extraction of ascites, systematic multiple peritoneal biopsies, including at the level of the omentum, and extraction of any suspicious element. For lymph node dissection, there is no indication for systematic pelvic and lumbo-aortic dissection in the absence of lymph node abnormalities, and a sample will be taken in case of scan-visible abnormality or palpable masses. For the contralateral ovary, careful inspection is necessary and some authors recommend a biopsy; there is no indication for systematic bilateral adnexectomy. For

the uterus no place has a hysterectomy. For grade 1 tumors, clinical follow-up seems sufficient after conservative surgical treatment alone. This attitude is confirmed by Carinelli in a large series of 245 immature ovarian teratomas, showing the absence of long-term recurrence in this subgroup of immature ovarian teratomas after unilateral adnexectomy. In case of immature grade 2 or 3 teratoma, the attitude to adopt, adjuvant chemotherapy or staging surgery, remains controversial. Adjuvant chemotherapy is usually reserved for grade 3 or even grade 2 tumors. The most widely used protocol includes three molecules taken from testicular cancer chemotherapies: BEP comprising bleomycin, etoposide and a platinum salt (cisplatin)[12].

In patients in whom complete surgical excision is not possible, multiple biopsies should be performed to gain a true picture of the residual tumor. If the growing tumors are not amenable to percutaneous biopsy, a follow-up laparotomy may be indicated[9].

Prognosis

Malignant transformation is very rare and occurs in only 0.17-2% of cases of mature teratoma. The most common malignant neoplasm arising in mature teratomas is squamous cell carcinoma[11,14,16].

In immature tumors, grade 1 tumors have a good prognosis because the five-year survival rate is evaluated in the literature between 81% and 94%. Immature grade 3 teratomas have a high malignant potential and their rapid local and distant evolution is responsible for higher rates of recurrence and death, with a 5-year survival rate of 90 to 100% with chemotherapy[12].

Recurrence

A few reports have shown the rate of post-surgical recurrence of MCT. It appears to be around 3–4% according to Anteby. The risk factors, however, are poorly known at the moment. Anteby et al. suggested that the risk of developing a subsequent MCT was higher in patients with bilateral or multiple MCT because two out of three cases with recurrence had bilateral or multiple MCT at the initial surgery. The present study suggested three factors - young age, large cyst, and bilaterality – to be predictive of recurrence, with a hazard ratio of 2.5–3.0. When a patient had at least two of these factors at surgery, the recurrence rate within an average follow-up period of 3.5 years rose to 10–20%, otherwise the rate was 2.5–3.5%, which would be the vital information to identify the patients with high risk of recurrence[19]. According to Harada et al., young age (<30 years), large cyst size (diameter, >8 cm), and bilateral occurrence are predictive risk factors for recurrence, with the risk of recurrence being especially high in the presence of more than one of these factors [21.] The presence of vitelline structures seems to be a predictive factor for the risk of recurrence[12].

Complications

Torsion of the pedicle has been reported to be the most frequent complication of ovarian teratomas, with a reported incidence of 3.2–16%. Torsion is caused by rotation of the pedicle to the tumor or the organ, resulting in venous, lymphatic, and finally arterial obstruction[3,14]. Torsion of ovarian tumor commonly involves the ovary and the fallopian tube concurrently rather than separately, since the broad ligament acts as a fulcrum. The appearance of the twisted ovarian pedicle is known as the “whirlpool sign” on imagings[5]. The most commonly identified features include an enlarged ovary, ovarian mass and an edematous thickened fallopian tube with a twisted vascular pedicle, which is the most specific imaging finding[14]. Teratoma is the most common ovarian mass associated with torsion[5]. Postmenopausal women with an adnexal mass or adolescents may be affected by torsion (about 17 % of cases); this may be because of changes in the weight of the adnexal. Postmenopausal women with ovarian teratomas need surgical intervention to avoid torsion[3].

Regarding torsion and tumor size, torsion is usually observed in tumors that measure between 5 and 10 cm. This may be because torsion does not occur, or tends to recover easily, in tumors that are less than 5 cm in size, whereas tumors that are larger than 10 cm are too large to rotate in the pelvic space[26].

A thick capsule has been postulated to account for relative rarity of spontaneous rupture noted in only 1.2– 3.8% of ovarian teratomas[14]. Acute rupture usually occurs in the setting of torsion, trauma, infection and labour and may lead to peritonitis[5]. In acute rupture, detection of discontinuity of the tumour wall is diagnostic[14].

Malignant transformation (MT) is very rare, occurring in only 0.17–2 % of mature teratoma cases. The most frequent malignancy arising in mature teratomas is squamous cell carcinoma (SCC) (88.3 %)[11,14,16], followed by adenocarcinoma, fibrosarcoma, carcinoid tumor, and mixed tumors [3,4]. MT usually occurs in postmenopausal women and may be associated with high tumor diameter[3]. The combination of criteria including patient’s age (>50 years), large tumours (>10 cm) and high concentrations of squamous cell carcinoma antigen and CA125 is considered marker for malignant transformation[3,14]. The ‘Rokitansky’ protuberance is a common site for malignant change. The contrast enhancement of the Rokitansky protuberance is an

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early indicator for the possibility of malignant change[14].

Pregnancy

Benign cystic teratoma is the most common ovarian tumor found in pregnancy. Traditional management of persistent ovarian cysts in pregnancy is exploratory laparotomy at 16 to 20 weeks of gestation and resection of the tumor. This approach has been a common practice because of several possible associated complications. The growth rate of dermoid cysts may be influenced by hormonal changes during pregnancy. After puberty, dermoid cysts may increase in size, presumably because of hormonal stimulation of the sebaceous glands[18].

Conclusion

Ovarian teratomas are the most common ovarian germ cell tumors, and account for 20% of all adult ovarian tumors and 50% of pediatric ovarian tumors. These tumors can originate from ectoderm, mesoderm or endodermal layers. Ovarian teratomas are classifed as mature, immature and monodermal teratomas. Malignant transformation is very rare, occurring in only 0.17–2% of mature teratoma cases. The most frequent malignancy arising in mature teratomas is squamous cell carcinoma (88.3 %). In 60% of cases, patients are asymptomatic Ultrasonography and tumor markers, such as CA125, CA19-9, and alpha-fetoprotein, are common tools used for the early detection and characterization of ovarian masses, such as mature or immature teratomas. CA19-9 is the most reliable biomarker of ovarian mature cystic teratomas; higher levels of serum CA19-9 are correlated with larger tumor sizes. Complete surgical excision is the standard of care for any teratomatous tumor, whether mature or immature.

Conflicts of Interests

The authors declare no conflict of interest.

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