

MUCOCELE APPENDIX: A LITERATURE REVIEW

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ABSTRACT

This review was written on data collected from case reports, cross-sectional studies, open-label studies and phase –II trials between 1989-2012. Web sites and other online resources of American college of surgeons, Medline, NCBI and Medscape resource centers were used to extract data. Mucocele of the appendix is a rare lesion characterized by the dilatation of the appendix lumen with mucus accumulation. It is more common in 5th and 6th decade with female preponderance. Appendiceal mucoceles can be classified into four histologic groups namely, mucinous cystadenomas, mucosal hyperplasia, simple or retention cysts & mucinous cystadenocarcinomas. The preoperative diagnosis is usually difficult due to nonspecific clinical presentation. The “onion skin sign” on ultrasound is considered to be specific for mucocele of the appendix. CT scan abdomen usually shows a cystic well-encapsulated mass, communicating directly with the cecum sometimes with mural punctate or curvilinear calcification which may be causing extrinsic pressure on the caecal wall without any surrounding inflammatory reaction. All patients who present with an asymptomatic mass or an incidental cystic lesion of the appendix should undergo surgical exploration, resection and is determined by the organ’s integrity, the dimensions of the base and histological type of the lesion.

KEY WORDS: Mucocele, appendix, appendectomy, Mucinouscystadenomas.

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INTRODUCTION

Rokitansky first describe mucocele of the appendix in 1842.¹ It is a as a rare lesion characterized by the dilation of the appendix lumen with mucus accumulation. It is more common in 5th and 6th decade with female preponderance and found in 0.2 to 0.3% of the appendectomy specimen.²⁻⁴ Mucocele of Appendix may be the result of cystadenomas (63%), cystadenocarcinomas (11%), mucosal hyperplasia or inflammatory process (25%) and rarely due to obstruction of lumen by endometriosis

or carcinoid tumours.⁵ Mucocele of the appendix due to mucinous cystadenoma is a rare clinical finding. Approximately half of the patients are asymptomatic.⁵ Early recognition and diagnosis is very important. The pseudomyxoma peritonei, as a result of rupture of the appendix, is the most dangerous complication. Apart from these causes, other tumor of appendix or caecum may present as mucocele and the main complication of mucocele is pseudomyxomaperitonei.⁶⁻⁸ Treatment is always surgical and determined by the organ’s integrity, dimensions of the base and histological type of the lesion. Latest

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literature search about treatment has revealed two different schools of thought. The first one defends the right colectomy as a treatment,⁹ and the second one recommends only appendectomy.¹⁰ The objective of this review is to analyze the literature as to mucocele, especially regarding diagnosis and treatment, besides discussing follow-up and prognosis of the individuals who have this disease.

Source of Data/Study Selection:

The data were collected from case reports, cross-sectional studies, Open-label studies and phase-II trials between 1989-2012.

Data Extraction:

Web sites and other online resources of American college of surgeons, Medline, ncbi and Medscape resource centers were used to extract data.

PATHOLOGY

Mucocele of the appendix is characterized by the accumulation of mucoid material in the lumen of appendix. Proximal obstruction of the appendiceal lumen causes distention and subsequent formation of a mucocele or appendicitis, so the mucocele appendix may be classified according to histological characteristics of luminal obstruction. The gross appearance of these benign conditions depends on the acute or chronic clinical presentation. An acute luminal obstruction with secondary infection having degenerated epithelial cells causing obstruction may mimic the clinical features acute appendicitis. A chronic insidious obstruction usually presents with a dilated appendix, with or without surrounding inflammation.

Appendiceal mucocele can be classified into the four histologic groups, which have relative frequencies of 52, 20, 18, and 10 percent, respectively.^{2,4} The course and prognosis of appendiceal mucoceles relate to their histologic subtypes. These types are:^{1,2,4}

- Mucinous cystadenomas (52%), are morphologically reminiscent of adenomatous colon polyps or villous adenomas, having dysplastic epithelium.
- Mucosal hyperplasia (20%), is histologically similar to a hyperplastic colon polyp, and mucus is usually acellular.
- Simple or retention cysts (18%), are characterized by degenerative epithelial changes due to obstruction (eg, fecalith) and distention.
- Mucinous cystadenocarcinomas (10%), demonstrate glandular invasion into the stroma, the cells having high grade of dysplasia. Rupture may lead to dissemination of mucin in peritoneal cavity causing mucinous ascites or pseudomyxomaperitonei.

Literature review shows analysis of 135 patients with mucocele of the appendix among them 129 had surgery and histological analyses. Among them 28.68% had pseudomyxomaperitonei. From these patients with pseudomyxomaperitonei, 95% had malignant mucocele and 83% of the perforated mucoceles were malignant.¹¹

CLINICAL PRESENTATION

Due to nonspecific clinical presentation of the mucocele in appendix the preoperative diagnosis is usually difficult. Mostly the patients are asymptomatic (23-50%) and usually it is discovered incidentally during surgery, ultrasound, and radiological examination or during endoscopic procedures.^{5,10} Right lower abdominal pain is the commonest clinical presentation (50%) which persist for months without any palpable mass in

right lower quadrant.^{9,10} Rarely patients present with symptoms of acute appendicitis. Change in bowel habits, unexplained anemia and rectal bleeding are rarely reported by patients.⁹ Simple or benign mucoceles, due to its insidious progression, has a rare chance of perforation as compared to malignant mucocele, which have a sudden onset similar to that of acute appendicitis, which usually present as an organ perforation.¹⁰ Hence due to lack of proper clinical symptomatology the preoperative clinical diagnosis of mucocele appendix is usually difficult.^{12,13} For all of the subgroups, patient presentation is extremely variable and may include right lower quadrant guarding and a palpable mass. Patients may also be completely asymptomatic. Mucocele appendix is also reported to few patients with inflammatory bowel disease.¹⁴

DIAGNOSIS

Early diagnosis and recognition can prevent the dreaded complications of pseudomyxomaperitonei, but it requires a very high index of suspicion during clinical assessment. The majority of appendiceal mucoceles are discovered incidentally during surgery. Radiology, sonography or endoscopy may facilitate preoperative detection of the lesion when this pathology is suspected by a clinician.

Ultrasound findings may be variable from purely cystic lesions with hypoechoic mass to anechoic fluid having fine internal echoes or complex hyperechoic masses depending on the contents.¹³ They can also mimic ovarian cyst on ultrasound scan.¹⁰ The “onion skin sign” is considered to be specific for mucocele of the appendix.^{6,10} Endoscopic U/S is a valuable modality that can be used to evaluate suspicious lesions of appendix like mucocele. Other than echogenicity, it can also identify architecture and wall layer of the origin of lesion.¹⁴

CT scan of the abdomen usually shows a cystic well-encapsulated mass which communicates directly with the cecum sometimes with mural punctate or curvilinear calcification which may be

causing extrinsic pressure on the caecal wall without any surrounding inflammatory reaction. Calcification in wall confirms the mucocele diagnosis and differs from the appendicular abscess, which does not have this characteristic.^{4,14}

Barium enema is not helpful and rarely shows a cecal filling defect, besides the lateral displacement of the cecum and terminal ileum.³

Colonoscopy may show a “volcano sign” which is an erythematous mass, with a central crater due to the protrusion of appendiceal ostium, which can increase or decrease with respiratory movements.¹⁴⁻¹⁶ So when a bulging appendiceal orifice is observed during surveillance colonoscopy, possibility of a mucocele appendix must be considered.¹⁵ Pre-operative levels of carcinoembryonic antigen (CEA) may suggest malignancy in appendix or colon.¹³

TREATMENT

The treatment of choice is Surgery. The underlying pathophysiology of the appendiceal mucocele dictates its management. If clinical presentation does not dictate emergent surgical intervention, then preoperative imaging and endoscopy may be beneficial. However, surgical exploration is required for tissue confirmation. If surgical intervention is warranted prior to preoperative studies, then management is dictated by the surgical findings. The surgical treatment of mucocele appendix depends upon some factors, such as the integrity of the organ wall, dimensions of its base and histopathology.^{17,18} For simple benign mucocele, the appendectomy with lymphadenectomy, including all the fat from the mesoappendix should be resected especially when the appendicular base is less than 2.0 cm in size.^{19,20} If lumen is more than 2.0 cm then the partial cecal resection including the site of implantation of the appendix is performed. This helps to prevent the dissemination of neoplastic cells to the abdominal cavity along with ensuring a negative resection margin. Specimen should be sent for frozen section immediately and if malignant

cells are found then the right hemicolectomy along with whole regional chain of lymphnodes should be performed. In the absence of frozen section facilities the hemicolectomy should be delayed till final histopathology report. A complete abdominal exploration is indicated due to the occurrence of synchronous lesions with other tumors, like colon and ovaries.²¹

Laparoscopic appendectomy in cases of mucocele is not indicated due to the risk of appendicular rupture and the dissemination of mucus leading to peritoneal implants. If mucocele is diagnosed during laparoscopy, the surgery should be converted into a laparotomy. However, some authors disagree and suggests a careful manipulation and use of protective envelopes.^{21,22}

In Perforated mucocele of the appendix mucus extravasation in peritoneal cavity may lead to the pseudomyxomaperitonei. Due to free mucinous fluid in the peritoneal cavity, the peritoneum would work as a defense against the dissemination of epithelial cells. Thus, it is recommended that the initial surgery should be as minimal as possible, in order to keep the peritoneum intact.^{23,24}

In pseudomyxomaperitonei or perforated mucocele appendix the mucus cytology should be immediately performed, because further surgical treatment will depend on cytology. Absence of adenomatous epithelial cells is an indication for hyperthermic intraoperative intraperitoneal chemotherapy. If cytology is positive, then beside operative chemotherapy, the cytoreductive surgery and postoperative intraperitoneal hyperthermic chemotherapy performed.^{25,26}

During cytoreductive surgery, deep implantation of malignant cells in the abdomen and pelvic viscera such as the ureter and blood vessels occurs during the extensive removal of the peritoneal surface especially if intraoperative intraperitoneal and immediate postoperative chemotherapies were not done.²⁶

The hyperthermic intraperitoneal chemotherapy is performed with mito-

mycin or heated oxaliplatin (42°C, for 60 to 120 min). Hyperthermia intensifies the cytotoxic effects of chemotherapy and increases the effect of the drug in the tissues. The postoperative chemotherapy is done with 5-fluorouracil during initial five postoperative days. This will prevent free tumor cells to fix on wound healing sites of peritonectomy and reduce the adhesion formation. Studies prove that even at the unsuccessful attempt of complete cytoreduction, a better outcome is observed when compared to those who have not been subjected to any procedure.^{27,28}

There is no need for intraperitoneal chemotherapy in those cases where cytoreduction is minimal. In these cases, systemic chemotherapy and palliative care is a better option.²⁹

FOLLOW UP

As to follow-up, a recent study suggests histological, clinical and genetic similarities in proliferative lesions of the appendix and colonic mucosa.²⁵⁻²⁷ So, simple and hyperplastic mucoceles would not require follow-up, benign mucocele would be followed-up as an adenomatous polyp with colonoscopies, according to the follow-up of colonic adenomas,²⁷ and the malignant one would be followed-up as a colonic adenocarcinoma, with regular monitoring of CEA and serial colonoscopies.²⁸

The follow-up of patients with perforated mucocele appendix is very important that the mucinous tumors of appendix rarely metastasise through haematogenesis or lymphatic pathways, and that the dissemination is confined to the peritoneal cavity which make it a localized disease, with healing chances.^{29,30} Literature review shows that there is no consensus as to the follow-up model. Meticulous clinical examination and CEA should be performed every three months, in patients who had cytoreductive surgery and intraperitoneal chemotherapy.³¹ Abdominal computed tomographies are performed every 6 to 12 months, or only when there is suspicion during clinical evaluation or CEA elevation.^{32,33}

PROGNOSIS

The prognosis of patients with benign mucocele is excellent with a 5-year survival rate of 91% to 100%.³⁴⁻³⁶ The prognosis of patients with pseudomyxoma peritonei is very poor, with limited life expectancy and no chances of healing.³⁵ Literature reveals that the cytoreduction associated with hyperthermic intraperitoneal chemotherapy has survival rates up to 50% to 96%, in five years among selected cases provided peritoneal cytoreduction is complete and there are no distant metastases.³⁷

CONCLUSION

Appendiceal mucoceles are best defined as appendices with proximal obstruction leading to distal dilation with mucin production. The term mucocele should be limited to the gross description of the appendix without inferring histopathology. The cause of the obstruction may be further classified based on histology into four subgroups. Mucocele is a rare tumor which often presents difficulties in diagnosis and must be considered in the differential diagnosis of a mass in the right lower quadrant of the abdomen. All patients who present with an asymptomatic mass or an incidental cystic lesion of the appendix should undergo surgical exploration, resection and is determined by the organ's integrity, the dimensions of the base and histological type of the lesion.

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