Cystic mesothelioma: Role of Tamoxifen in preventing recurrence in the post-operative setting

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SUMMARY

Cystic mesothelioma is a rare benign tumor of the peritoneal cavity arising from mesothelial cells. It is characteristically found in women during the reproductive years. No more than 130 cases have been reported in the English literature so far. Curative resection is often required to establish diagnosis and also for definitive management. Local recurrences without distant metastases are a feature of this pathology, hence long-term follow-up is necessary. Therapy with the antiestrogen tamoxifen in the post-operative settings may provide an option for long-term medical management in cases of symptomatic recurrent cystic mesotheliomas. Prognosis is good despite frequent recurrences. Here we present the case-report of a female with cystic mesothelioma who underwent surgical management, remained symptom-free for 10 months, and then again started having similar symptoms as were present prior to surgery. The patient refused explorative second-look surgery. Thereafter, the patient has been put on Tab Tamoxifen 20 mg once daily, has responded well, and is subjectively and objectively disease-free since 24 months. Hence Tamoxifen may have a role not only in the treatment of symptomatic recurrent cystic mesothelioma, but also in preventing recurrences in selected cases.

Key words: Cystic mesothelioma, Peritoneum, Surgical management, Tamoxifen

INTRODUCTION

Peritoneal benign cystic mesothelioma is a rare tumour of unknown aetiology. It is characteristically found in women during the reproductive years. The correct diagnosis can be made by histopathological examination of the operative specimen in conjunction with immunohistochemical and ultrastructural evaluations. Surgery is thus mandatory both for diagnosis and treatment. Surgical management, unfortunately, is not always curative, since there is a recurrence rate of 50%. Regular postoperative radiological and clinical follow-up is recommended to check for possible recurrence. Antiestrogens may have a role in the medical management of these rare estrogen-dependent neoplasms.

CASE REPORT

A 35 years old fertile, pre-menopausal female presented with 4 months history of chronic abdominal pain. The pain was colicky in nature, moderately severe in intensity, localized mainly in bilateral flanks, occasionally radiated to lower back; and was later associated with vomiting. There was no history of urinary or bowel or gynaecological complaints. Complete hemogram and blood biochemistry was within normal limits. The general physical and systemic examination was normal. Pre-operative ultrasonography and CT scan of the abdomen revealed multiple cystic masses in left side of abdomen lying anterior to left kidney, at the tail of pancreas, and posteromedial to left kidney. There were grade-II hydronephrotic changes in left kidney. An exploratory lapotomy was done with the provisional diagnosis of pseudopancreatic cyst.

At exploratory lapotomy, a multiloculated big cyst was found lying posterior and inferior to transverse colon, another cyst was present posterior to left kidney communicating with anterior cyst, and one cyst was densely adherent to transverse colon. The cysts were compressing the pelvi-ureteric junction causing hydronephrotic changes in left kidney. The patient underwent partial cystectomy with cystojejunostomy with transverse colectomy with colocolic anastomosis. The post-operative period was uneventful. Microscopic examination of the operative specimen revealed cysts within the thin cyst wall that were composed of fibrous connective tissue and lined by a single layer of cuboidal or flattened epithelium with variable nuclear atypia. Based on these histological findings, a diagnosis of cystic mesothelioma was made.
DISCUSSION

Cystic mesothelioma is a rare benign tumor of the abdominal and pelvic peritoneum, consisting of solitary or multiple cysts. No more than 130 cases have been reported so far in the surgical-pathological literature. Several risk factors such as chronic peritoneal irritation caused by foreign bodies, infection or endometriosis have been hypothesized; but the exact etiology and origin remains doubtful.

The tumor is more frequent (85%) in adult women of reproductive age group and rarely occurs in children. McCullagh M et al reported the first case of cystic mesothelioma of the peritoneum in a 2-year old girl; while De Toma G et al reported cystic mesothelioma in a 92 year old female.

Cystic mesothelioma may present as abdominal pain, distension, urinary apparatus involvement, abdominal-pelvic mass, and other mass symptoms such as early satiety. The clinical features of a patient with an intra-abdominal cystic mass, however, do not lead to a specific diagnosis, and the diagnosis is often difficult because of their insidious symptomatology. The tumor may reach enormous size before being detected, Hafner et al reported a 33 kg cystic tumour originating from the peritoneum resected en bloc at laparotomy in their male patient.

Cystic mesothelioma of the peritoneum has a nonspecific multilocular cystic appearance on images, which does not permit it to be differentiated from other cystic lesions. Hence diagnostic modalities such as plain radiography, ultrasonography, and computed tomography (CT) scan can suggest the diagnosis; confirmation can be accomplished only at surgery. The differential diagnosis with adenomatoid tumors, lymphangiomas, cystic malignant mesotheliomas and metastatic serous cystic tumors of the ovary is supported by immunohistochemistry.

A recurrence rate of 50% has been reported. Local recurrence is thought to be related to incomplete resection of the tumor.

Methods to contain local recurrences following surgical resection has continued to prove a medical challenge over the last few years. After several unsuccessful attempts at surgical resection, Benson RC Jr reported a case of multilocular mesothelial cyst of the peritoneum by a combination of conservative surgical resection and sclerosive therapy with tetracycline. At 4-year followup evaluation no recurrence was noted. Surgical excision with adjunct sclerosive therapy appears to be an alternative to radical surgery and may decrease the incidence of recurrence in some cases of peritoneal multilocular cysts. In another series, Sethna K et al treated all five patients of cystic peritoneal mesothelioma with cytoreductive surgery plus intraperitoneal chemotherapy. They concluded that cytoreductive surgery to remove all visible tumor and intraperitoneal chemotherapy to control microscopic residual disease will help patients with peritoneal cystic mesothelioma to remain symptom- and disease-free over an extended time period with a single surgical intervention.

The role of laproscopic surgery in the management of cystic mesothelioma is controversial. Ricci F et al reported a minimally invasive laparoscopic approach for histological diagnosis as well as successful surgical management of benign cystic mesothelioma in a 44 year old male. On the other hand, some surgeons feel that it is very difficult during laparoscopy to differentiate these benign cystic mesotheliomas from peritoneal metastases or tuberculous lesions, debating whether the surgeon should continue or terminate the laparoscopic procedure in these ambivalent and potentially risky circumstances.

Since this tumor is characteristically found in women during the reproductive years and is rare after bilateral oophorectomy or menopause, hormonal sensitivity is suggested. Letterie GS treated a patient of recurrent cystic mesothelioma with monthly administrations of a long-acting GnRH agonist as an alternative to radical surgery. A rapid and continued reduction in volume corresponded to the induction and maintenance of a hypoestrogenic state over a 6-month period. However, the subsequent addition of a combination of estrogen and progestin (known as add-back therapy) resulted in a gradual increase in cyst volume, which reduced again with resumption of GnRH-analogue therapy, suggesting extreme sensitivity of tumor to one or both hormones. The potential role for antiestrogens in medical management of recurrent cystic mesothelioma and as an alternative to radical surgery became evident when a 19-year-old woman with a
symptomatic pelvic mass secondary to a recurrent benign cystic mesothelioma 2 years after radical surgery was treated with the antiestrogen tamoxifen. An initial reduction in volume and arrest of growth was followed by stabilization in size and disappearance of symptoms. Therapy with the antiestrogen tamoxifen in this setting may provide an option for long-term medical management in cases of symptomatic recurrent cystic mesotheliomas.  

Our patient of cystic mesothelioma presented with pain abdomen, underwent surgical management, remained symptom-free for 10 months, and then again started having similar symptoms as were present previously. She refused re-exploration. She has been put on Tablet Tamoxifen 20mg once daily. She has been followed up for about two years, and is subjectively and objectively disease free since then. Tamoxifen has anecdotally been found useful in the management of patients with cystic mesothelioma of peritoneum who had relapsed following surgery. Thus there is a possible role of Tamoxifen in preventing recurrence of disease in patients of cystic mesothelioma of peritoneum, being followed up post operatively. In our case, tamoxifen provided rapid and prolonged effect and was well tolerated. This suggests that antiestrogens may have a role not only in the medical management of recurrent disease, but also in preventing recurrence in these rare estrogen-dependent neoplasms.

REFERENCES