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Appendicular mucocele: two case reports and literature review

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SUMMARY: **Appendicular mucocele: two case reports and literature review.**

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The classification of mucinous tumors of the vermiform appendix is quite controversial, and includes a spectrum of neoplastic lesions ranging from benign proliferations, intraluminal, to invasive adenocarcinomas. Among the complications of appendicular mucinous neoplasms we should mention the "pseudomyxoma peritonei", a condition caused by cancerous cells (mucinous adenocarcinoma) that produce abundant mucin or gelationous ascites. Mucinous neoplasms of the appendix are rare diseases of unknown etiology. The diagnosis is difficult because of poorly specific clinical, biochemical and imaging parameters, and their detection can be occasional. Most of the reported cases involving women of reproductive age (with a history of endometriosis, abdominal surgery or pelvic inflammatory disease). The definitive diagnosis requires histology and immunohistochemistry. Cytoredutive surgery combined with hyperthermic intraperitoneal chemoterapy (HIPEC) is now considered the best treatment for this disease.

We present two cases treated with surgery and HIPEC.

KEY WORDS: Mucocele - Surgery - Appendix.

Case report 1

L.R., a 45-years-old woman, Caucasian race. Past medical history: tonsillectomy in childhood; Laparoscopic cholecystectomy in 1993; in 2004 ATC-HCV positivity (transaminases always remained normal and HCV-RNA quantitative research always negative). Menarche at 12 years; regular menstrual cycles; abortion 18 years; abortion 36 years for fetal genetic disease; then subsequent pregnancy terminated in the first quarter; 3 attempts at artificial insemination with ovarian stimulation, without success.

She comes to our attention in October 2012 for relapsing pelvic effusion in the absence of other symptoms of note. The general physical examination does not reveal any pathologies of organs or systems. The periodic ultrasound scans performed in the fall of 2011 to March 2012 showed hypoechoic fluid in the pelvis (50x25 mm) posterior to the uterus, and attached to the uterus towards the space with the bladder; hypoechoic area in the content of superimposed layers of different densities compatible with psudomyxoma peritonei or pseudocyst adhesions; hypoechoic collection in Douglas 6 cm in content more dense with small marginal hyperechoic area. Blood tests and tumor markers (CA 19.9, CA 125) were still in the normal range.

In October 2014 the patient underwent diagnostic laparoscopy. Exploring the abdominal cavity we found an important effusion of gelatinous material, which also involved other abdominal organs, and an appendicular neoplasm, which was removed. We also appreciated peritoneal soft-consistency nodes; some of them were removed and sent for histology.

Cytology on gelatinous intraperitoneal substance showed fibrous tissue containing mucoid material and inflammatory cells; histology of peritoneal nodes showed hyperplastic mesothelium, with chronic inflammatory infiltrate and focal deposits of mucoid material. Definitive histology showed appendicular mucinous neoplasm of low grade, extensive tissue and serous.

Due to the results of the histological results, the patient was sent to a specialized center for the treatment of the peritoneal cavity diseases.

During the follow up, the patient underwent CT abdomen (December 2014), that revealed the presence of small flap of abdominal effusion disposed around the li-

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ver and in the pelvis. Adnexa and uterus appeared normal. There was not abdominopelvic lymphoadenomegaly, neither focal densitometric alterations in liver, spleen and pancreas parenchyma. Kidneys and adrenals were in the normal range. CT-PET did not reveal areas of increased uptake. The transvaginal ultrasound scan revealed no dimensional or morphological alterations of pelvic organs and Fallopian tubes. In the right adnexal region and Douglas inhomogeneous fluid appeared as mucinous content.

In January 2015 open debulking surgery with right colectomy and HIPEC were performed. During the exploration, mucin's deposits were found into all abdominal regions, especially in the pelvis, along the right parieto-colic space and engaging the diaphragm. Pelvic peritonectomy, hystero-adnexectomy and Douglassectomy, right hemicolectomy and total omentectomy were performed.

All the mucin's nodes affecting diaphragm, liver capsula, the mesentery and the bowel serosa were removed using diathermy. An ileo-colic anastomosis was performed, and at the end the patient underwent intra-peritoneal chemohyperthermia.

The final histological examination on 25 cm of right colon, 14 cm of last ileal loop and omentum showed the presence of deposits of mucoid material at the level of the peritoneum, inflammatory aspects of serosa and some reactive lymph nodes. Resection margins were free from disease. In mucin's deposits were not any cancer cells; ovaries, Fallopian tubes and cervix had no pathological changes.

The first follow-up was performed one month after surgery: the physical examination was negative.

Case report 2

G.F. , 42-years-old woman; Caucasian race. Past medical history: silent.

The patient had a 7 cm adnexal cyst which was monitored over time by MRI and ultrasound. She came to our attention in January 2014 after last radiological control with the suspicion of appendicular mucocele because of increased size of lesion , with a liquid content in contact with cecum, developing in the right-iliac fossa. Complete blood count and laboratory results were in normal ranges, such as the values for other parameters. A diagnostic laparoscopy was performed. Adnexa and uterus appeared normal, while the appendix was surrounded by free fluid with mucinous aspects and small gelatinous cysts were present in the pelvis.

Definitive histology showed a mucinous appendicular low grade neoplasm (WHO classification 2010).

Even in this case the patient was sent to a specialized center in treatment of pathologies of the peritoneal cavity. In July 2014, chest CT did not reveal pleural-parenchymal adhesions or pleural effusion, neither significant hilar, mediastinal and axillary lymphadenopathy. CT abdomen showed scarce peritoneal fluid in the Douglas pouch (maximum thickness of 12 mm), two cystic lesions (diameter 10 mm and 11 mm) in the right adnexa's area. The intraperitoneal parenchymal organs were normal.

Debulking surgery with right colectomy by open approach and HIPEC were performed: during the exploration, mucin's deposits were found in the pelvis, especially in the Douglas pouch and above the right adnexum, in right parieto-colic space, in the last ileal loop mesentery. Pelvic peritonectomy, right hemicolectomy, and total omentectomy were performed. Right broad ligament of the uterus was also removed.

All the mucin's nodes affecting peritoneum have been removed by using diathermy. Finally, intraperitoneal chemo-hyperthermia was performed.

The pathological examination was performed on 29 cm of right colon, terminal ileum and omental specimen: the serous surface appeared smooth in the colonic tract and hyperemic and wrinkled in the ileal segment. The bowel sections showed follicular lymphatic hyperplasia and focal aspects of erosive mucosa. There were no neoplastic cells. All lymph nodes were hyperplastic-reactive. The final diagnosis was: low-grade pseudomyxoma peritonei.

Discussion

The mucocele is a rare disease that occurs in 0.2-0.3% of appendectomies, more frequently in women than in men (3:1), average age of 55 years (1-5). For several reasons, due to obstacle to emptying from the mucus-secreting tumors, the appendix undergoes a progressive accumulation of mucus in the lumen with dilation until it can tear. Appendicular mucocele may also be associated with other cancers, such as cystadenoma and cystadenocarcinoma, colon and ovarian mucin-secreting cells cancers (2, 5-7).

Macroscopically the appendicular mucocele appears as a diffuse thickening of the bowel, or as a large cyst filled with mucus secreted by neoplastic epithelium.

The natural evolution of this heteroplasia is conditioned by the anatomical features of the bowel. In particular, the wall is thinner than that of the other sections of the gastrointestinal tract, in some areas the submucosa is juxtaposed to the peritoneum for the lack or incompleteness of the muscle layers. The blood supply is given by appendicular vessel, which is a terminal one. The neoplasm rarely spreads through the lymphatic system and blood, while has a particular tendency to perforation, which can achieve the picture of the pseudomyxoma peritonei characterized by installations of gelatinous masses mixed with malignant epithelial cells in the peritoneal cavity (3, 8-10).

The development of the neoplasm in the appendix causes the early occlusion. The thickness of the wall and the

vascular compression cause inflammatory reaction which predisposes to perforation of the appendix, which usually occurs at its apex. In other cases, this complication occurs by infiltration of the wall by the tumor (11, 12).

The preoperative diagnosis of mucocele is rare because of the low incidence of this tumor, the non-specificity of symptoms and the low amount of biochemical parameters and significant imaging.

20-25% of the appendicular mucocele is asymptomatic and the diagnosis is accidental (1, 3). In 50-65% of cases symptoms and signs of acute inflammation of the appendix, in 10-20% of cases intestinal obstruction or palpable mass in the right lower abdominal quadrant are present (1-3, 9). Melena (8), intussusception (13, 14), infiltration of the bladder (15), vaginal penetration with colporragia (16), and pionephrosis by compression of the right ureter (17) are rarer occurences.

Preoperative ultrasound may be useful to suspect a lesion of the appendix. Ultrasound and abdominal and pelvic CT can be useful to identify swelling in the right iliac fossa or thickening of the wall of the cecum, but these findings may be common with other diseases, such as adenocarcinoma of the cecum, Crohn's disease, ileo-colonic intussusception (14, 18, 19).

Endoscopy with targeted biopsies is the only procedure that can allow to define preoperatively neoplastic lesion. However, the endoscopic study of the appendix, which plans to inspect carefully the appendicular orifice and the surrounding cecal mucosa, is quite difficult for the narrowness of the lumen. In literature are reported only two cases of adenocarcinoma of the appendix whose diagnosis was achieved preoperatively by colonoscopy with biopsies (2.29).

In our cases, neither clinical nor the several surveys performed preoperatively allowed the diagnosis, if not suspicious, of mucinous appendicular neoplasm. Intraoperative diagnosis is also difficult because the tumor is often hidden by the inflammation of the appendix.

Sometimes the disease is an incidental finding during surgery performed for other indications (10 to 20.2% of cases) (2, 4, 10, 20). Therefore the diagnosis is achieved with definitive histology of the surgical specimen.

The treatment of appendicular mucinous cystadenoma is essentially surgical and should be based on histological results and disease's spreading. The best treatment of mucinous cystadenoma is laparoscopic appendectomy; in the case of broad-based implant desease or extended to the cecum, the best approach is cecum resection or right hemicolectomy (1, 2, 5, 13). However it is better to check both ovaries, Fallopian tubes and colon to exclude other associated neoplasms.

In the presence of pseudomyxoma peritonei most authors recommend a surgical aggressive attitude, which includes right hemicolectomy, omentectomy, bilateral resection of adnexa and removal of all peritoneal mucin's masses. In addition, these patients should undergo intraperitoneal chemotherapy (18, 21-23).

After the surgery the patient needs a regular follow-up in order to identify early metachronous neoplastic growths (20, 21, 24). According to literature, the 5-year survival ranges are between 35-55% and depends on the stage of the disease and the type of surgery performed (3, 4, 7, 20, 25).

The prognosis of mucinous cystadenoma of the appendix is good, even in the case of extension outside the appendix, with a survival rate of 91-100%.

Conclusion

Appendicular mucocele is a rather rare disease of unknown etiology and difficult diagnosis because it does not have a specific clinical presentation neither biochemical parameters or imaging; therefore it requires a long diagnostic multidisciplinary path.

The best therapeutic approach involves radical surgery combined with HIPEC.

Due to the complexity of the procedure and the rarity of the disease, patients with a diagnosis of appendicular mucinous neoplasm should be treated in centers with experience in peritoneal surface disease to achieve the best result in terms of disease-free and all survival rate.

It is important to emphasize the good prognosis of a low-grade mucinous neoplasm, but it involves a rigorous follow-up because of the possibility of recurrence.

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