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Case Report

Familial Cystic Teratomas: Four Case Reports and Review of the Literature

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ABSTRACT Mature cystic teratomas (MCTs) are some of the most common ovarian neoplasms in women of reproductive age. However, familial teratomas are exceedingly rare. We present 4 cases of dermoid cysts seen in a mother and her 3 daughters with left MCTs. None of the patients had symptoms at the time of diagnosis, but all of them were diagnosed in their twenties during an annual gynecologic examination. In this report, we elaborate on MCTs familial incidence, genetic linkage, theories of pathogenesis, diagnosis, complications, and surgical management. To our knowledge, after extensive review of the literature, there have been only 2 cases, in addition to the present case, of unilateral MCTs across generations reported. Journal of Minimally Invasive Gynecology (2010) 17, 782–786 © 2010 AAGL. All rights reserved.

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Mature cystic teratomas (MCTs), also known as ovarian dermoid cysts or dermoids, are relatively common benign ovarian neoplasms derived from ovarian primordial germ cells. Dermoid cysts may arise from both gonadal and nongonadal tissue [1]. The most common nongonadal dermoid cysts are found in the fronto nasal and presacral regions. Ovarian dermoid cysts or cystic teratomas are divided into 3 categories: mature (cystic or solid, benign), immature (malignant), and monodermal or highly specialized (benign). MCTs have a predominance of ectodermal elements, containing sebaceous material in 97% of cases. They are the most common germ cell tumor of the ovaries. They are often unilateral, with an estimated bilaterality rate of 13.2% [2]. Mature ovarian teratomas account for 90% of all ovarian tumors in premenarchal girls and 60% of all ovarian tumors in females younger than 20 years of age [3]. They comprise approximately 10% to 20% of all ovarian neoplasms in the general population [2,4] but account for only 1% to 5% of all malignant ovarian neoplasms [5,6]. Although dermoid cysts are fairly common, the incidence of familial cases is extremely rare, limited to a handful of case reports [3]. Table 1 summarizes reported familial MCTs from Plattner et al [3]. Although MCTs have been reported in siblings, there are only two case reports, in addition to the present case, of familial dermoid cysts occurring in a mother and her 2 daughters [7,8].

Case Presentation

Here we report on a mother and her 3 daughters who all had left ovarian dermoids. Patient 1 is a 57-year-old Korean woman, gravida 4 para 4 (three females, one male), who has been postmenopausal for the past 7 years. She gave a history of ovarian cysts detected during prenatal care for her first pregnancy. At age 26, she underwent a postpartum exploratory laparotomy with a left ovarian cystectomy. Pathologic study confirmed a benign dermoid cyst. She subsequently delivered 3 more children without any complications.

Patient 2 is the eldest daughter. She is a 32-year-old woman, gravida 0 para 0, who presented with a left dermoid cyst, detected on annual gynecologic examination at age 27. The patient underwent exploratory laparotomy with left

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Table 1
Familial incidence of ovarian dermoid cysts

Year	Author	Ovarian condition
1924	Sippel	Ovarian dermoids in 3 sisters
1958	Schauffler	Ovarian dermoids in twins
1966	Feld	Ovarian dermoids in triplets
1973	Plattner	Bilateral dermoids in mother and 2 daughters
1983	Brenner	1 family, three successive generations of dermoids
1988	Gustavson	Dermoids in a mother and her two daughters

salphingooophrectomy in her home country. Pathologic study confirmed MCT. The results of clinical follow-up to the present date have been normal.

Patient 3 is the middle daughter. She is a 25-year-old woman, gravida 0 para 0. After her first annual gynecologic examination at age 22, ultrasonography revealed a left ovarian dermoid cyst. The dermoid was removed by laparoscopy, and pathologic study confirmed an MCT. The ovary was preserved.

Patient 4 is the youngest daughter. She is a 22-year-old woman, gravida 0 para 0, who came to us for her first annual gynecologic examination. The patient's ultrasound scan revealed a 6.5- × 5.5- × 4.2-cm left ovarian dermoid cyst. The patient underwent laparoscopic removal of the MCT, with conservation of her ovary and has an uneventful postoperative course.

Discussion

The characteristics common to these 4 cases are as follow: all were symptom free at the time of diagnosis, and all were uncomplicated, left-sided MCTs, diagnosed with ultrasonography. The women are from a well-educated Korean family, and they provided a very detailed, accurate medical history. The only common environmental finding was the use of several Korean herbal medications to help regulate their menstrual cycles and relieve cramping.

Malignant transformation is quite rare, occurring in 1% to 3% of cases, primarily in postmenopausal women (average age 60) [6,9–11]. It should be noted that pelvic examinations are not performed on unmarried Korean women. Before marriage, a typical annual gynecologic examination in Korea consists of a blood draw for CA125 levels and abdominal ultrasound scanning. Because of these differences in clinical practice, it is possible that ovarian tumors, including MCTs, may be detected at earlier stages and at higher frequency in Korea than in the United States.

Interestingly, a study by Smith et al [12] reports an increased frequency of malignant ovarian germ cell teratomas in women of Asian descent in the United States. They also report that 56.7% of women presented with localized disease. In 2009, a study performed in Korea by Lee et al [13] reports that 65% of detected malignant ovarian germ cell tumors were stage I. It is possible that early-stage ovarian malignancies are detected at a higher frequency in Korea as a result of their standard gynecologic screening, with yearly abdominal ultrasound scannning. Further investigation of gynecologic practices may be required to understand better the rates of MCT and malignant teratomas and their potential differences in Korea and the United States. There are several theories on the pathogenesis of teratomas. In the theory of incomplete twinning, embryonic remnants of 1 twin are believed to be incorporated into the tissue remnants of another twin. This is supported by the increased frequency of dermoids in families with a history of twins [3]. The theory of blastomere inclusions suggests that sequestered totipotent primordial germ cells or blastomeres undergo neoplastic proliferation. Derepression of totipotent genetic information in somatic cell nuclei and ovarian pregnancies have been also mentioned briefly in the literature [3]. In 2001, another theory of coalescence of primary follicles was proposed [14]. Biovular follicles in residual ovarian tissue were found in several patients with MCTs. Imperfect parthenogenesis or parthenogenic development of the ova is the most widely accepted theory for ovarian teratomas [14]. Undifferentiated germ cells from yolk sac endoderm give rise to teratomas. They migrate into gonads later in development and undergo imperfect parthenogenesis. This theory explains the propensity teratomas have for ovaries. It suggests that teratomas arise from an endogenous cell line, supported by the observation that most MCTs have Barr bodies and a 46 XX karyotype [14]. The theory provides a better explanation for familial dermoid cyst cause, because it implies a genetic defect that results in MCTs, which is passed down from 1 generation to the next [3,13]. A study of the molecular pathogenesis of ovarian teratomas also lends support to the idea that inherited gene mutations could confer increased risk of MCTs within families [15]. Tate et al [16] recently reported their finding that loss of heterogeneity of the PTEN region (a tumor suppressor gene) is one of the molecular alterations involved in the development of mature ovarian teratomas. They also found that mutations in KIT (a protooncogene) are associated with melanomas arising from ovarian mature teratomas.

Detection of MCTs in patients is often incidental, with 21.1% of women diagnosed are asymptomatic [2]. They are commonly found during pelvic surgery (eg, for ectopic pregnancy or cesarean section) or routine pelvic examination.

Although MCTs are slow-growing benign tumors, once they reach a critical size or develop malignant or hormonal properties, symptoms may arise. They may cause pain because of torsion or pressure on adjacent structures. Rupture, hemorrhage, and abnormal uterine bleeding may also occur. Lower abdominal pain is the most common complaint, found in 44.1% of cases. Ayhan et al [2] report a palpable pelvic or abdominal mass with or without abdominal distension in 25.1% of cases. Torsion occurs in approximately 16% of cases and rupture in 1% to 4% [4].

Malignant transformation is a more rare complication, occurring in 1% to 3% of cases, primarily in postmenopausal women [6]. There have been reports of MCT transformation

into adenocarcinoma, malignant melanoma, squamous cell carcinoma, osteogenic sarcoma, leiomyosarcoma angiosarcoma, carcinoid tumor, and thyroid adenocarcinoma [2,5,17–21]. Squamous cell carcinoma is the most common malignant transformation, occurring in 80% of cases, primarily in women older than 50 years of age [20]. Squamous cell carcinoma, arising from dermoid cysts, accounts for approximately 1% of malignancy. Ovarian teratomas causing virilization are exceedingly rare and mostly occur in postmenopausal women. These patients present with masculinization demonstrated by deepening of the voice and clitoromegaly [22]. Benign cystic teratomas may also produce beta HCG, thyroid-stimulating hormone, estrogen, and prolactin [22,23].

Ayhan et al [2] reported thyroid tissue in 3.5% of mature teratomas. Dalmau et al [24] reported 11 cases of paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis, resulting in neuropsychiatric symptoms. Other unusual manifestations of MCT include infection, invasion to adjacent viscera, and autoimmune hemolytic anemia [4]. In 1994, Pothula et al [25] reported a case of MCT who presented with hemoperitoneum and acute abdomen.

Care must be taken when surgically removing dermoid cysts because they are prone to rupture. Spillage of sebaceous material into the abdominal cavity can occur and lead to shock and hemorrhage. A ruptured MCT can consequently lead to a marked granulomatous reaction (chemical peritonitis).

Ultrasonography is the primary diagnostic imaging tool for patients with potential ovarian cysts (Fig. 1). It is useful in determining morphologic characteristics such as multilocularity, thickened walls, projections, or irregular cyst contents. Mature ovarian teratomas can contain hair, skin, teeth, bones, and neural elements, appearing quite variable on ultrasonography. However, they often appear as solid masses, because of their greasy, sebaceous contents, allowing for reasonably accurate diagnosis. A 98% positive predictive value with 85% to 94.4% sensitivity has been reported for the diagnosis and identification of MCTs with transabdominal ultrasonography [26,27]. Endovaginal ultrasonography helps detail the cyst structure, as does a transabdominal approach. The advantages of transabdominal ultrasonography are better visualization of larger cysts and assessment of other structures (e.g., kidney, liver and ascites). Three-dimensional ultrasonography may help visualize blood flow within and around the cyst.

Magnetic resonance imaging is often not necessary but may be performed with gadolinium to evaluate better the soft tissue lesions after ultrasonography (Fig. 2). Despite the availability of high-quality imaging, histopathologic characterization of ovarian cysts provides the definitive diagnosis. Historically, medical management of MCTs included monitoring with ultrasonography and use of oral contraceptive pills for their ability to suppress the hypothalamicpituitary-ovarian axis. Recent studies have shown that oral contraceptive pills do not influence ovarian cyst growth or regression [28–30]. Another reason that medical management alone is no longer used is due to the potential of MCTs to grow, rupture, and spill into the abdomen.

Surgical management of dermoid cysts typically requires simple cystectomy alone to preserve ovarian function (Fig. 3). Cystectomy is typically the treatment of choice, with laparoscopy as the most commonly used approach for the past 15 years [27]. However, a recent retrospective study from the United Kingdom suggests that expectant management of MCTs is feasible in symptom-free women in whom incidental detection occurred on ultrasonography. They concluded that surgical intervention should be considered in the following cases: younger age, parity ≥ 2, bilateral cysts, and larger cyst diameter. No morphologic features or demographic predicted growth rates of MCTs. Laparoscopy is preferred because there are fewer postoperative complications, less scarring, less postoperative pain, and fewer days in the hospital [31–33]. A Cochrane review from 2005 found reduced incidence of fever, urinary tract infection,

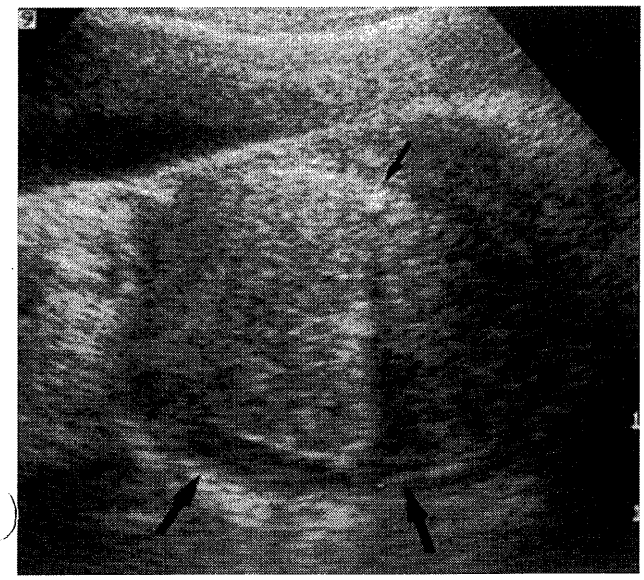

Fig. 1. Mature cystic teratoma on ultrasound scanning.

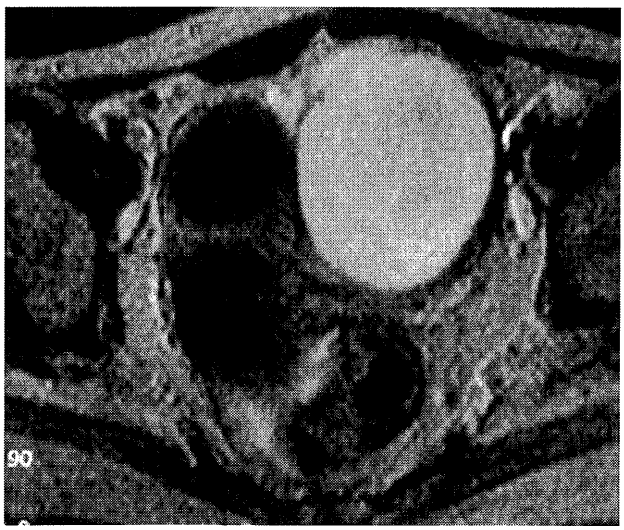

Fig. 2. Mature cystic teratoma on magnetic resonance imaging.

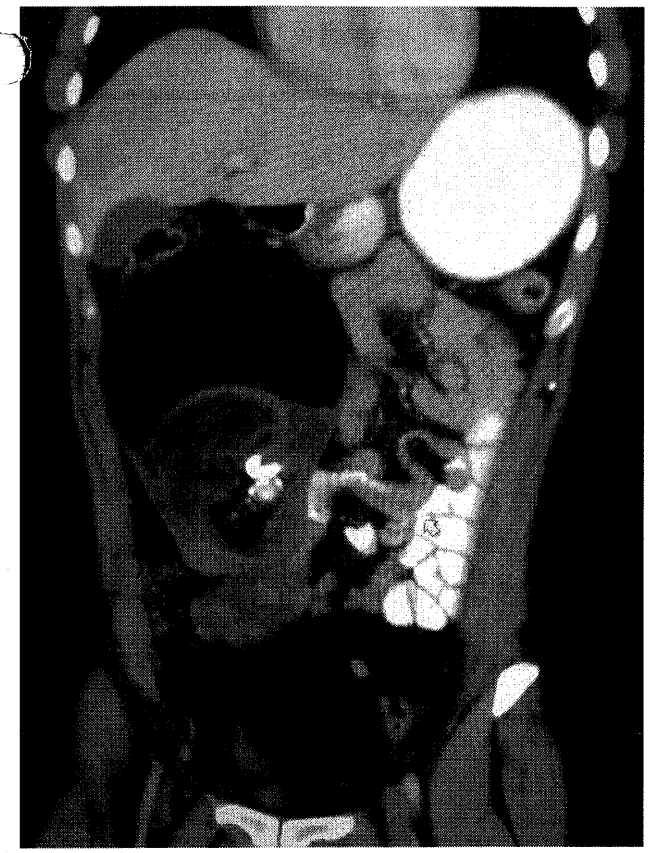

Fig. 3. Mature cystic teratoma on computed tomography.

postoperative complications, postoperative pain, number of days in the hospital, and total cost with laparoscopy [32]. Although a 12% to 18% spillage rate has been reported with the laparoscopic "endobag," spillage does not increase the postoperative morbidity rate as long as thorough washing of the peritoneal cavity takes place [34,35]. It has been our experience that the laparoscopic bag generally decreases incidence of rupture and spillage of tumor contents [35]. It has been suggested that laparoscopy is preferable for tumors less than 10 cm in diameter [2]. Larger dermoid cysts may require laparotomy. However, regardless of size, in our experience, the limiting factors for laparoscopic management of dermoid cysts are the skill and experience of the surgeon and the availability of proper instrumentation. Copious peritoneal lavage should be performed to avoid a chemical peritonitis from spillage of the sebaceous cyst fluid. Patients should be followed up after surgery because recurrence is known to occur in some women. A retrospective Canadian study from 2005 reported 7.6% probability of recurrence in women treated with laparoscopy [36]. Besides this 1 factor, it is still unclear what increases the risk of ovarian dermoid recurrence.

MCTs are sometimes found alongside other pelvic neoplasms (endometrial adenocarcinoma, squamous carcinoma in situ, serous cystadenomas; Fig. 4) [2]. For cases of malignancy, pelvic washings, bilateral oophorectomy with or without a hysterectomy and surgical staging may be

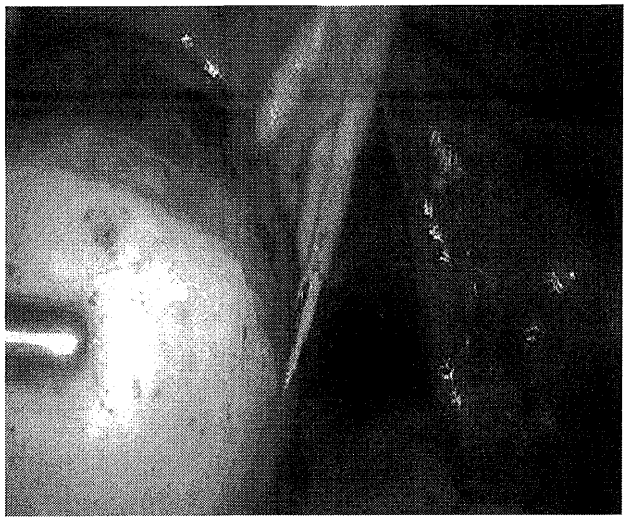

Fig. 4. Mature cystic teratoma on laparoscopy.

required. In general, surgical treatment should be tailored to the individual patient and should take into consideration age, fertility, bilaterality, and the co-occurrence of other pelvic disease [2].

Conclusion

This is a unique case of unilateral MCTs in a family across generations. The only common finding of interest was the use of Korean herbal medications. In general, preoperative diagnosis of MCT is difficult because of nonspecific signs and symptoms. Pelvic ultrasonography can aid in the diagnosis, but surgical excision with histopathologic characterization is required for confirmation. Almost all dermoid cysts can be removed laparoscopically or laparoscopically assisted without complications. With either technique, the abdomen should be copiously irrigated to avoid a chemical peritonitis [37].

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