International Journal of Surgery Case Reports 99 (2022) 107665

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.elsevier.com/locate/ijscr

Case report

Benign multicystic mesothelioma of appendiceal origin treated by hyperthermic intraperitoneal chemotherapy: A case report

Suk Jun Lee [a], Ji Hae Nahm [b], Jeonghyun Kang [c], Seung Hyuk Baik [c], Eun Jung Park [c,*]

[a] Division of Breast Surgery, Department of Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea
[b] Department of Pathology, Yonsei University College of Medicine, Seoul, Republic of Korea
[c] Division of Colon and Rectal Surgery, Department of Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Keywords:
Cystic mesothelioma
Appendix
Hyperthermic intraperitoneal chemotherapy

ABSTRACT

Introduction and importance: Peritoneal benign cystic mesothelioma is a rare benign tumor that originates from a mesothelial proliferative lesion of the peritoneum. However, proper surgical management remains unclear due to its low incidence. We report a clinical case of peritoneal benign cystic mesothelioma treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC).

Case presentation: A 60-year-old female who underwent laparoscopic appendectomy in 2015 presented with abdominal pain in right lower quadrant area. Computed tomography of the abdomen and pelvis revealed a ruptured appendiceal mucocele or mucinous neoplasm, and several seeding-like small nodules in the greater omentum and right peritoneum. Cytoreductive surgery followed by HIPEC was performed; right hemicolectomy and lymph node dissection, omentectomy, and right abdominal partial peritonectomy. HIPEC with mitomycin was conducted for 90 min and an anastomosis between the ileum and colon was made after HIPEC. The pathologic results revealed the colonic mass was a multi-loculated cyst lined by mesothelial cells containing amorphous eosinophilic fibrinoid material, which are common features of benign cystic mesothelioma.

Clinical discussion: Peritoneal benign cystic mesothelioma is known as a borderline disease of mesothelial tumors. Because its etiology is unknown, treatment strategies are not determined.

Conclusion: Cytoreductive surgery followed by HIPEC can be considered to treat peritoneal benign cystic mesothelioma and prevent its malignant transformation.

1. Introduction

Peritoneal benign cystic mesothelioma (PBCM) is an uncommon benign tumor that originates from a mesothelial proliferative lesion of the peritoneum. The annual incidence of PBCM is 0.015/100, 000 and it is more frequent in young females [1]. PBCM was first described in 1979 by Mennemeyer and Smith, and only 200 cases have been reported worldwide until the present [2]. The pathophysiology of this disease is uncertain. However, several hypotheses have been proposed, such as conditions related to inflammatory response to previous abdominal surgery, endometriosis, pelvic inflammatory disease and other similar causes [3]. Apart from symptoms, physical examination is also non-specific, and therefore PBCM is usually diagnosed by chance. There are no evidence-based guidelines for treatment but it is generally believed that surgical resection with hyperthermic intraperitoneal chemotherapy (HIPEC) is the best option [4]. Here we report a case of PBCM diagnosed in a woman who underwent cytoreductive surgery with HIPEC.

2. Case presentation

A 60-year-old woman who underwent laparoscopic appendectomy to treat appendiceal mucocele three years ago visited our institution due to abdominal pain for four days. Physical examination revealed focal abdominal tenderness in the right lower quadrant area. C-reactive protein was 0.1 mg/L, white blood cell count 4080/μL and other blood

Abbreviations: PBCM, peritoneal benign cystic mesothelioma; HIPEC, hyperthermic intraperitoneal chemotherapy; CA, cancer antigen; CEA, carcinoembryonic antigen; CT, computed tomography; PMP, pseudomyxoma peritonei.

* Corresponding author at: Division of Colon and Rectal Surgery, Department of Surgery, Gangnam Severance Hospital, Yonsei University College of Medicine, 20, Eonju-ro 63-gil, Gangnam-gu, 06229 Seoul, Republic of Korea.
E-mail address: camp79@yuhs.ac (E.J. Park).

https://doi.org/10.1016/j.ijscr.2022.107665
Received 5 August 2022; Received in revised form 11 September 2022; Accepted 13 September 2022
Available online 16 September 2022

laboratory results were within normal limits. Serum cancer antigen (CA) 19-9 levels were less than 0.8 U/mL and carcinoembryonic antigen (CEA) levels were normal at 3.2 ng/mL. Abdominopelvic computed tomography (CT) revealed a ruptured appendiceal mucocele or mucinous neoplasm, several seeding-like small low attenuating nodules in the greater omentum and right peritoneum, segmental and fundal adenomyomatosis of the gallbladder and a 3.0 cm sized calcified uterine myoma (Fig. 1A). Because there were possibilities of pseudomyxoma peritonei (PMP) from appendiceal mucinous neoplasm, we planned to perform cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy. According to the intraoperative findings, jelly-like mucin masses in the abdominal cavity were observed in the cecum, omentum, right paracolic gutter, pelvic cavity, and lesser sac. (Fig. 1B) Most of them were easily removed manually as they did not infiltrate into the peritoneum. Thus, right hemicolectomy and lymph node dissection, omentectomy, and right abdominal partial peritonectomy were performed. Other jelly-like spreading lesions in the pelvic cavity and lesser sac were surgically removed. Then, HIPEC using mitomycin-C of 35 mg/m^2 was administered for 90 min. The patient showed hyperkalemia at the postoperative 7th days along with neutropenia, defined as absolute neutrophil count below 1500/mm^3. The patient was discharged on postoperative 11th days. The pathologic results showed that the colonic mass was a multiloculated cyst lined by mesothelial cells containing amorphous eosinophilic fibrinoid material, consistent with benign cystic mesothelioma. The SCARE 2020 guideline was used to report clinical progress for this case report [5].

3. Discussion

Three different mesothelial tumors occur in the abdominal cavity, namely: malignant tubulopapillary mesothelioma, cystic mesothelioma and adenomatoid tumor [6,7]. The incidence of malignant mesothelioma is 0.9–1.0/1,000,000 annually. The median survival of malignant mesothelioma is about 6–10 months. Adenomatoid tumors are a rare benign disease mostly located in the genital tract, which rarely recur. Benign cystic mesothelioma is a borderline disease, containing features of both these tumors [8].

Since Mennemeyer and Smith first described benign cystic mesothelioma [9], almost 200 cases have been reported in the literature [10]. It occurs more frequently in women of reproductive age. The etiology and pathogenesis are unknown. However, three hypotheses have been proposed. First that, PBCM originates from chronic inflammatory conditions related to the peritoneum, which alters mesothelial cells into reactive hyperplastic and dysplastic lesions. Second, there is a more fundamental neoplastic origin of the peritoneal serosa without any relationship with coexistent chronic inflammatory events. Lastly, the development and progression of PBCM are associated with its sensitivity to sex hormones [10]. This theory is supported by the evidence of PBCM demonstrating a higher incidence in women of reproductive age and its responsiveness to endocrine drugs, such as tamoxifen and gonadotropin-releasing hormone analogs [11]. Although there is no critical evidence, the first hypothesis, in which chronic inflammation is a crucial factor for the proliferation and metaplasia of mesothelial cells is the most widely accepted [12].

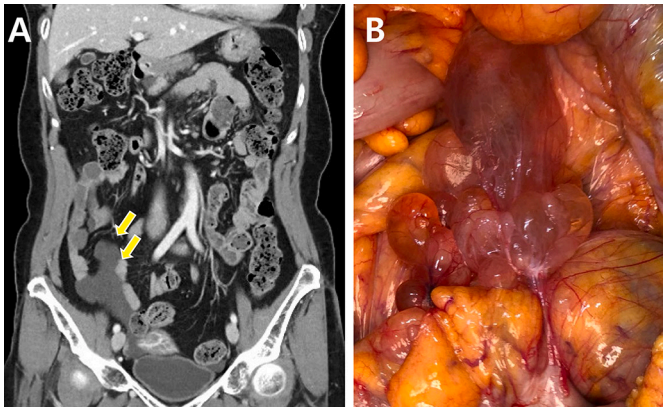

Fig. 1. Perioperative images of peritoneal benign cystic mesothelioma; A. preoperative computed tomography image (arrow, PBCM lesions), B. the intraoperative image.

However, the symptoms of PBCM are usually uncertain. Patients with PBCM complain of abdominal discomfort or pain when the tumor grows sufficiently large to exert pressure on other organs. Other symptoms of PBCM include abdominal distension, pelvic pain, palpable mass, weight loss, nausea, vomiting, constipation, signs of intestinal obstruction, and urinary retention [12]. In our case, the patient had a right lower quadrant pain in the abdomen which resembled the symptoms of acute appendicitis [13]. Physical examination may help to discover PBCM but does not aid in distinguishing PBCM from other diseases. The clinical symptoms of PBCM include abdominal distension, abdominal tenderness and one or more palpable abdominal masses. In our case, the patient presented only with a right lower quadrant tenderness without any other signs.

Radiological studies may be helpful in the diagnosis of PBCM. Ultrasound studies of the abdomen reveal anechoic to mildly echogenic, multi-septate cystic structures. On the CT scan, PBCM appears as a low-density, multi-loculated, multi-cystic, and thin-walled lesion. However, CT does not allow differentiation with other cystic lesions [14]. On the contrary, MRI can define the peritoneal origin of the lesions and differentiate PBCM from other cystic lesions. MRI findings are hypointense on T1-weighted images and hyper to intermediately intense on T2-weighted sequences with mild contrast enhancement of the wall [15].

Microscopic features of PBCM show that the cysts are lined with cuboidal or flattened mesothelial cells. The septa typically consist of loose fibrovascular connective tissue with a sparse inflammatory infiltrate accompanied by fibrin, granulation tissue, and hemorrhages in the cyst walls. However, many unusual morphological features make it difficult to differentiate benign and malignant lesions. For instance, the cells lining the cysts demonstrate atypia with hyperchromatic enlarged nuclei and intraluminal small papillae, gland-like structures and cribriform patterns [16]. Mesothelial cells are immunoreactive for calretinin, WT1 and no staining is observed for FVIII-RA, CA19.9, CA-125 and CEA antibodies [6]. In our case, the immune-histochemical stain showed that only Calretinin is positive and other factors (CD34, CDX-2, MUC-2, Alcian blue, PAS) are negative (Fig. 2).

Multiple treatment strategies for BPCM have been reported so far. However, the best treatment option remains controversial. Adjuvant hormonal therapy, sclerotherapy with tetracycline, and HIPEC has been suggested as treatment options [17]. However, it is believed that surgery with complete removal of cystic lesions is the only effective treatment, and provides the only chance for avoiding local recurrence. In addition, highly invasive surgical treatment such as cytoreductive surgery with HIPEC is recommended because BPCM can transform into malignant mesothelioma.

The prognosis of BPCM appears to be favorable with no reports of metastasis or malignant degeneration. One case of fatal complications has been reported: a 14-year-old patient died 12 years after diagnosis due to refusal of surgery [18,19]. However, the recurrence rate of PBCM remains high, at approximately 50 % in women and 33 % in men, even after complete cytoreduction with HIPEC. Therefore, long-term follow-up after treatment is recommended. Some recommend a follow-up CT scan every 3 months for the first year after surgery, and then annually for the next 5 years. This may lead to early detection of relapse, but the impact of this strategy on overall survival is yet to be established [20].

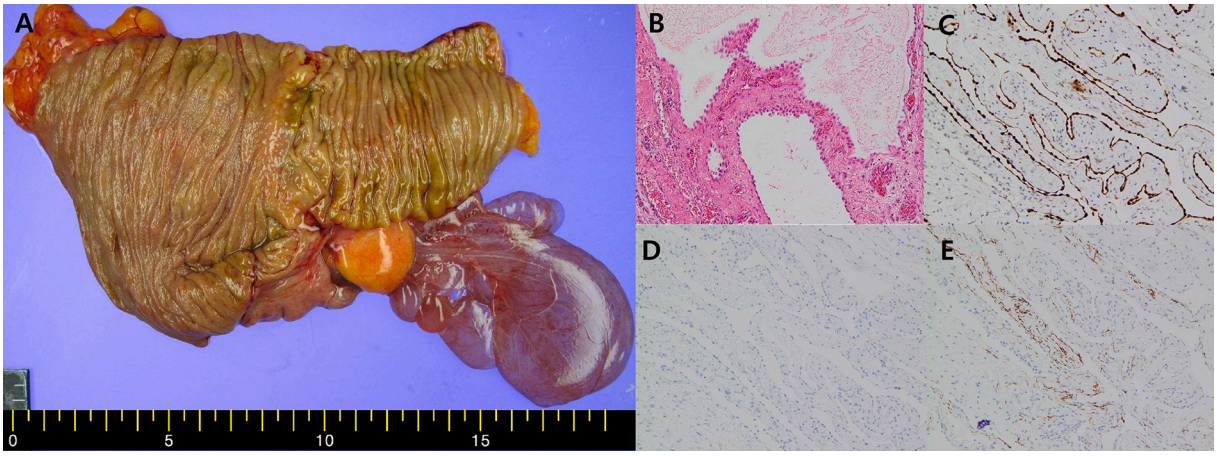

Fig. 2. The immunohistochemical staining results of PBCM; A. resected bowel and PBCM, B. H&E pathology staining, C. Carletinin staining (Positive in the lining cells), D. CDX-2 staining, E. CD34 staining.

4. Conclusions

We have presented a rare case of peritoneal benign cystic mesothelioma. Until now, there is no consensus for diagnosis, treatment, and follow-up. PBCM has a low mortality and a high recurrence rate, though complete resection significantly reduces local recurrence. Therefore, cytoreductive surgery followed by HIPEC can be considered to treat PBCM and prevent its malignant transformation.

Sources of funding

There was no funding for this research.

Ethical approval

This study was approved by the Institutional Review Board of Yonsei University Gangnam Severance Hospital. (IRB No.3-2021-0119).

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Suk Jun Lee collected data and wrote the first draft of this manuscript. Jeonghyun Kang and Seung Hyuk Baik had full access to all the information of the cases. Ji Hae Nahm contributed to interpret pathologic results of this study. Eun Jung Park contributed for study design and reviewed for this manuscript.

Research registration

Not applicable.

Guarantor

Eun Jung Park MD, PhD, FACS.

Declaration of competing interest

All authors have no disclosure for any financial and personal relationships.

References

[1] J.A. Snyder, R. Carman Jr., A.A. Aggon, J.P. Cardinale, Benign multicystic peritoneal mesothelioma: a rare case presenting as pneumoperitoneum and pneumotosis intestinalis, J. Gastrointest. Oncol. 2 (1) (2011) 55–58.
[2] S. Gussago, P. Spina, A. Guerra, Benign multicystic peritoneal mesothelioma (BMPM) as a rare cause of abdominal pain in a young male: case report and review of the literature, J. Surg. Case Rep. 2019 (3) (2019), rjz057.
[3] H.-m. Ahn, S.-H. Lee, Impending rupture with a twisted huge appendiceal mucocele treated with totally laparoscopic resection: a case series, Ann. Coloproctol. 37 (Suppl 1) (2021) S34–S38.
[4] S.J. Roh, S.C. Park, J. Choi, J.S. Lee, D.W. Lee, C.W. Hong, et al., Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy with mitomycin C used for colorectal peritoneal carcinomatosis, Ann. Coloproctol. 36 (1) (2020) 22–29.
[5] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.
[6] S. van Ruth, M.W. Bronkhorst, F. van Coevorden, F.A. Zoetmulder, Peritoneal benign cystic mesothelioma: a case report and review of the literature, Eur. J. Surg. Oncol. 28 (2) (2002) 192–195.
[7] J. Son, Y.J. Park, S.R. Lee, H.O. Kim, K.U. Jung, Increased risk of neoplasms in adult patients undergoing interval appendectomy, Ann. Coloproctol. 36 (5) (2020) 311–315.
[8] Y. Katsube, K. Mukai, S.G. Silverberg, Cystic mesothelioma of the peritoneum: a report of five cases and review of the literature, Cancer 50 (8) (1982) 1615–1622.
[9] R. Mennemeyer, M. Smith, Multicystic, peritoneal mesothelioma: a report with electron microscopy of a case mimicking intra-abdominal cystic hygroma (lymphangioma), Cancer 44 (2) (1979) 692–698.
[10] M. Momeni, E. Pereira, G. Grigoryan, K. Zakashansky, Multicystic benign cystic mesothelioma presenting as a pelvic mass, Case Rep. Obstet. Gynecol. 2014 (2014), 852583.
[11] M.S. Khurram, H. Shaikh, U. Khan, J. Edens, W. Ibrar, A. Hamza, et al., Benign multicystic peritoneal mesothelioma: a rare condition in an uncommon gender, Case Rep. Pathol. 2017 (2017), 9752908.
[12] A.M.C. Rapisarda, A. Cianci, S. Caruso, S.G. Vitale, G. Valenti, E. Piombino, et al., Benign multicystic mesothelioma and peritoneal inclusion cysts: are they the same clinical and histopathological entities? A systematic review to find an evidence-based management, Arch. Gynecol. Obstet. 297 (6) (2018) 1353–1375.
[13] I.S. Cho, S.U. Bae, H.R. Jung, K.S. Park, W.K. Jeong, S.K. Baek, Actinomycosis of the appendix mimicking cecal tumor treated by single-port laparoscopic approach, Ann. Coloproctol. 37 (2) (2021) 125–128.
[14] J.D. O'Neil, P.R. Ros, B.L. Storm, J.L. Buck, E.J. Wilkinson, Cystic mesothelioma of the peritoneum, Radiology 170 (2) (1989) 333–337.
[15] V. Mehta, V. Chowdhary, R. Sharma, J.S. Golia Pernicka, Imaging appearance of benign multicystic peritoneal mesothelioma: a case report and review of the literature, Clin. Imaging 42 (2017) 133–137.
[16] D.E. McFadden, P.B. Clement, Peritoneal inclusion cysts with mural mesothelial proliferation. A clinicopathological analysis of six cases, Am. J. Surg. Pathol. 10 (12) (1986) 844–854.
[17] Y.J. Kim, C.H. Kim, Treatment for peritoneal metastasis of patients with colorectal cancer, Ann. Coloproctol. 37 (6) (2021) 425–433.

[18] F. Raafat, M. Egan, Benign cystic mesothelioma of the peritoneum: immunohistochemical and ultrastructural features in a child, Pediatr. Pathol. 8 (3) (1988) 321–329.
[19] I.J. Yang, M. Seo, H.-K. Oh, J. Lee, J.W. Suh, D.-W. Kim, et al., Surgical outcomes of single-port laparoscopic surgery compared with conventional laparoscopic surgery for appendiceal mucinous neoplasm, Ann. Coloproctol. 37 (4) (2021) 239–243.
[20] M.C. Safioleas, K. Constantinos, S. Michael, G. Konstantinos, S. Constantinos, K. Alkiviadis, Benign multicystic peritoneal mesothelioma: a case report and review of the literature, World J. Gastroenterol. 12 (35) (2006) 5739–5742.