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Benign Multicystic Omental Mesothelioma in Pregnancy: A Case Report and Review of the Literature

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Benign Multicystic Peritoneal Mesothelioma (BMPM) is a very rare condition of unknown pathogenesis, that occurs mainly in women in their reproductive age (5:1 female/male ratio). The pathogenesis of BMPM is unclear and doubts regarding its neoplastic and reactive nature exist. Furthermore, the differential diagnosis with other diseases remains uncertain. In most cases the diagnosis is accidental, during a laparotomy performed for other reasons, since the diagnostic imaging does not allow a definite diagnosis preoperatively. Radical surgical resection is the "gold standard" for treatment of BMPM, despite a high rate of recurrence (about 50%). We report on a case of a 30-year-old pregnant woman with multilocular omental cystic mass, 36 x 22 cm in size, underwent elective caesarean section at term of pregnancy. The definitive histologic diagnosis was benign multicystic mesothelioma of the omentum. BMPM detected in pregnancy or during cesarean delivery is very rare; in fact only three other cases have been reported. Particularly, we present the only case, described in the literature, of a young female with benign multicystic omental mesothelioma in pregnancy that was treated solely by surgery, without recurrence after

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three years follow-up. In this article we also describe diagnostic evaluation, treatment, prognosis of this rare disease as the possible positive effects of adjuvants medical treatments.

Keywords: Benign multicystic peritoneal mesothelioma; pregnancy; complete surgical resection; optimal therapeutic management; hormonal involvement.

1. INTRODUCTION

Benign Multicystic Peritoneal Mesothelioma (BMPM) is an uncommon lesion arising from the peritoneal mesothelium that covers the serous cavity [1-5]; it accounts for about one third of all mesotheliomas, and is not related to asbestos exposure [6,7,8]. It is more common in women (5:1 female/male ratio) in reproductive age (median age, 28 years; range, 18-54 years), but may also occur after menopause. To date, approximately 130 cases have been reported; 85% of the cases occur in the early or mid-reproductive ages, only three during the pregnancy [9,10,11]. Clinically, there is no specific symptomatology; many patients are asymptomatic and the tumor is typically found incidentally, but symptoms of variable intensity can occur depending on the size of the tumor. Preoperative diagnosis of BMPM is still problematic; diagnosis confirmation is achieved only with the pathological examination, at the time of surgery [12]. Complete surgical excision is the optimal treatment choice [9,10,13]. The biological behavior of BMPM is characterized by its slowly progressive process and high rate of recurrence after surgical resection; in addition this lesion does not metastasize and has no tendency to malignant transformation [7,8]. The higher frequency of BMPM in women of childbearing age and the decrease in cyst size after treatment by a gonadotropin-releasing hormone analogue agonist and tamoxifen, have suggested the hormone sensitivity of the lesion [14,15,16]. However, in a recent immunohistochemical analysis, estrogen and/or progesterone receptor were found in only 3 (17.64%) of 17 women with BMPM [15].

We here report a case of BMPM admitted to our Department with a review of the literature.

2. CASE REPORT

A 30-year-old woman, primigravida, with negative medical and gynecological history; ultrasonographic examination revealed a 9-week intrauterine pregnancy and a large, 8 x 9 cm right adnexal multilocularipo-anechoic cystic mass. Tumor markers were negative. Magnetic Resonance Imaging (MRI) performed at the 17th week, showed a massive multilocular thin-walled cystic mass, hypointense on T1W and hyperintense on T2W images, that displaced the ascending colon, extending cranially, to the liver and, caudally, to the right iliac region (Fig. 1). The lesion measured about 16 X 9 X 22 cm in its maximum transverse, anteroposterior, and craniocaudal diameters, respectively (Figs. 2–3). During pregnancy, the patient was subjected to ultrasound scans that highlighted the regular monthly evolution of pregnancy, a normal fetal growth and the progressive increase in size of the cystic mass. She was referred to our Department for worsening dyspnea. During the hospitalization, she was subjected to routine blood tests. Tumor markers were within normal limits (CA 125: 11.6 U/ml, CA 19-9: 27 U/ml, CEA: 1.2 ng/ml) except CA 15-3: 101 U/ml (range 0-43 U/ml). A xipho-pubic laparotomy was performed and the patient underwent a cesarean section delivery during the 39 weeks of pregnancy with the birth of a fetus alive and kicking, male, weighing 3200 g, Apgar score 9/10. Peritoneal cavity inspection showed an omental mass, adherent to the parietal peritoneum, consisting of a conglomeration of cystic structures grouped in clusters of variable diameter from 10 mm to about 8 cm. No cystic lesion was noted in the parietal and visceral peritoneum, liver, kidney or spleen. A part of cystic omental mass (3 cm) was taken and sent for frozen section examination, which demonstrated multiple mesothelial cysts, without atypia or mitoses. With this result, we performed total omentectomy. The specimen consisted of omentum measuring 36 x 22 cm with multiple serous-filled cysts and thin walls (Fig. 4). Definitive histological examination was "Benign multicysticomental mesothelioma". Microscopic examination demonstrated multiple cystic spaces lined by flat to low cuboidal cells, with occasional hobnail cell features, and no atypia or mitoses; the cysts were separated by fibrous septa with areas of acute and chronic inflammation and slight stromal cell proliferation (Fig. 5). In addition, the mesothelial lining was negative for estrogen and progesterone receptors, on immunohistochemical stains. The patient had an uneventful recovery and was closely followed-up

by UltraSonography (US) and Magnetic Resonance Imaging (MRI). She remained free of symptoms and had no recurrence three years after surgery.

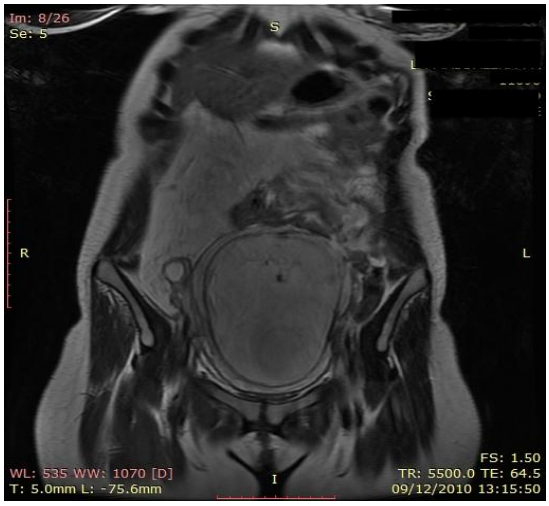

Fig. 1. MR coronal image

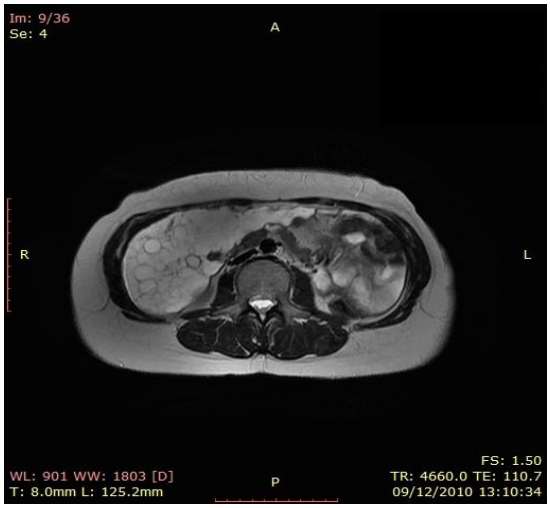

Fig. 2. MR axial image

3. DISCUSSION

Benign Multicystic Peritoneal Mesothelioma (BMPM) is a rare tumor, first described in 1979 by Menemeyer and Smith [17]. Since then approximately 130 cases have been reported [10], but the information regarding BMPM remains incomplete and fragmentary to the lack of data especially concerning the follow-up [1]. BMPM is localized mainly at the surface of the pelvic viscera, at the serosal surfaces of the intestine and omentum or in the retroperitoneal space, spleen and liver. Its pathogenesis is still controversial. The close relationship with inflammation, a history of prior surgery, endometriosis or uterine leiomyoma suggests the reactive nature of BMPM to chronic irritative stimuli, also confirmed by the presence of an inflammatory component microscopic examination; on the other hand the slow but progressive growth of the untreated lesions and the marked tendency to recur after surgical resection, suggest the neoplastic origin of the lesion [1,5]; however, lesions do not metastatize. Moreover, the histogenetic relationship with Cystic Adenomatoid Tumor, although rare, has led some authors to suggest that BMPM represents possibly a borderline lesion between an adenomatoid tumor and a malignant mesothelioma.

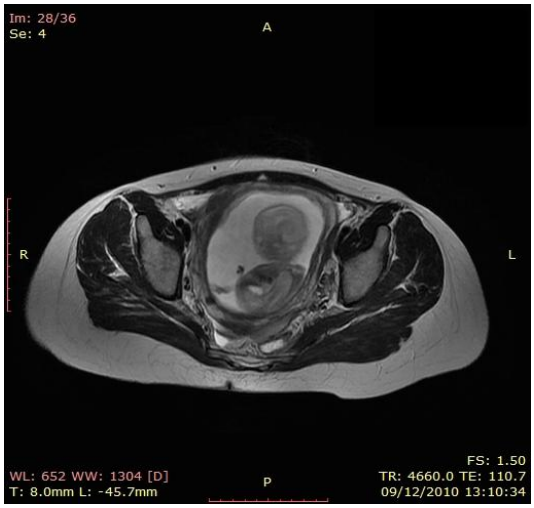

Fig. 3. MR axial image

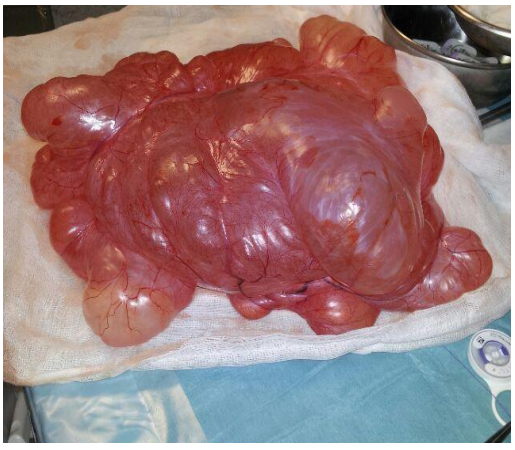

Fig. 4. Surgical specimen

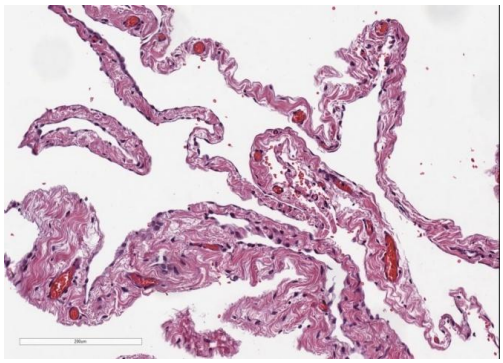

Fig. 5. Photomicrograph of the lesion after surgical removal using the H and E stain with a ×100 magnification

Often, BMPM remains silent in abdominal cavity; sometimes it is manifested as acute abdomen [18]. The classic presenting signs and symptoms are abdominal pain, tenderness, and an abdominal or pelvic mass. Most patients are diagnosed incidentally during examination or laparotomies for other reasons, as in the our case. The available modern imaging techniques, such as UltraSonography (US), Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI), can demonstrate the lesion, but a differential diagnosis from other cystic lesions arising from these anatomical areas, is difficult [19,20,21]. On ultrasonography, the cysts are solitary or multiloculated, translucent, anechoic and arranged in grape/honeycomb-like clusters separated by fibrous tissue, thin-walled, either filled with serous or bloody fluid; the size of BMPM may vary from a few millimeters to >30 cm; CT and MRI confirm the ultrasonographic findings [20]. Rarely, free intraabdominal fluid or hemorrhage and calcification in the walls of cysts have also been documented [20]. Although distortion of adjacent organs is a main characteristic of this tumor depending on its size, neither invasion/ infiltration nor lymphadenopaty, have been reported [12,20]. The definitive diagnosis is achieving only at the time of surgery with the anatomical-pathological examination [12]. Microscopic examination of the specimens demonstrate multiple cystic spaces lined by flat-to-low cuboidal cells; the cells lining the cysts are positive for cytokeratin and calretinin markers on immunohistochemical stains.

Pathological differential diagnosis include benign and malignant lesions that present as cystic or multicystic abdominal masses. Benign lesions include cystic lymphangioma (cystic hygroma), cystic forms of endosalpingiosis, endometriosis, mullerian cysts involving the retroperitoneum, cystic adenomatoid tumors and cystic mesonephric duct remnants. Malignant lesions include malignant mesothelioma and serous tumors involving the peritoneum [2]. The differential diagnosis of BMPM from cystic ovarian tumors is a key point, since BMPM may be treated by local excision with preservation of the ovaries. Preoperative fine-needle aspiration biopsy of cystic lesions may contribute to the differential diagnosis [22,23], but in most cases this method is not informative and it is considered hazardous from an oncological point of view. Although an invasive procedure, laparoscopy is the most accurate diagnostic method since it allows local biopsy of the suspected tissue specimens; the diagnosis can be confirmed by electron microscopy and immunohistochemistry [22].

Complete removal of the cystic lesion if possible, remains the "gold standard" for treatment and the only hope to avoid local recurrence, therefore, aggressive surgical approaches including cytoreductive surgery is recommended [13]. In 1997, Datta and Paty introduced the concept of peritoneal stripping for these patients [24]. The lateral margins of the lesion can often be seen to merge with the surrounding normal mesothelial covering, making complete excision difficult if not impossible. Another surgical option is combined modality treatment with cytoreductive surgery plus hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC), using cisplatin or doxorubicin; preliminary results have demonstrated safety and efficacy in several series of patients with peritoneal dissemination, demonstrating a prolonged disease-free survival and a minimal risk of recurrence.

The use of HIPEC may eradicate free tumor cells, therefore it is useful in the control of microscopic residual disease [25]; this strategy has been introduced for the treatment of pseudomyxoma peritonei [26] and has been applied successfully for patients with BMPM.

Based on the predominance of benign multicystic mesothelioma in women in the reproductive age, three case reports suggest some degree of hormonal involvement of the tumor. The use of tamoxifen and long-acting GnRH analogues leads to a reduction in cyst volume and cyst growth [14,15,16]; therefore, hormonal therapy could be a therapeutic option for tumor reduction before anticipated surgery or management of recurrent lesions in some cases [12-16,27]. Rosen and Sutton used potassium titanyl

phosphate laser to treat these lesions; the laser penetrates to a depth of 2 mm, its primary effect being coagulation and vaporization. The authors consider this method to be efficacious in the treatment of multiple sites disease and, in addition, may reduce the need for repeated laparotomies [28].

Recurrence rate is 41,7% and, according to data reported in the literature, it can occur from 3 months to 22 years after surgery [9]; the best predictive factor remains the completeness of initial surgical resection. Recurrences can be treated by hormonal therapy with antioestrogens [15] and gonadotrophin-releasing analogues [16]; other treatment options are hyperthermic intraperitoneal chemotherapy [29,30], and sclerotherapy with tetracycline [31]. Adjuvant chemotherapy and radiotherapy are not indicated because these tumors have a prevailing benign character. It should be emphasized that these are experimental treatment and evaluating the degree of success following these procedures is difficult because of the rarity of desease.

Malignant transformation of peritoneal cystic mesotheliomas is a rare event; only two case have been reported in literature [7,8]. This fact mandates a re-evaluation of the term 'benign' and systematic clinical follow-up of these patients for prolonged periods, perhaps for life [7]. Unfortunately, the difficulty in further follow-up is compounded by the fact that there are no tumor markers and pathognomonic clinical findings for diagnosis and recurrence of this pathology.

BMPM detected in pregnancy or during cesarean delivery is very rare; in fact only three other cases have been reported. Particularly, we present the only case, described in the literature, of a young female with benign multicystic omental mesothelioma in pregnancy that was treated solely by surgery, without recurrence after three years follow-up. (Table 1).

The first case, described by Nayak et al. in 2005 [11], regards a 26-years-old woman. During the cesarean section, a multicystic peritoneal mass, with a thin translucent wall and serous clear content, was detected accidentally and excised. The post-operative pathology report was defined as a BMPM.

In 2006, Jerbi et al. [10] described the case of a 35-year-old woman, gravida 2, para 2, with a history of cesarean section, which had been experiencing lower abdominal pain for almost 5 months. Ultrasonographic studies revealed a 5-week intrauterine pregnancy and a large, 8 x 9 cm anechoic multicystic mass occupying the pelvis. On laparotomy, multiple grapelike clusters of cysts filled the entire pelvis. The cysts were attached to the peritoneal surface of the pouch of Douglas. All macroscopically visible cysts were excised and pregnancy was allowed to continue. Histologic studies revealed that the cysts were lined with a flat cuboidal epithelium without atypia, and immunohistochemical staining for HBME-1 confirm the mesothelial character of the cells. In addition, the mesothelial lining was diffusely positive for estrogen receptor but not for progesterone receptor. Six weeks later, a control ultrasonographic examination showed a recurring pelvic mass, which was 5 x 6 cm. Operative termination of pregnancy was accepted and performed. After counseling, a daily course of 20 mg of tamoxifen was started. Three months later, the patient remains stable, without significant increase in the mass size.

Table 1. Overview of BMPM in pregnancy cases

	Nayak et al. 2005 [11]	Jerbi et al. 2006 [10]	Akbayir et al. 2011 [9]	Our case
Age	26	35	38	30
Symptoms	None	Lower abdominal pain	None	Worsening dyspnea
Timing of disease found	During caesarean section	A 5 week intrauterine pregnancy	During caesarean section	A 9 week intrauterine pregnancy
Localization	Multicystic peritoneal mass	Pelvis	Right paracolic region	Omentum
Size at US	Unspecified	8 x 9 cm	9 x 7 cm	22 x 15 cm
Treatment	Surgery	Surgery. Voluntary Interruption of Pregnancy and Tamoxifen after recurrence	Surgery	Surgery

The third case described by Akbayir et al. in 2011 [9], regards a 38-years-old woman, primigravida, underwent a cesarean section delivery because of advanced maternal age and request for cesarean delivery. In her medical records she received hysterosalpingography and hysteroscopy for infertility research. During the cesarean section, a multicystic mass measuring 9 x 7 cm was detected incidentally in the right paracolic region and total resection of the mass was performed. The postoperative pathology report was defined as a BMPM.

4. CONCLUSION

In conclusion, we have presented the only case, described in the literature, of a young female with benign multicysticomental mesothelioma detected in pregnancy. Radical surgical resection is the "gold standard" of treatment. However, because of the rarity of this entity, uncertainties remain about the follow-up strategies and the therapeutic management of local recurrences.

Further studies are needed to evaluate the real benefit, in terms of overall survival, of aggressive surgical treatment or more conservative therapies.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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