CASE REPORT

RJME
Romanian Journal of Morphology & Embryology
http://www.rjme.ro/

An unusual cause of acute surgical abdomen: benign multicystic peritoneal mesothelioma associated with adenomatous tumor

CRISTIAN MEŞINĂ[1)], THEODOR VIOREL DUMITRESCU[1)], STELIAN ŞTEFĂNIŢĂ MOGOANTĂ[1)], MIHAI CĂLIN CIORBAGIU[1)], DANIEL ALIN CRISTIAN[2)], MIHAELA-IUSTINA MEŞINĂ-BOTORAN[3)], CORINA-LAVINIA GRUIA[4)], MARIA CAMELIA FOARFĂ[4)], MIHAI MEŞINĂ[5)], MARIUS EUGEN CIUREA[6)], DANIELA CIOBANU[7)]

[1)]*Department of Surgery, University of Medicine and Pharmacy of Craiova, Romania; Department of Surgery, Emergency County Hospital, Craiova, Romania*

[2)]*Department of Surgery, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; Department of Surgery, "Colţea" Clinical Hospital, Bucharest, Romania*

[3)]*Department of Human Anatomy, University of Medicine and Pharmacy of Craiova, Romania*

[4)]*Department of Pathology, University of Medicine and Pharmacy of Craiova, Romania; Department of Pathology, Emergency County Hospital, Craiova, Romania*

[5)]*"Prof. C. C. Iliescu" Emergency Institute for Cardiovascular Diseases, Bucharest, Romania*

[6)]*Department of Plastic Surgery and Reconstructive Microsurgery, University of Medicine and Pharmacy of Craiova, Romania; Department of Plastic Surgery and Reconstructive Microsurgery, Emergency County Hospital, Craiova, Romania*

[7)]*Department of Gastroenterology, University of Medicine and Pharmacy of Craiova, Romania; Department of Gastroenterology, Emergency County Hospital, Craiova, Romania*

Abstract

Benign multicystic peritoneal mesothelioma (BMPM) is a rare disease that primarily affects fertile women with previous abdominal surgery. BMPM associated with adenomatous tumor is a single case report, according to our opinion. The patient had a history of abdominal surgery nine years ago for ovarian cysts. Upon admission, the diagnosis was acute surgical abdomen with acute peritonitis signs. The treatment applied consisted in the removal of peritoneal cysts and partial omentectomy. Only immunohistochemical examination established the diagnosis. The aim is to discuss diagnostic and therapeutic difficulties, underlining that there is no consensus on the use of chemotherapeutics. In conclusion, establishing a preoperative diagnosis is difficult if not impossible. One of the causes of acute surgical abdomen may be BMPM. The malignant transformation of this disease is rare, but the disease recurrence rate is over 50%, and it is often recommended to be monitored through abdominal computed tomography.

Keywords: benign multicystic peritoneal mesothelioma, adenomatoid tumor, omentectomy.

Introduction

Benign multicystic peritoneal mesothelioma (BMPM), known as multilocular peritoneal cysts, is an extremely rare disease, which has the peritoneal mesothelium as a starting point. Although this disease is considered benign, relapse after surgery is reported in over 50% of cases [1] and two cases of malignant transformation have been reported [2]. Pathogenesis of the disease is unknown. There is a discussion of a possible etiopathogenicity related to pelvic inflammatory disease, Mediterranean fever, endometriosis and a history of abdominal surgery. BMPM is more common in premenopausal women and rarely in men [3–5]. In this article, we present a case of BMPM associated with adenomatous tumor and we review the literature on this problem.

Aim

We describe the case of a 53-year-old female who was admitted as an acute surgical abdomen caused by BMPM, our case being unique in literature. Only immunohistochemical (IHC) exam after surgical removal established the final diagnostic: BMPM associated with adenomatous tumor.

Case presentation

R.V., a 53-year-old female patient, was admitted in the 2nd Surgical Clinic, Emergency County Hospital, Craiova, Romania, in December 2017, with diffuse abdominal pain, vomiting. Patient history was significant for hypertension and type 2 diabetes mellitus. Physical examination showed a postoperative infraumbilical scar on the abdomen for ovarian cyst and appendectomy (in the same surgical session nine years ago). There was a little abdominal distension, with diffused pain, having muscle defense in the right flank and right iliac fossa and right lower quadrant tenderness.

Laboratory investigations showed: hemoglobin (Hb) 12.9 g/dL, white blood cells (WBC) count 22 330/mm^3,

platelets 245 000/mm^3, urea 36 mg%, creatinine 0.87 mg%, serum glutamic oxaloacetic transaminase (SGOT) 13 IU/L, alanine aminotransferase (ALAT) 12 IU/L, glycemia 302 mg%, Na^+ 137 mEq/L, Cl^- 103 mEq/L, K^+ 3.7 mEq/L, cancer antigen (CA) 125 level 34 U/mL (reference range: 0–39 U/mL), CA 19-9 level 5.22 U/mL (reference range: 0–35 U/mL) and carcinoembryonic antigen (CEA) level 8 ng/mL (reference value 2.5 ng/mL and for smokers <5 ng/mL).

Computed tomography (CT) examination of the abdomen and pelvis performed post-contrast revealed a 40 mm interhepato-gastric cystic mass, diffuse peritoneal thickening and large cystic lesion in the right lower quadrant (Figure 1).

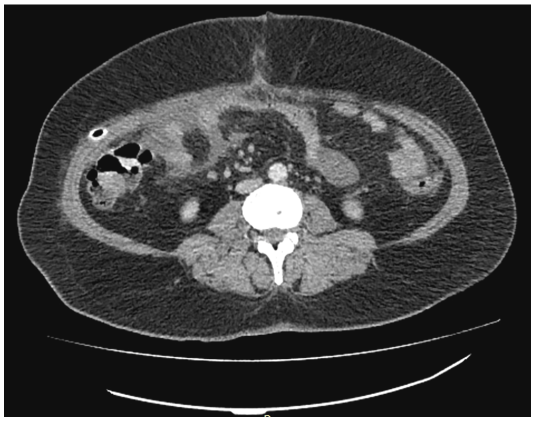

Figure 1 – ***Diffuse peritoneal thickening and well-defined low attenuating (cystic) mass in the right lower quadrant.***

With preoperative diagnosis of acute peritonitis, surgical intervention occurs revealing the presence of multiple cysts with clear fluid, having variable sizes (3–40 mm) disposed on the peritoneum covering the small bowel, the mesentery, the omentum and a 40 mm diameter interhepato-gastric cyst. Exploratory laparotomy discovered numerous thin-walled and pelvis forming multicystic mass. The cysts measured from a few millimeters to a few centimeters in diameter and had clear fluid. There have been multiple filamentous adhesions between the peritoneum, intestine and viscera. The great epiploon was thickened, edematous, infiltrated. The performed surgery consisted in partial omentectomy, surgical excision of the large cysts with adhesiolysis by laparotomy, peritoneal lavage and multiple peritoneal drainage.

The macroscopic examination of the surgically removed large omentum revealed the presence of multiple cysts, with clear fluid, having dimensions from 3 mm to 12 mm in diameter (Figure 2). Extracted surgical tissue fragments were fixed within three weeks in 10% formalin solution. Then, 1 cm sections were included in the paraffin and the five-µm sections were stained with Hematoxylin–Eosin (HE). Immunohistochemistry was performed on formalin-fixed paraffin-embedded tissue.

The microscopic examination revealed multiple, irregular or round cysts, cuboidal or flattened mesothelial cell walls, sometimes with fenestrated edges (Figure 3). The intercystic spaces were separated by loose, edematous tissue, often containing chronic inflammatory cells with abundant cytoplasm and eccentric nucleus (Figure 4), fibrin deposits and sometimes-entrapped mesothelial cells resembling infiltrating carcinoma (Figure 5). The described aspects have suggested the existence of a BMPM associated with adenomatous tumor.

IHC examination of the lesions highlighted a diffuse and highly positive immunoreactivity for anti-calretinin antibody (Figures 6 and 7) and for anti-epithelial membrane antigen (EMA) antibody (Figures 8 and 9) in the ciliate epithelium of the cysts, which compose the lesion and in areas of the adenomatous tumor and negative immuno-reactivity for anti-CD34 antibody in the epithelium covering the cystic spaces and in areas of the adenomatous tumor (Figure 10). Immunoreactivity for anti-CD34 antibody was positive in the vessels of surrounding tissues (Figure 11). The differentiation between abdominal cystic lymph-angioma and multicystic peritoneal mesothelioma was based on the immunoexpression for CD34: positive in lymphangioma and negative in BMPM. Most epithelial mesotheliomas exhibit extensive, strong linear membrane staining using anti-EMA antibodies, in contrast to the weak or undetectable staining seen in reactive mesothelial hyperplasia. HBME-1 was positive in mesothelial cells of multicystic peritoneal mesothelioma, but also in adenomatous tumor cells (Figure 12).

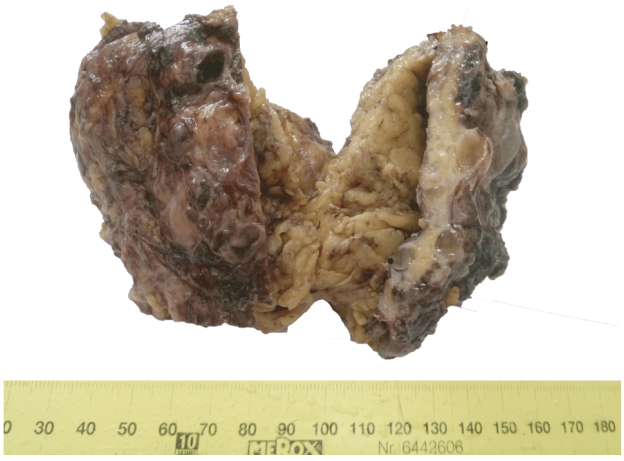

Figure 2 – ***The macroscopic aspect of the large omentum with multiple cysts with clear fluid and dimensions from 3 mm to 12 mm in diameter.***

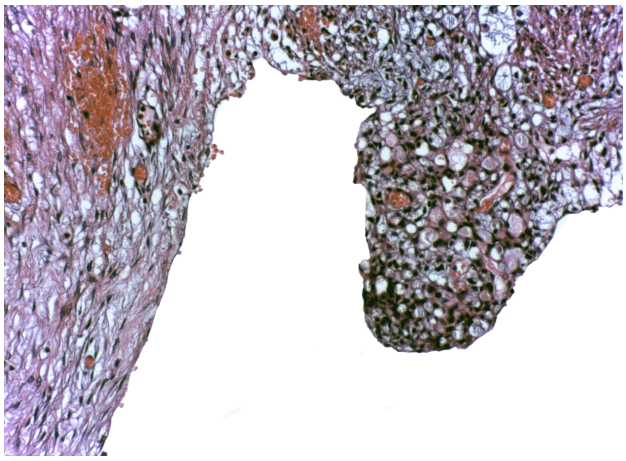

Figure 3 – ***Multicystic peritoneal mesothelioma with foci resembling adenomatoid tumor. HE staining, ×200.***

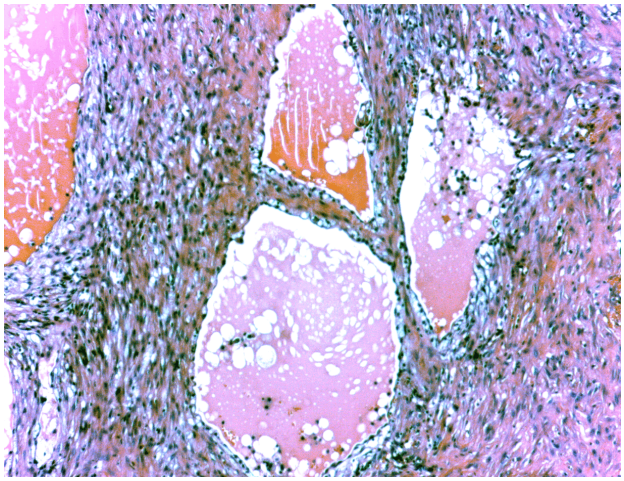

Figure 4 – *Mesothelial cells entrapped in the wall of a multicystic peritoneal mesothelioma. HE staining, ×40.*

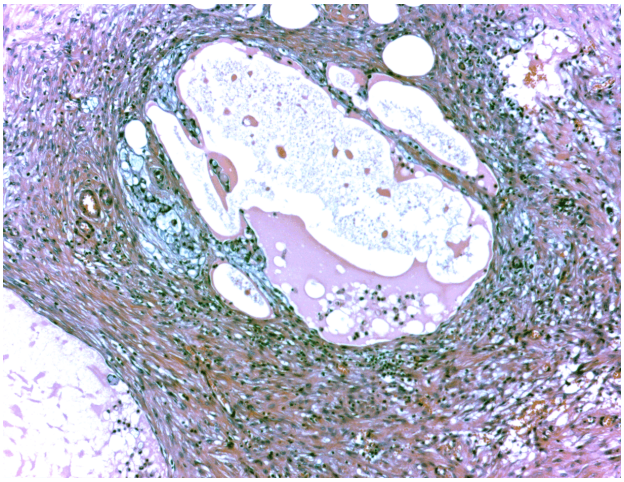

Figure 5 – *Multicystic peritoneal mesothelioma with secondary inflammatory changes. Mesothelial spaces lie in an edematous spindled stroma contain inflammatory cells. HE staining, ×200.*

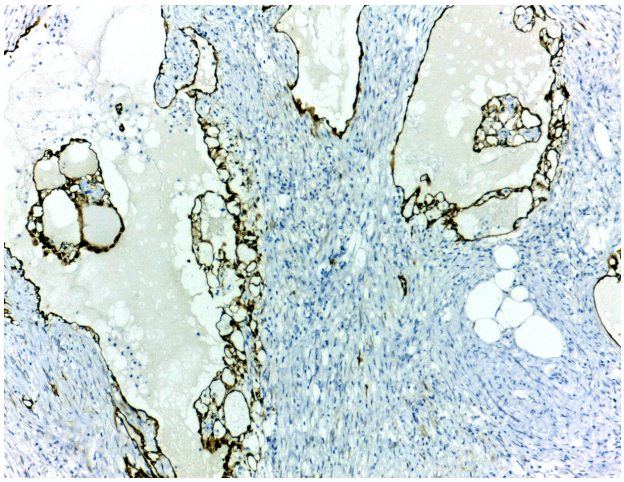

Figure 6 – *Multicystic peritoneal mesothelioma: calretinin-positive immunostaining in the ciliate epithelium of the cyst. Anti-calretinin antibody immunostaining, ×100.*

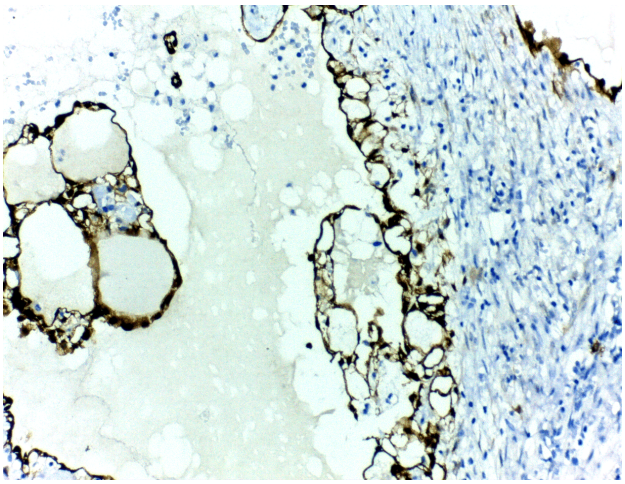

Figure 7 – *Multicystic peritoneal mesothelioma: calretinin-positive immunostaining in areas of the adenomatous tumor. Anti-calretinin antibody immunostaining, ×200.*

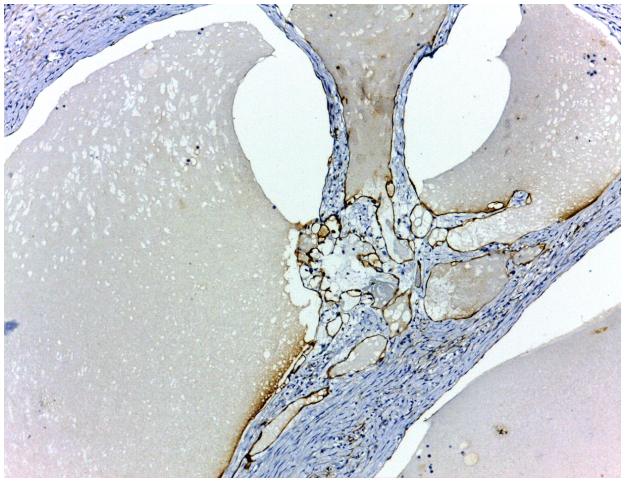

Figure 8 – *Multicystic peritoneal mesothelioma: EMA positive immunostaining in ciliate epithelium of the cyst. Anti-EMA antibody immunostaining, ×40.*

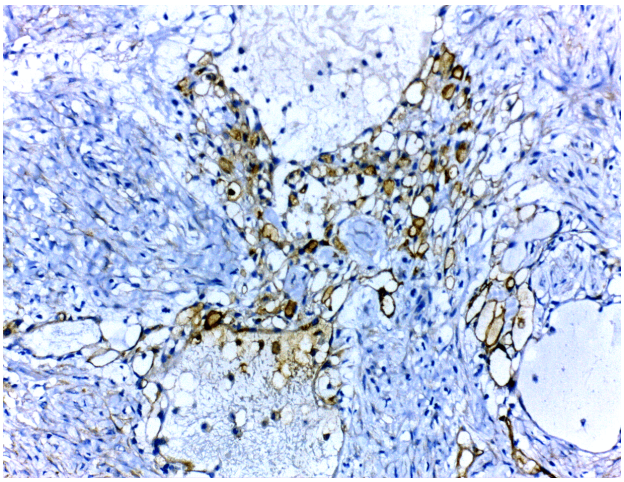

Figure 9 – *Multicystic peritoneal mesothelioma: EMA positive immunostaining in areas of the adenomatous tumor. Anti-EMA antibody immunostaining, ×200.*

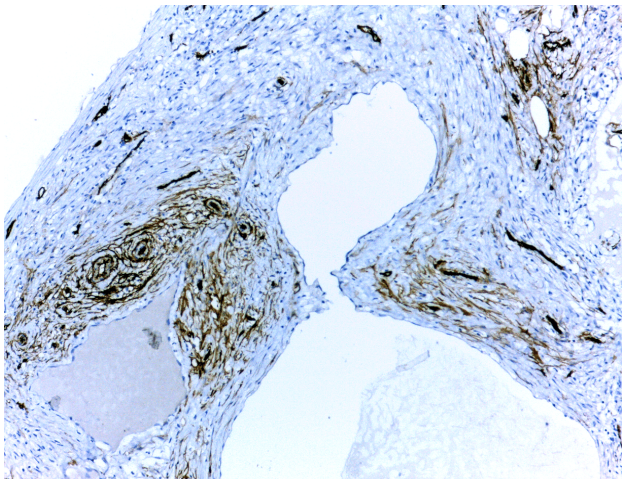

Figure 10 – ***Muticystic peritoneal mesothelioma: CD34 negative immunostaining in the epithelium of the lining of the cystic spaces and in areas of the adenomatous tumor. Anti-CD34 antibody immunostaining, ×100.***

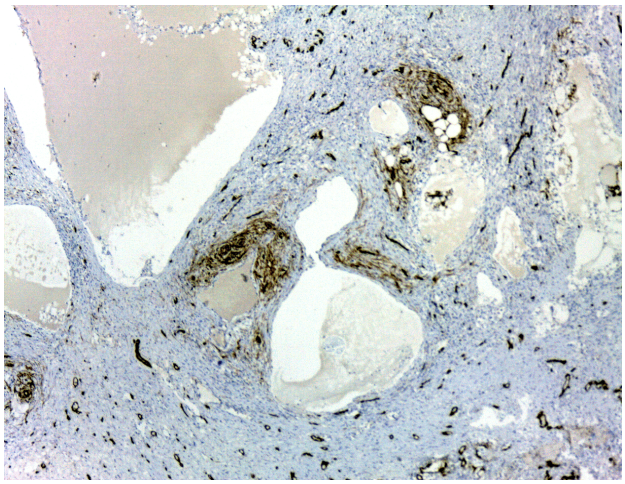

Figure 11 – ***Multicystic peritoneal mesothelioma: CD34 positive immunostaining in the vessels of the surrounding tissue. Anti-CD34 antibody immunostaining, ×40.***

Mouse anti-mesothelioma monoclonal antibody (clone Hector Battifora mesothelial-1 (HBME-1)] reacts with an unknown antigen of the surface of mesothelioma cells microvilli. This antibody stains normal mesothelial cells but also mesothelioma cells in a thick membrane model due to the abundance of long microvilli on the surface of these cells. Using polyclonal antibodies against human recombinant calretinin, many researchers have demonstrated calretinin immunoexpression in all mesothelioma investigated. HBME-1 and calretinin have been used as mesothelioma-related markers.

Ki67 proliferative index was positive at a rate of 7% (Figure 13).

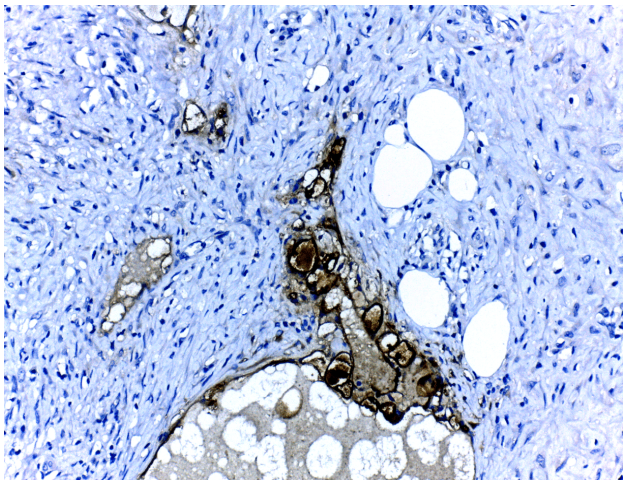

Figure 12 – ***Multicystic peritoneal mesothelioma: HBME-1 positive immunostaining in the mesothelial cells of multicystic peritoneal mesothelioma and adenomatous tumor cells. Anti-HBME-1 antibody immunostaining, ×200.***

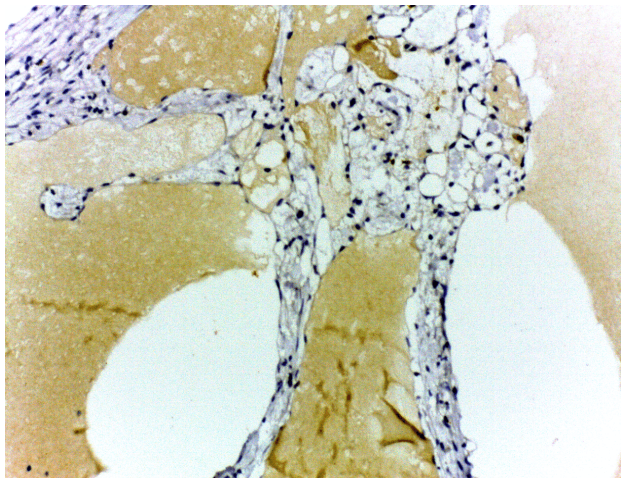

Figure 13 – ***Multicystic peritoneal mesothelioma: Ki67 low nuclear (7%) immunostaining in tumor cells. Anti-Ki67 antibody immunostaining, ×200.***

Discussions

BMPM is a rare disease with unknown pathogenesis. There is a discussion of a possible etiopathogenesis associated with pelvic inflammatory disease. Three hypotheses have been proposed in the etiology of BMPM disease. One hypothesis argues that BMPM arises from an inflammatory process involving peritoneum, which results in hyperplastic and dysplastic reactive transformation of peritoneal mesothelial cells. Another theory supports the primary neoplastic origin without the involvement of a chronic inflammatory process. Other authors support the hormonal theory, in which the development and progression of BMPM is closely related to sensitivity to sexual hormones. This theory is supported by the fact that BMPM has a higher incidence in women during the reproductive period, and that BMPM responds to Tamoxifen and gonadotropin-releasing hormone analogues [6]. Most authors agree on the fact that chronic peritoneal inflammatory process causes proliferation and migration of peripheral mesothelial cells often associated with metaplasia of the underlying connective tissue [6–8]. Transition between multicystic mesothelioma and adenomatoid tumor has been observed on several occasions [9, 10].

The symptoms of BMPM are insignificant, but become apparent when the cystic tumors are large enough to produce mass effect on surrounding organs, or if the cysts

break and produce an acute peritonitis-like reaction, as we have shown. Symptoms may be chronic abdominal and/or pelvic pain, abdominal distension, intestinal obstruction, intestinal transit disorders [1, 11–13].

The physical examination may reveal muscle defense, abdominal distension or acute appendicitis-like symptoms [14]. In our case, the abdominal pain was diffuse and the symptoms mimed an acute peritonitis.

There are benign or malignant diseases that can mime BMPM. These diseases are intestinal lymphangioma [15, 16] and malignant peritoneal mesothelioma. Lymphangioma can be diagnosed when the cysts contain predominantly chylous fluid and when there is discovered the presence of lymphoid aggregates, smooth muscle cells and D2-40 positive immunoexpression in the IHC examination. Malignant peritoneal mesothelioma has a history of asbestos exposure, abdominal pain, weight loss.

The abdominal CT reveals the presence of ascites fluid and diffuse thickening of the peritoneum [11, 12, 17].

Multiple therapeutic strategies for BMPM have been proposed. Complete cytoreduction with instillation of hyperthermic intraperitoneal chemotherapy (HIPEC) remains the best treatment. The appropriate surgical treatment appears to be excision of localized cysts to healthy tissue or debulking procedures for invasion of neighboring tissues. However, the disease recurrence remains about 50% in women and 33% in men after complete cytoreduction. For surveillance, CT scan is recommended every three months in the first year after full cytoreduction and then one year in the next five years.

This algorithm is used for an earlier detection of relapse that allows less invasive surgical resection and can thus reduce the risk of malignant transformation [1, 12, 18]. Various chemotherapeutic agents were used intraoperatively. The chemotherapeutic agents used are related to the type of malignancy and the experience of the oncologist surgeon. The most used combination in this disease is Cisplatin + Doxorubicin [19]. Preoperative diagnosis of BMPM is difficult to establish, paraclinical imaging experiments such as ultrasonography (US), CT or magnetic resonance imaging (MRI) are non-specific with a low diagnostic value. The definitive diagnosis is established on the histopathological examination of the surgical specimens combined with the IHC examination [20]. There is still no consensus on therapeutic conduct, although surgical removal of lesions remains the optimal therapeutic option. There are different opinions regarding aggressive surgery *versus* traditional resection surgery through healthy tissue. Alternative therapies include: hormonal supplementation, laser vaporization and sclerotherapy with inconclusive results. Furthermore, it has been observed that lesions do not respond to adjuvant chemotherapy or radiotherapy.

Stallone *et al.* reported a 65-year-old patient who had been surgically treated for multiple peritoneal cysts, but who had recurrence four months after surgery, being treated with low-dose Rapamycin, which is an mammalian target of Rapamycin (mTOR) inhibitor [21, 22].

Conclusions

Establishing a preoperative diagnosis of BMPM is difficult, if not impossible. One of the causes of acute surgical abdomen may be BMPM. The malignant transformation of this disease is rare, but the disease recurrence rate is over 50%, and it is often recommended to be monitored through CT abdomen.

Conflict of interests

The authors declare that they have no conflict of interests.

References

[1] Vyas D, Pihl K, Kavuturu S, Vyas A. Mesothelioma as a rapidly developing giant abdominal cyst. World J Surg Oncol, 2012, 10:277.

[2] González-Moreno S, Yan H, Alcorn KW, Sugarbaker PH. Malignant transformation of "benign" cystic mesothelioma of the peritoneum. J Surg Oncol, 2002, 79(4):243–251.

[3] Snyder JA, Carman R Jr, Aggon AA, Cardinale JP. Benign multicystic peritoneal mesothelioma: a rare case presenting as pneumoperitoneum and *pneumatosis intestinalis*. J Gastrointest Oncol, 2011, 2(1):55–58.

[4] Shetty S, Nagaraj H, Prabhakar SP, Rajput A. Benign cystic peritoneal mesothelioma. Int J Res Med Sci, 2014, 2(2):762–764.

[5] Gupta A, Rao HK, Pande R, Gupta S. A rare case of benign multicystic peritoneal mesothelioma: a clinical dilemma. Indian J Surg, 2013, 75(Suppl 1):27–29.

[6] Occhionorelli S, Tartarini D, Pascale G, Maccatrozzo S, Stano R, Vasquez G. Benign multicystic mesothelioma of peritoneum complicating acute appendicitis in a man: a case report. J Med Case Rep, 2016, 10:44.

[7] Momeni M, Pereira E, Grigoryan G, Zakashansky K. Multicystic benign cystic mesothelioma presenting as a pelvic mass. Case Rep Obstet Gynecol, 2014, 2014:852583.

[8] Oks M, He T, Palkar A, Esposito MJ, Koenig SJ. Benign multicystic mesothelioma causing bilateral pneumothoraces. Ann Am Thorac Soc, 2015, 12(7):1106–1109.

[9] Chan JKC, Fong MH. Composite multicystic mesothelioma and adenomatoid tumour of the uterus: different morphological manifestations of the same process? Histopathology, 1996, 29(4):375–377.

[10] Livingston EG, Guis MS, Pearl ML, Stern JL, Brescia RJ. Diffuse adenomatoid tumor of the uterus with a serosal papillary cystic component. Int J Gynecol Pathol, 1992, 11(4): 288–292.

[11] Wang TB, Dai WG, Liu DW, Shi HP, Dong WG. Diagnosis and treatment of benign multicystic peritoneal mesothelioma. World J Gastroenterol, 2013, 19(39):6689–6692.

[12] Safioleas MC, Constantinos K, Michael S, Konstantinos G, Constantinos S, Alkiviadis K. Benign multicystic peritoneal mesothelioma: a case report and review of the literature. World J Gastroenterol, 2006, 12(35):5739–5742.

[13] Meşină C, Vasile I, Vîlcea ID, Paşalega M, Calotă F, Enache DS, Dumitrescu T, Mirea C, Mogoanta S. Carcinoid tumour of the appendix: problems of diagnosis and treatment. Chirurgia (Bucur), 2011, 106(2):239–245.

[14] Khuri S, Gilshtein H, Abboud W, Assalia A, Kluger Y. Benign cystic mesothelioma of the peritoneum: a rare case and review of the literature. Case Rep Oncol, 2012, 5(3):667–670.

[15] Meşină C, Paşalega M, Calotă F, Comănescu V, Vîlcea D, Ţenea T, Mirea C, Vasile I. Limfangiomul intestinal hemoragic – prezentare de caz. Chirurgia (Bucur), 2006, 101(2):201–202.

[16] Meşină C, Vasile I, Paşalega M, Calotă F, Vâlcea D, Meşină-Botoran MI, Paraliov T, Foarfă C, Ghiluşi M. Mesenteric inflammatory veno-occlusive disease as a rare cause of acute abdomen. Rom J Morphol Embryol, 2007, 48(1):83–86.

[17] Meşină C, Vasile I, Ciobanu D, Calotă F, Gruia CL, Streba L, Mogoantă SŞ, Pârvănescu H, Georgescu CV, Tarniţă DN. Collision tumor of recto-sigmoidian junction – case presentation. Rom J Morphol Embryol, 2014, 55(2 Suppl):643–647.

[18] Tentes AA, Zorbas G, Pallas N, Fiska A. Multicystic peritoneal mesothelioma. Am J Case Rep, 2012, 13:262–264.

[19] Baratti D, Vaira M, Kusamura S, D'Amico S, Balestra MR, Cioppa T, Mingrone E, De Simone M, Deraco M. Multicystic peritoneal mesothelioma: outcomes and patho-biological features in a multi-institutional series treated by cytoreductive surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC). Eur J Surg Oncol, 2010, 36(11):1047–1053.
[20] Meşină C, Mogoantă SŞ, Cristian DA, Dumitrescu TV, Drăgoescu PO, Meşină-Botoran MI, Ciurea ME, Ghiluşi MC, Ciobanu D. Retroperitoneal ancient schwannoma – case presentation. Rom J Morphol Embryol, 2015, 56(4):1517–1522.
[21] Stallone G, Infante B, Cormio L, Macarini L, Grandaliano G. Rapamycin treatment for benign multicystic peritoneal mesothelioma: a rare disease with a difficult management. Am J Case Rep, 2017, 18:632–636.
[22] Ciobanu D, Meşină C, Streba L, Gruia CL, Diţescu D, Şarlă CG, Enescu A, Petrescu F. The role of immunohistochemistry in diagnosis a synchronous colon tumor. Rom J Morphol Embryol, 2014, 55(3 Suppl):1209–1213.

Corresponding author
Mihaela-Iustina Meşină-Botoran, Lecturer, MD, PhD, Department of Human Anatomy, University of Medicine and Pharmacy of Craiova, 2 Petru Rareş Street, 200349 Craiova, Dolj County, Romania; Phone +40724–513 221, e-mail: mesina.cristian@doctor.com

Received: March 30, 2018

Accepted: November 27, 2018