Appendiceal mucocele.
A case report and literature review.

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Appendiceal mucocele is a rare disease (0.3% of all appendectomy) and is characterized by the accumulation of mucoid material in the appendiceal lumen. Etiopathogenesis can be inflammatory or neoplastic. Four entities can be distinguished on the basis of histopathologic epithelial characteristics: simple appendiceal mucocele (AM), mucocele with epithelial hyperplasia, cystadenoma and cystadenocarcinoma; the last two subgroups represent neoplastic forms. Dissemination of neoplastic cells and mucoid material in abdominal cavity, caused by appendiceal perforation, clinically results in pseudomyxoma peritonei which is the dramatic evolution in 10-15% of cases. Clinically it can remain either asymptomatic for long time or it can manifest with abdominal pain that can be associated with the presence of a palpable mass. The most common clinical manifestation is pain in the right iliac fossa. Preoperative diagnosis is rare, while it is more frequently intraoperative. Therapy is fundamentally surgical: appendectomy is curative for simple AM, for AM with epithelial hyperplasia and for cystadenoma with intact appendiceal base; cecum resection is indicated for cystadenoma with larger base of implantation; right hemicolectomy has been the elective treatment in case of cystadenocarcinoma for several years although Gonzalez-Moreno and Sugarbaker have recently demonstrated its validity as definitive treatment only if it is performed in order to obtain complete cytoreduction, if there is lymph node involvement, or if histopathological examination indicates non-mucinous type. We report the case of a 60-year-old woman that presented with cystic neoformation in the right iliac fossa, that was preoperatively considered deriving from the ovary. We intraoperatively found the presence of appendiceal mucocele that histological examination defined as mucinous cystadenoma.

KEY WORDS: Appendiceal mucocele, Laparoscopic appendectomy, Pseudomixoma peritonei.

Introduction

Appendiceal mucocele (AM) is a rare disease characterized by cystic dilation of appendiceal lumen caused by accumulation of mucoid material. It is detected in 0.3% of all appendectomy, represents 8% of all appendiceal tumors and less than 0.5% of all gastrointestinal tumors.

The incidence has a peak in the population over 50 years old.

As for the etiopathogenesis, mucocele may be the expression of an inflammatory or a neoplastic process. It is frequently asymptomatic and often incidentally found during radiological or endoscopic procedures or during laparotomy and laparoscopy performed to treat other pathologies. Nevertheless in 50% of cases pain in the right iliac fossa is evocative of appendiceal pathology.

Preoperative diagnosis is rare, while it is more usually defined during the surgical intervention. When the diagnosis is made, it is fundamental to perform adequate surgical treatment and program a close follow-up in order to early recognize signs and symptoms suggestive of progression to pseudomyxoma peritonei (PMP) that repre-
resents the evolution of appendiceal mucocele in 10-15% of cases.

We report the case of a 60-year-old woman diagnosed with ovarian neoformation and therefore candidate for laparoscopic ovarian excision. During the exploratory phase, we noticed that the mass did not originate from the ovary but was instead the expression of appendiceal mucocele.

Case report

A 60-year-old woman was referred to our attention because of a cystic mass with thick internal septi, with maximum diameter of 36 mm in the right adnexa at ecographic examination. Gynecologic evaluation confirmed the presence of a neoformation with both solid and liquid aspects with scarce vascularity. MRI showed a bilobed cystic neoformation with a thin inner septum with maximum diameter of 45 mm in the right adnexa. Her medical history was positive for hypothyroidism, arterial hypertension, hyperuricemia and colic diverticulosis.

Preoperative hematological exams showed a modest increase of GPT (52 UI/L), Gamma-GT (130 UI/L) and LDH (516 UI/L), modest hypokalemia (3.2 mEq/L) and normal levels of tumor markers.

During exploratory laparoscopy the voluminous mass at preoperative imaging resulted deriving from the appendix, while the right ovary did not present anatomo-pathological relevant findings. We decided to perform appendectomy using Endo-GIA 35 (Ethicon EndoSurgery, Cincinnati, OH, USA) since we found the integrity of the appendiceal base. In order to avoid the contact between the mass and adjacent structures and organs, the appendix was immediately inserted in the endobag and extracted from the abdominal cavity.

Post-operative period was regular with canalization in day III, removal of drainage in day IV, and discharge in day VII. Macroscopic histological examination revealed dilated appendix of 5 x 3 x 3.5 cm of diameter, containing gelatinous thick material, fibrous wall and atrophic mucosa. Macroscopic examination defined the mass as mucinous cystadenoma with mucoid infiltration and microscopic focal interruption of the wall.

On the basis of the oncologic evaluation and of the anatomo-pathological characteristics of the lesion, the patient started a close clinical and instrumental follow-up in order to identify possible successive signs of evolution to PMP.

Discussion

The term “appendiceal mucocele” (AM) is not indicative of a specific histopathological diagnosis, rather it refers to a dilation of appendiceal lumen caused by the accumulation of mucous material. AM was recognized as pathological entity by Rokitansky in 1842 and was formally defined by Feren in 1876. There are four pathological subgroups that are differentiated on the basis of epithelial characteristics:

A) retention cysts or simple mucocele: generated from the obstruction of appendiceal lumen, usually caused by fecal impaction. It is characterized by normal epithelium or epithelium with degenerative alterations due to the obstruction and it presents a medium dilation of 1-2 cm. This histological type constitutes almost 20% of all mucoceles;

B) mucocele with epithelial hyperplasia: it is histologically similar to hyperplastic polyps of colon; the dilation of the lumen is analogous to the above type. This subgroup in found in 20% of all mucoceles;
C) cystadenoma: it is characterized by tubular adenomatous epithelium with some grades of epithelial atypia, similar to adenomatous colon polyps or villous adenomas, it produces abundant quantities of mucus and presents prominent dilation of the lumen up to 6 cm. It constitutes the most common form with almost 50% of cases; 

D) cystadenocarcinoma: this type is characterized by invasion of glandular stroma and/or the presence of implants of epithelial cells in the peritoneum; some lesions are similar to mucinous tumors of colon; also in this case the lumen dilation is prominent. This form represents 11-20% of all cases.

Cystadenoma and cystadenocarcinoma are neoplastic appendiceal mucoceles and their incidence is 35% of primary appendiceal carcinomas. These lesions may be either preceded by simple mucocele or may arise de novo. Their perforation is responsible for mucous material dissemination in the peritoneal cavity. The material can be acellular or it can contain cells with several grades of dysplasia. Cystadenoma is associated with perforation in 20% of cases; extravasated mucous material deposits in the periappendiceal region and in the peritoneal cavity (attached to serosa or lying free within the peritoneal cavity). Neoplastic cells are not found on histological examination of mucus and appendectomy is curative in this case. It has been reported that cystadenoma can undergo malignant modification. In fact, although there aren’t conclusive evidences demonstrating progression from cystadenoma to appendiceal cystadenocarcinoma, several investigators believe that the sequence adenoma-adenocarcinoma is comparable to the evolution from polyp to adenocarcinoma of colon. Macroscopically cystadenocarcinoma causes appendiceal dilation and mucus production indistinguishable from cystadenoma and undergoes spontaneous rupture in 6% of cases.

Nevertheless neoplastic cells can pass the appendiceal wall through micro perforations and diffuse in peritoneum even without macroscopically evident ruptures. When this occurs, peritoneal cavity is progressively extended by the accumulation of gelatinous, mucous, semisolid material in which neoplastic adenocarcinomatous cells can be found: this condition is known as peritoneal pseudomyxoma. The abundant quantity of mucus that is present in the peritoneal cavity distributes, for gravitational reasons, in the most declivous spaces, as the pelvis or the retrohepatic space. Continuous peristaltic movements prevent cells implantation on the surface of bowel. Therefore the majority of patients undergoes a silent and asymptomatic progression of the disease that can remain ignored for years. This dissemination needs to be considered similarly to a metastatic spread. Intrapertioneal diffusion of this mucin secreting tumor is identical to mucinous cystadenocarcinoma of the ovary, colon, stomach and pancreas.

Malignant mucocele rarely metastasizes through blood and lymph nodes and tends to remain in peritoneal cavity, even though retroperitoneal and pleuric implantations have been occasionally observed.

Discordant data exist on gender distribution: some authors report higher incidence among women, others a similar incidence in males and females, while others a higher incidence in men. Relatively to age, AM presents a peak of incidence over the fifth decade of life.

The symptomatology of mucocele can vary from asymptomatic to the presence of severe abdominal pain with or without a palpable mass. Even lesions that are particularly voluminous can be asymptomatic in 25% of cases. When symptomatic, the most common clinical manifestation is acute or chronic pain in right iliac fossa followed, in decreasing order of frequency, by signs and symptoms as: abdominal mass, weight loss, nausea, vomiting and acute appendicitis.
Unusual manifestations are gastrointestinal bleeding associated with mucocele intussusceptions, intestinal obstruction, sepsis and genitourinary symptoms. Rupture can clinically manifest with signs and symptoms of acute appendicitis. The subsequent implantation of epithelial cells on peritoneal surface and the accumulation of mucus frequently lead to a gradual increase of abdominal circumference and to chronic abdominal pain. Clinical onset can be the appearance of an inguinal hernia or of an ovarian mass in men and women respectively. The association with other tumors localized in the gastrointestinal tract, ovary, breast and kidney have been described in one third of all patients. Since the association with colorectal tumors is overall the most frequent, being present in 20% of cases, an accurate intraoperative exploration of colon and ovary is required.

Even if nowadays the availability of more sensitive and specific diagnostic techniques increases the number of AM that are diagnosed before surgery, a definitive preoperative diagnosis is not possible and is considered exceptional in the majority of cases. Diagnostic techniques that preoperatively allow the identification of the lesion are the radiographic, ecographic and endoscopic examinations. Ultrasonography shows encapsulated cystic lesion, firmly attached to the cecum, containing liquid of variable echogenicity according to the composition of mucus. The presence of multiple echogenic layers along the dilated lumen produces the pathognomonic sign of "onion-skin-like" circles. Typical findings on computed tomography are a round, low-density, thin-walled, encapsulated cystic mass communicating with the cecum; calcifications are present in 50% of cases. Accretion nodules in the mucocele right meso, removed en bloc with the appendix, are negative, right hemicolectomy is not necessary. The presence of mucus in abdominal recesses (parietocolic, inter-hepatico-diaphragmatic spaces, Douglas pouch), on the peritoneum or of adjacent organs, presents a good long-term prognosis after a large surgical excision has been performed. If evocative signs of progression to pseudomyxoma peritonei are found, 5-year survival ranges from 18% to 55% and the cause of death is related to complications of repeated intestinal obstructions or to the onset of renal failure.

Therapy is surgical. It is essential to proceed to the excision of the appendix according to the "not-touch" technique, avoiding incautious manipulations that can favor appendicolical perforation and the consequent dissemination of mucoid material or of epithelial cells in peritoneum. The choice of the surgical treatment is determined by the dimensions of the mass and by the histological subgroup. Appendectomy is indicated for simple mucocele and for cystadenoma when the base of the appendix is intact. Resection of the cecum is necessary for cystadenoma with large and firm base and when cytostatic sectioning gives positive margins at the appendectomy site. For laparoscopy it is strongly recommended the use of endobag in order to reduce the risk of neo-plastic dissemination.

Right hemicolectomy has been considered for years the treatment of choice for cystadenocarcinoma. Hesketh reported that patients treated with hemicolectomy had definitively better long-term prognosis respect to those who underwent appendectomy alone. In a recent review published in 2004, Gonzalez-Moreno e Sugarbaker criticized and confuted this hypothesis, selectively identifying the specific situations in which right hemicolectomy gives advantage in terms of survival respect to appendectomy alone. In fact if the margins of resection are free and if lymph nodes of appendiceal meso, removed en bloc with the appendix, are negative, right hemicolectomy is not necessary. Right hemicolectomy is instead indicated only if (a) it is necessary to obtain a radical excision of the primary tumor and a complete cytoreduction; (b) appendiceal or ileocolic lymph node involvement is histologically shown; (c) histopathological exam gives evidence of a non-mucinous subgroup. An accurate exploration of abdominal cavity must exclude the presence of accumulation of mucoid material in abdominal recesses (parietocolic, inter-hepato-diaphragmatic spaces, Douglas pouch), on the peritoneum and the omentum. The exploration must also exclude the association with other tumors in particular tumors of colon (11-20%) and the ovary (2-24%). If during the exploratory phase the rupture of the mucocele with diffusion of mucus in abdominal cavity is discovered, Dhage-Ivatury and Sugarbaker suggest that it is fundamental to first define the histological nature of the mucous material and the lesion. If in the abdominal mucous fluid epithelial cells are not found, the patient needs to start a careful follow-up. If instead in the intraperitoneal fluid epithelial cells are detected, the diagnosis of PMP is made and in this case it is necessary to radically treat the peritoneal carcinoma with cura-

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Appendiceal mucocele is a rare disease and is hardly preoperatively diagnosed. Symptomatology is aspecific and does not present pathognomonic signs. In the majority of cases definitive diagnosis is established during laparoscopy performed for other pathologies or for suspected acute appendicitis. Surgical treatment strictly depends on histological type and therefore appendectomy alone is indicated for AM without epithelial atypia and for cystadenoma with intact base. In enlarged forms of cystadenoma, with large base of implantation, in which cellular atypia is found, cecum resection is indicated. Right hemicolectomy is required in case of cystadenocarcinoma, in which prognosis is highly correlated with disease extension, grade of cellular atypia and lymph node involvement. The operation can be performed with minimally invasive technique if manipulation of the mass is avoided with the “not-touch” procedure. After surgical treatment, even patients with benign lesions must undergo careful follow-up because of the possible progression to PMP.

### Conclusion

Appendiceal mucocele is a rare disease and is hardly preoperatively diagnosed. Symptomatology is aspecific and does not present pathognomonic signs. In the majority

### Riassunto

Il mucocele appendicolare (MA) è una patologia rara caratterizzata dalla dilatazione cistica del lume appendicolare conseguente all’accumulo di materiale mucoso al suo interno. Si riscontra nello 0,3% di tutte le appendicectomie, rappresenta l’8% di tutti i tumori appendicolari e meno dello 0,5% dei tumori gastrointestinali. Presenta un picco di incidenza nella popolazione oltre i 50 anni.

Da un punto di vista eziopatogenetico, il mucocele può essere espressione di un processo infiammatorio o neoplastico. In base alle caratteristiche istopatologiche dell’epitelio si distinguono quattro entità: mucocele semplice, mucocele con iperplasia epiteliale, cistoadenoma e cistoadenocarcinoma; le ultime due rappresentano le forme neoplastiche. La disseminazione di cellule neoplastiche e di materiale mucoso nella cavità addominale, a causa della perforazione dell’appendice, configura il quadro clinico dello pseudomixoma peritoneo, temibile evoluzione nel 10%-15% dei casi. Clinicamente può rimanere a lungo asintomatico o manifestarsi con dolori addominali associati o meno a massa palpabile. La manifestazione clinica più comune è il dolore in fossa iliaca destra. La diagnosi preoperatoria è rara e viene posta frequentemente in fase intraoperatoria. La terapia è essenzialmente chirurgica: l’appendicectomia è curativa per il MA semplice, con iperplasia epiteliale e per il cistoadenoma con base appendicolare intatta; la resezione del ceco è indicata per i cistoadenomi con larga base d’impianto; l’emicolecotomia destra è stata per anni il trattamento elettivo nel caso di cistoadenocarcinoma, ma recentemente Gonzalez-Moreno e Sugarbaker ne hanno dimostrato l’utilità solo laddove necessaria al fine di ottenere una completa citoriduzione, o nel caso di coinvolgimento linfonodale, o qualora l’esame istopatologico deponga per un tipo non mucinoso.
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