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Struma ovarii complicating pregnancy. Case report and literature review

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SUMMARY: **Struma ovarii complicating pregnancy. Case report and literature review.**

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A 19-year-old woman at 12th week of pregnancy was referred to our hospital with severe acute abdominal pain, nausea and vomiting. Patient's abdomen was untreatable. Routine examinations, except neutrophilic leukocytosis, were normal. Ultrasound imaging showed the presence of intrauterine pregnancy corresponding to amenorrhea and a right complex ovarian mass, with well defined margins without papillary projection, 14x12 cm in diameter. No free fluid was evident. Due to untreatable abdomen and suspecting torsion of the ovarian tumor the patient underwent laparotomy under general anesthesia. The pregnant uterus was normal. The right ovary had increased volume for a cystic-solid mass of the size of 14 cm with smooth surface and twisted on the vascular peduncle. A right adnexectomy was performed. Intraoperative frozen section was negative for malignancy and postoperative histological examination revealed a struma ovarii without atypia of the follicular cells. Postoperative course was normal. The patient was discharged after three days and she delivered at term a normal baby. Mostly struma ovarii represents an incidental finding during cesarean section, but in rare case it may be cause of complications such as torsion, rupture, hypertiroidism and rarely may be a malignant tumor. The AA describe literature data on struma ovarii diagnosed in pregnancy.

KEY WORDS: Pregnancy - Ovarian tumor - Struma ovarii - Adnexal torsion - Dermoid cysts.

Introduction

The diagnosis of abdominal masses during pregnancy has increased because routine obstetric ultrasound (1) and it is estimated that 2-10% of all pregnancies show ovarian masses (2, 3). Mostly they are functional cysts that resolve by 16 weeks of pregnancy, but 3-6% are ovarian cancers that represent the second gynecological cancer complicating pregnancy (2, 3). Malignant germ cell tumors are the most frequent ovarian cancer in pregnancy and ovarian dermoid is the most frequent benign tumor. Approximately 15% of ovarian teratomas contains a small, non-significant focus of thyroid tissue (4). The rare struma ovarii is a monodermal teratoma described in 1899 by Boettlin (5, 60), usually diagnosed in fertile age, and rarely in prepubertal age and very seldom in pregnant women. By definition it is composed of mature thyroid tissue in more than 50% of the tumor and rarely thyroid tissue occupies most of the mass (6, 7). Struma ovarii cells typically stain for thyroglobulin and TTF-1 confirming the thyroid nature of the tissue (8). It represents approximately 1% of all ovarian tumors and 2,7% of all dermoid tumors (9). 1-3% of struma ovarii are characterized by the presence of functional thyroid tissue with symptoms and signs of hyperthyroidism, as a result of autonomous activation of the thyroid tissue (4). It is well known that persistent hyperemesis gravidarum (10) or hyperthyroidism in pregnancy (11, 12) may be consequent to functionally active thyroid in struma ovarii. The association with serous or mucinous or cystoadenoma and Brenner tumors have been reported (13). Malignant transformation

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is reported in 5 to 10% of cases and the prognosis is usually favorable (14).

Adnexal torsion has been described both in not pregnant and pregnant patients, and the presence of ovarian mass increases the risk of ovarian torsion leading to ischemia and necrosis of the ovarian tissue following persistent obstruction of veins, arteries and lymphatic flow. Usually it is a gynecological emergency. The literature reports that overall incidence of adnexal torsion is 1/10 per 10,000 of spontaneous pregnancies, mostly in patients with adnexal tumors (15). The diagnosis of adnexal torsion in pregnancy may be difficult owing to the symptoms of pregnancy and the presence of growing uterus with dislocation of the mass.

The Authors present a rare case of struma ovarii causing acute adnexal torsion in the 13th week of pregnancy in a patient clinically and biochemically euthyroid. The patients underwent laparotomy with adnexectomy.

Case presentation

A 19-year-old woman at 12th week of pregnancy was referred to our hospital with severe acute abdominal pain, nausea and vomiting. She was afebrile. Family and personal history were negative. A right ovarian mass has been incidentally discovered during a routine follow-up examination in the 8th weeks of pregnancy. It was a mass of 14x12 cm in diameter, with septum, a regular contour, no solid component, and a content partially showing groundglass echogenicity. The contralateral ovary was normal. There was no evidence of peritoneal fluid. Fetal development was corresponding to amenorrhea. The patient didn't report symptoms of hyperemesis gravidarum. At the entrance to the hospital the vital parameters were regular as well as routine examinations, except neutrophilic leukocytosis. The abdomen was untreatable. Ultrasound examination confirmed the presence of intrauterine pregnancy corresponding to amenorrhea and a right complex ovarian mass, with well defined margins without papillary projection, 14x12 cm in diameter (Figure 1). No free fluid was evident in the Douglas. Routine antenatal tests including thyroid function (commonly performed in our population) tests were normal. CA 125 was slightly increased and other humoral markers were negative. Suspecting ovarian torsion due to increasing pain and untreatable abdomen, the patient underwent laparotomy under general anesthesia. The right ovary had increased volume for a smooth cystic-solid mass of the size of 14 cm (Figure 2) twisted on the vascular peduncle but without necrotic aspect. Ovary and tube were excised and sent for frozen examination which reported a benign unruptured lesion. Contralateral ovary was normal as well as the inspection of peritoneum and abdominal cavity. Laparotomy lasted 45 minutes. Postoperative course was uneventful without tocolitic therapy and the patient was discharged three days after surgery with a regular pregnancy. Postoperative histological examination diagnosed a mature cystic teratoma with predominantly development of mature thyroid tissue (struma ovarii) (Figures 3, 4, 5) with positive stain for thyroglobulin (Figure 6) and TTF-1 (Figures 7, 8). There was no atypia of the follicular cells. The patient spontaneously delivered at term a normal baby.

Figure 1 - Ultrasound imaging of the right ovarian tumor.

Discussion

The prevalence of adnexal masses ranges from 1 in 81 to 1 in 8,000 pregnancies (16) and average gestational age at diagnosis and surgery were 12 and 20 weeks respectively (17). Functional cysts are the most common adnexal mass associated with pregnancy (2, 3) and resolve spontaneously in early pregnancy. The benign masses are prevalently dermoid cysts, serous or mucinous cyst adenomas and on rare occasions, endometriomas, hydrosalpinx, or leiomy-

Figure 2 - Macroscopic aspect of right ovarian tumor.

Figure 3 - On histologic examination a mature cystic teratoma is diagnosed with mature thyroid tissue, skin and annexes pilosebaceous.

omas (18). Adnexal mass may requiring surgery due to complications as reported in dermoid cysts that undergo torsion (1-22%), rupture (0-9%), obstruction of labor (2-17%) (19) or very seldom infection (20) or autoimmune hemolytic anemia (21). Only 3-6% of all ovarian cysts associated with pregnancy are malignant (1) and 5-15% of struma ovarii presents malignant changes (22). Papillary carcinoma and follicular carcinoma are the most frequent type of carcinoma in struma ovarii, diagnosed respectively in 21% and in 54% of malignant struma ovarii (23). Cellular atypia, increased hyperplasia, nuclear pleomorphism, mitotic activity and vascular and or capsulate invasion are the main histological characteristics of malignant struma ovarii (24). Distant metastases of malignant struma ovarii are described in <5% of patients in the liver, peritoneum, lungs, and bone with usually a favorable prognosis (25-27).

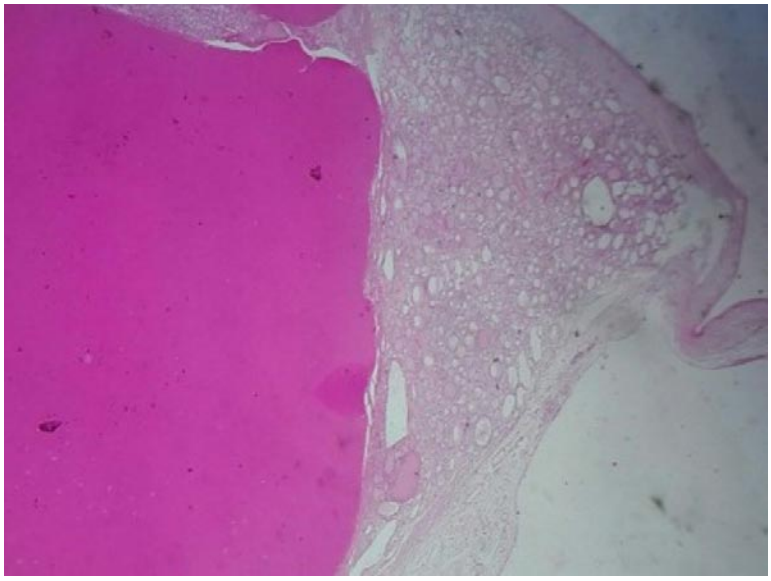

Figure 4 - Mature cystic teratoma. The tumor is composed predominantly of acini lined by a single layer of eosinophilic, low-cuboidal cells with round nuclei and filled with colloid, as seen in the eutopic thyroid.

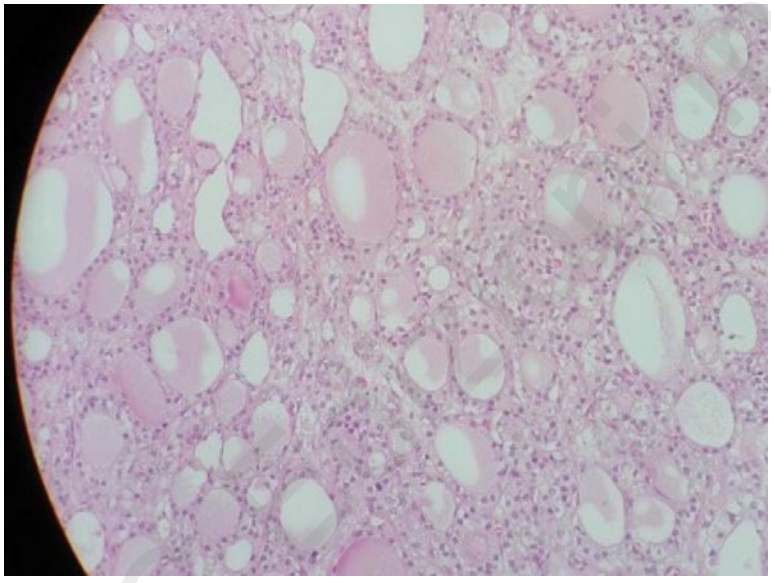

Figure 5 - Mature cystic teratoma: this type of teratoma is composed predominantly of mature thyroid follicles.

Lee et al. (28) reported a patient with metastatic follicular struma ovarii complicating pregnancy. Poor prognostic factors for malignancy are spread to surrounding organs initial extra-ovarian involvement, dimension >5 cm and >50% proliferating thyroid tissue (29). When an ovarian mass is diagnosed during laparotomy a careful inspection of pelvis and abdominal cavity is mandatory to detect signs of malignancy and to diagnose other masses because dermoid tumor may be bilateral in 10% of cases (30), multiple in the same, contralateral ovary and in other anatomical sites (31, 32). It should be also remembered that usually the diagnosis of struma ovarii is incidental during a cesarean section and frozen section during laparotomy may be faulty in diagnosis cancer degeneration. Zorlu et al. (33) reported that malignancy was diagnosed in frozen sections in only 50% of cases, but other studies data show that, although the diagnosis of tumors of borderline malignancy may be difficult, the sensitivity and specificity of frozen section in diagnosis of ovarian tumors is high and better than showed by Zorlu (33).

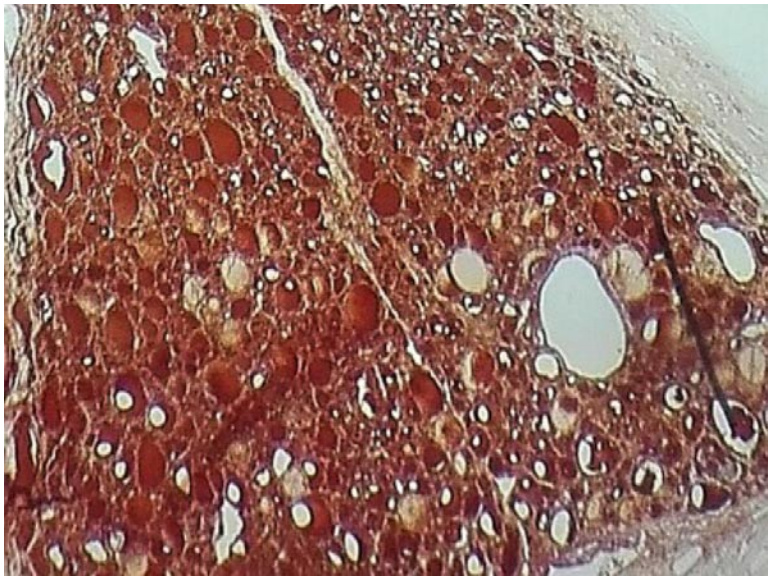

Figure 6 - Immunostains for thyroglobulin are positive in the colloid and in the cytoplasm of the follicular cells in mature cystic teratoma.

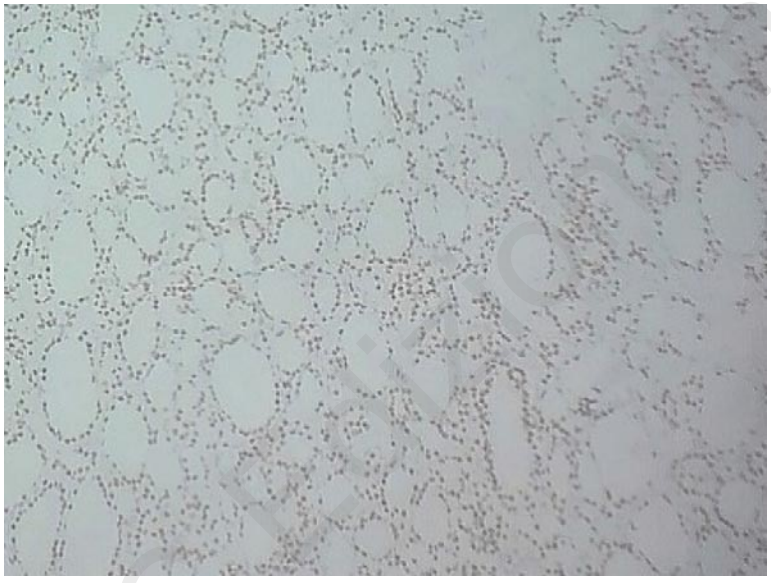

Figure 7 - Mature cystic teratoma: immunostains for thyroid transcription factor-1 (TTF-1) are positive in the tumor cell nuclei.

The histologic criteria for cancer diagnosis in struma ovarii within the thyroid gland may be also not predictive of metastatic potential in struma ovarii (35).

Torsion is a complication of adnexal mass due to rotation of the ovary around the axis represented by the uterus-ovarian and infundibulum-pelvic ligaments. Its overall incidence in the literature is 1/10 per 10,000 spontaneous pregnancies, and it has been also described in a normal fallopian tube and or ovary. The right adnexa is most involved because the right utero-ovarian ligament is longer than the left (36) leading to hypermobility. Increased ovarian size/weight as well hyperstimulated ovaries (37) increase the risk of torsion.

The symptoms of struma ovarii torsion are not specific and may arise suddenly with acute pain localized on the side of the torsion, associated with nausea, abdominal defense generally usually without fever (38). The diagnosis may be difficult especially during pregnancy. Blood markers are not specific, because may be present only sign of inflammation.

Figure 8 - Mature cystic teratoma: the cyst is prevalently lined by follicular cells positive for TTF-1.

Ca-125 may be increased in non pregnant women with struma ovary (22) and usually in patients with ascites due to the peritoneal irritation. The differential diagnosis with appendicitis, PID, adnexal or ovarian cyst, ectopic pregnancy, necrotising fibroma, sigmoid diverticulitis may be difficult in some cases (39). Ultrasound examination shows useful data, but it is not able to differentiate between benign and low malignant potential tumors. Size, complex echo structure, papillary structure, internal septa, irregulars borders, increased vascularity and low resistance to blood flow are well known signs of possible malignancy. Magnetic resonance imaging may be safety performed in the second and third trimester of pregnancy (40). On Doppler blood the flow may be abnormal and the "whirlpool sign" is the main sign of adnexal torsion (41, 42): the ovary is twisted around the ovarian ligament or infundibulopelvic ligament as a whirlpool or a spiral. The color Doppler sign increases the sensitivity of ultrasound in the diagnosis of ovarian torsion and may be predictive of non-viability of the ovary, but in some cases the flow may be normal according to severity of torsion (41).

In acute abdomen surgery is mandatory. Suspected asymptomatic ovarian masses should be removed between the 16th and 24th week of pregnancy (43, 44), when is low the risk of complications for mother and fetus. The surgical treatment must be conservative in patient in fertile age, but unfortunately an adnexectomy is often indicated. Specific issues discussed with the patients are the possible nature of the mass, the suspect of ovarian torsion, the rupture of the cyst, the necessity of surgical treatment, the possible obstetric complications (risk of miscarriage or preterm delivery), the potential effect of general anesthesia on developing fetus, and the necessity of follow-up even in benign lesion owing to the possibility of occurrence or a new dermoid or very rarely late diagnosis of highly differentiated follicular carcinoma (45). The literature review in ovarian torsion shows that the conservative treatment is correlated with the time of the surgical indication. This is the reason why emergency physicians must be trained to avoid a delay in the diagnosis with a wide use of Doppler study and thus try to preserve the ovary for future pregnancies. However the clinical appearance of an ovarian torsion does not well correlate with the residual ovarian function. In our case the twisted ovary was completely transformed into an apparently benign complex mass without evidence of normal ovarian tissue, thus requiring adnexectomy. It was also performed an accurate exploration of abdominal cavity avoiding uterine manipulation with the aim to diagnose other associated tumors or sign of malignant degeneration. In some case report and small series the mass has been removed safety by laparoscopy (46), and this experience is growing also for treatment of non obstetrical

surgical disease in pregnancy (47), but we opted for open laparotomy.

If the patient has to be submitted to surgery a relevant issue is the fetal risk due to pharmacological treatment during anesthesia and the complications linked to surgical manipulation of uterus. During anesthesia it should be minimized or avoided aorto-caval compression (possible from 13th weeks of pregnancy), avoiding uteroplacental hypoperfusion and fetal asphyxia (48). Although many studies have described the potential for neuroapoptosis and neurodegenerative changes in the developing mammalian brain following general anesthesia, the risk seems particularly evident for prolonged or repeated exposure (49). Data show that pharmacological effects are greater during organogenesis, complete only around the 12th week. For this reason it would be advisable not to perform any surgical and anesthetic procedures before 13th week of pregnancy when an asymptomatic adnexal mass is evident. The best time to perform surgery is the second trimester of pregnancy.

Preoperative evaluation with detailed ultrasound imaging of the entire parenchyma of the contralateral ovary is mandatory due to the association with other ovarian dermoid tumor as well inspection of pelvic cavity during surgery, because dermoid are bilateral in 10% of cases (50) or multiple (31, 32) in different organs. Usta et al. (32) described an ovarian dermoid in a pregnant woman associated with a dermoid in the round ligament. Surgical recurrence of dermoid cysts on the same ovary has been described in 3-4% of patients in follow-up (31).

Previous reports have shown that patients with struma ovarii are largely without symptoms, or are accompanied by non-specific symptoms that are similar to other ovarian neoplasms (22): lower abdominal pain, nausea, vomiting, palpable lower abdominal mass, abnormal vaginal bleeding, ascites, hydrothorax, elevated thyroid function (4, 14). It rarely produces adequate thyroid hormone leading to hyperthyroidism and thyrotoxicosis has been reported in 5-15% of cases. It is more common in tumors more than 3 cm in size. The expression of TSH receptor in ovarian tissue in the presence of TRAb is indicative of a functioning struma ovarii (19, 51). Some cases of hyperemesis gravidarum may be due to TSH secretion by struma ovarii. Thyroid hyperfunction is diagnosed in 5-8% of patients with struma ovarii (47, 52).

Struma ovarii in pregnancy has been reported only in few cases in the literature and torsion is even more rare. Kung et al. (11) described a woman affected and treated by Graves disease 4 years before a pregnancy, when she underwent in the 41 week of pregnancy a laparotomy due to sudden onset of severe pain. Cystectomy was performed and fetus delivered by cesarean section. Histological examination showed a functional struma ovarii. The AA reported that the patient developed hyperthyrodism due to coexistence of struma ovary and Grave disease. Bhanap and Kulkarni (53) described a struma ovarii diagnosed incidentally during cesarean section after an uneventful pregnancy. Merza et al. (12) reported a patient with hyperthyroidism due to struma ovarii and Mimura et al. (54) a patient with coexistence of Grave's disease and struma ovarii. Usta et al. (2006) (32) diagnosed a round ligament dermoid cysts coexistent with a struma ovarii in pregnancy. Other cases are reported by Sifakis et al. (55) and Novac et al. (56), who report that a bilateral struma ovary mimicked an ovarian neoplasm. Wilhelm et al. (57) described a puerpera with massive ascites due to struma ovarii, while Lager et al. (58) discussed a metastatic malignant struma ovarii diagnosed in pregnancy. The opportunity of long-term follow-up is evident in Riggs'case report (45); a woman was treated with a right adnexectomy after delivery due to a previously ruptured complex ovarian cysts consistent with struma ovarii at final pathology. After two years she underwent another diagnostic laparoscopy and biopsy diagnosed a highly differentiated thyroid follicular carcinoma of ovarian origin.

The cases presented underline the rarity of struma ovarii diagnosed in pregnancy. Dede et al. (59) in a retrospective study on 68 incidental masses discovered during a caesarean section detected only 1 (1.5%) struma ovarii.

In conclusion, our case deals with struma ovarii diagnosed in the 13th week of pregnancy following torsion of the mass. The patient was surgically treated through a laparotomy and was discharged after few days in good condition. Successfully she spontaneously delivered at term a healthy baby. The case shows the typical history of this rare tumor because an ovary transformed in an evident mass apparently benign went to acute torsion and revealed on definitive histologic exam a benign struma ovarii.

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