Primary retroperitoneal mucinous cystadenoma

Malak S. Abedalthagafi, MD, *Patrick G. Jackson,* MD, *Metin Ozdemirli,* MD, PhD.

ABSTRACT

تتضمن أورام خلف الصفاق الأولي: السرطان الكيسي المخاطي، الأورام المخاطية ذات الحد الفاصل، الأورام النادرة والمتواجدة في النساء والمتضمنة الحزام المخاطي. وحيث أن خلف الصفاق الأولي لا يحتوي على ظاهرة مخاطية، تبقى نظرية حدوث هذه الأورام غير معروفة. نستنتج أن حدوث هذه الأورام قد يأتي من الأورام المسخية، أو من المبايض الزائدة، أو من التحول المخاطي للطبقة المتوسطة لخلف الصفاق. نستعرض في هذا التقرير حالة للخدام المخاطي خلف الصفاق الأولي لمريضة تبلغ من العمر 44 عاماً، والتي حضرت بسبب ورم بطني. بعد استئصال الورم بجراحة المنظار لم يكن هناك أية أثر لعودة الورم بعد 16 شهراً. الشكل المجهري والتحليل للصبغات النسيجية يدعم فرضية التحول المخاطي لطبقة خلف الصفاق المتوسطة والمسبوقة بتكوين كيسي اشتمالي والتي تؤدي إلى حدوث أورام خلف الصفاق المخاطية.

Primary mucinous neoplasms of the retroperitoneum, including mucinous cystadenocarcinomas, mucinous borderline tumors, and mucinous cystadenomas are uncommon tumors found exclusively in women. Since the retroperitoneum does not contain mucinous epithelium, the origin, and histogenesis of these tumors remain unclear. It is speculated that these tumors can arise from teratomas, supernumerary ovaries, or mucinous metaplasia of the retroperitoneal mesothelium. We describe a case of a primary mucinous cystadenoma of the retroperitoneum in a 44 year-old female that presented as a palpable abdominal mass. There was no evidence of recurrence 16 months after complete laparoscopic excision of the tumor. The morphology and immunohistochemical analysis in this case support the hypothesis that mucinous metaplasia of the retroperitoneal mesothelium overlying a preceding inclusion cyst can give rise to retroperitoneal mucinous tumors.

Saudi Med J 2009; Vol. 30 (1): 146-149

From the Department of Pathology (Abedalthagafi, Ozdemirli) and Surgery (Jackson), Lombardi Comprehensive Cancer Center, Georgetown University Hospital, Washington, DC, United States of America.

Received 13th August 2008. Accepted 12th December 2008.

Address correspondence and reprint request to: Dr. Malak Abedalthagafi, Department of Pathology, Georgetown University Hospital 3900 Reservoir Road, N.W., Washington DC, 20007, United States of Americal. Tel. +1 (202) 7843637. Fax. +1 (202) 6878935. E-mail: mxa212@gunet.georgetown.edu

Primary mucinous cystadenomas of the retroperitoneum are extremely rare tumors. Although very rare cases were reported in men and children, these tumors are found exclusively in women.[1-3] Like most retroperitoneal tumors, they can cause symptoms through exertion of pressure or by obstructing adjacent organs if they are large enough. They have potential for malignant transformation. There is no unanimous opinion on the genesis of these tumors and due to their extreme rarity, their histogenesis, biological behavior, and their optimal management remains at a speculative level. In this paper, we present a case of primary retroperitoneal mucinous cystadenoma and review the clinicopathological features, therapeutic options, and outcome in respect to the cases reported in the literature. The morphologic and immunohistochemical analysis observed in this case directly supports the hypothesis that mucinous metaplasia of the retroperitoneal mesothelium can give rise to retroperitoneal mucinous tumors.

Case Report. A 44-year-old female presented with bloating and abdominal pain for 6 months. The abdominal pain was described as intermittently cramping and the intensity of pain was exacerbated with time. She denied any systemic disease or history of drug abuse. Physical examination and pelvic examination showed no remarkable findings. The laboratory data were within reference ranges including serum tumor markers. An MRI and abdominal ultrasound revealed a large cystic lesion that measured 14x11x8 cm in size, occupying the left retroperitoneal space along the posterior portion of the stomach adjacent to the body of pancreas. Initially, this was interpreted as a pseudocyst and the contents were drained on 2 occasions. Cytological examination of the cyst fluid was nondiagnostic due to its acellular contents. However, the cyst recurred after drainage each time. Workup was negative for any other tumors. The cyst was completely excised by laparoscopic surgery. During the surgery, the colon was reflected medially by incising the white line of Toldt and the obvious retroperitoneal large inclusion cyst was identified. This was dissected free in its entirety and, just prior to removal, it was incised and drained laparoscopically. It was, therefore, removed intact. The

decompressed cyst was then placed in an EndoCatch bag that was brought out through the Hasson trocar site. Inspection of the area revealed an obvious left ureter that was intact and without injury. The colon was put back in its anatomic location and all trocars were removed under direct vision. She was awakened from anesthesia and brought to the post-anesthesia care unit in a stable condition. The specimen received was a single deflated, pink-tan, multilocular cyst measuring 11x7x0.5 cm. Histological examination showed a thin-walled cyst containing either mostly endocervical type columnar mucinous epithelium or adjacent simple cuboidal epithelium without atypia and hypocellular fibrous stroma with focal microcalcifications. There was also a minor component of intestinal type columnar mucinous epithelium with occasional goblet cells (**Figure 1**). The tumor was extensively sampled and no atypia for consideration of mucinous borderline tumor or invasive carcinoma was identified. There was no evidence of teratoma. Immunohistochemistry was performed. Both types of epithelium were positive for keratin and epithelial membrane antigen. The mucinous cells were positive for cytokeratin-7, LeuM1, focally positive for cytokeratin-20 and carcinoembryonic antigen (CEA) and negative for calretinin and CD10. The cuboidal cells were positive for calretinin and cytokeratin-7 and negative for cytokeratin-20, CD15, CD10, and CEA (similar to mesothelial cells) (**Figure 2**). Neither estrogen nor progesterone receptor positive stromal cells were identified in the fibrous stroma. The results are summarized in **Table 1**. She remains free from recurrence 16 months after complete laparoscopic excision of the tumor.

Discussion. Primary retroperitoneal mucinous cystadenoma is rare and found exclusively in women, the sole exception is a report of a 65-year-old man in association with fallopian tube-like structure and aberrant epididymal tissue, and was interpreted as a result of müllerian and wolffian embryonic development disorder.[4] In a recent review by Isse et al[5] only 10 cases were published in the English language literature. Since then a few additional cases have been reported.[6-12] The reported cases were all women ranging in age from 14-85 and with tumor size ranging from 6-30 cm. The most common complaint has been described as abdominal pain or discomfort and a slow growing pelvic or abdominal mass. Retroperitoneal mucinous cystadenomas are grossly, ultrastructurally, and histologically similar to mucinous cystadenomas of the ovary.[2] However, little information is available concerning their pathogenesis, optimal treatment schedule, and prognosis. The usual preoperative differential diagnosis of retroperitoneal cystic masses includes cystic mesothelioma, cystic lymphangioma, cystic teratoma, müllerian cyst, pancreatic or nonpancreatic pseudocyst in addition to mucinous cystadenoma.[13] For diagnosis, blood tests are not helpful. Imaging studies cannot provide a definitive diagnosis although they might help to determine the anatomic location preoperatively. Although aspiration is a good method for delineating the nature of cysts, cytologic analysis of the aspirated fluid frequently fails to reveal the type of epithelium lining the cysts. Moreover, because of the potential for malignant transformation, exploratory laparotomy with complete excision of the cyst is usually indicated for both diagnosis and treatment.[13] Histologically, mucinous cystadenomas contain cystic spaces containing cellular fibrous stroma and lined by endocervical or intestinal type columnar mucinous epithelium without any atypia or invasion into the underling stroma. In some cases, the stromal cells have estrogen and progesterone receptors.[4] However, inclusion cysts contain simple

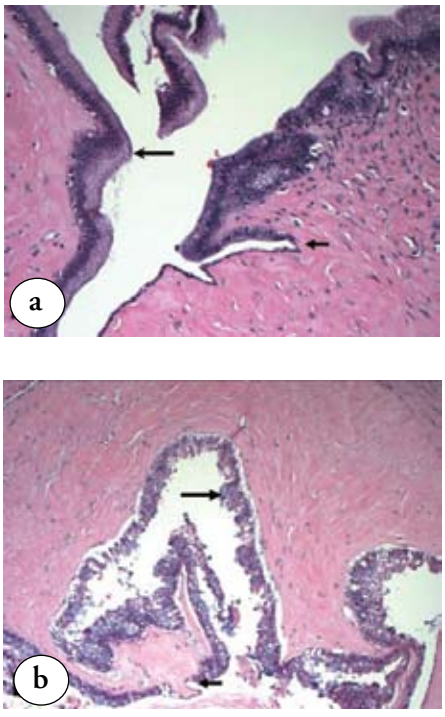

Figure 1 - Representative morphologic features from formalin fixed paraffin embedded sections show **a)** columnar cervical type mucinous epithelial lining (long arrow) and abrupt transition from simple cuboidal epithelium (short arrow), **b)** intestinal type mucinous epithelium with goblet cells (long arrow) and abrupt transition from simple cuboidal epithelium (short arrow) (hematoxylin and eosin x 200, each).

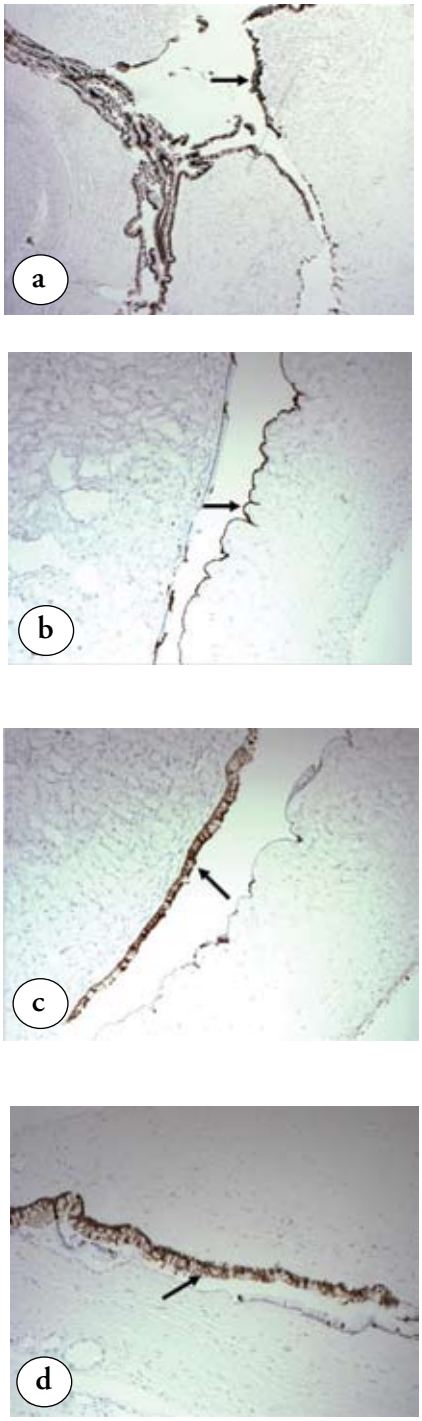

Figure 2 - Immunohistochemistry showing the epithelial lining cells are diffusely positive for keratin (arrow) **a**) Cuboidal cells are positive for calretinin (arrow) **b**) Mucinous columnar cells are positive for CD15 (arrow) **c**) and focally positive for cytokeratin 20 (arrow) **d**) (x100, each).

Table 1 - The results of immunohistochemical analysis.

Antibody	Mucinous cells	Cuboidal cells
Pankeratin	+	+
Epithelial membrane antigen	+	+
Cytokeratin 7	+	+
Cytokeratin 20	+/-	-
Calretinin	-	+
CD15	+	-
CD10	-	-
CEA*	+/-	-
Estrogen receptor	-	-
Progesterone receptor	-	-

*carcinoembryonic antigen

cuboidal epithelium lining similar to mesothelium and lack fibrous cellular stroma. The cyst described in this case has both columnar mucinous epithelium lining in addition to simple cuboidal mesothelial lining. The presence of abrupt changes from one type epithelium to the other (**Figure 2a**) indicates mucinous metaplasia. To prove this, immunohistochemistry was performed. Mesothelial epithelium is typically positive for keratin, cytokeratin 7, and calretinin, whereas it is negative for CD15 (LeuM1) and CEA. Typical ovarian mucinous tumors express cytokeratin 7 and cytokeratin 20.[14] In our case, the mucinous cells expressed cytokeratin 7 and focally cytokeratin 20 similar to ovarian mucinous cystadenomas and cuboidal cells expressed mesothelial markers. These results also prove that mucinous metaplasia of mesothelium can give rise to mucinous tumors. Only few reports include description of the immunohistochemical profile for retroperitoneal mucinous cystadenomas. One of the cases reported by Isse et al[5] was similar to ours in that calretinin was present in the cuboidal epithelium, but the cytokeratin profile was not reported. The case described by Rizzardi et al4 expressed epithelial membrane antigen, keratin (AE1/AE3), and cytokeratins 8, 18, and 19, but not cytokeratin 7.4. As for the management of primary retroperitoneal mucinous cystadenomas, complete surgical excision is recommended to eliminate the risk of infection, recurrence, and malignant transformation. Traditionally exploratory laparotomy with complete enucleation of the cyst is performed, although successful laparoscopic excision has been reported similar to our case.[12] Based on the review of the literature, these tumors seem to behave in a benign fashion with no recurrences after complete surgical removal, as has been demonstrated in our case.

In conclusion, this case details the immunohistochemical analysis for mucinous cystadenoma in the retroperitoneum and provides

additional morphologic and immunohistochemical data to support the hypothesis that mucinous tumors can arise as a result of mucinous metaplasia of the retroperitoneal mesothelial cells in this location.

References

1. Tangjitgamol S, Manusirivithaya S, Sheanakul C, Leelahakorn S, Thawaramara T, Kaewpila N. Retroperitoneal mucinous cystadenocarcinoma: a case report and review of literature. ***Int J Gynecol Cancer*** 2002; 12: 403-408.
2. Banerjee R, Gough J. Cystic mucinous tumours of the mesentery and retroperitoneum: report of three cases. ***Histopathology*** 1988; 12: 527-532.
3. Matsubara M, Shiozawa T, Tachibana R, Hondo T, Osasda K, Kawaguchi K, et al. Primary retroperitoneal mucinous cystadenoma of borderline malignancy: a case report and review of the literature. ***Int J Gynecol Pathol*** 2005; 24: 218-223.
4. Rizzardi C, Brollo A, Thomann B, Santirocco C, Melato M. Intra-abdominal ovarian-type mucinous cystadenoma associated with fallopian tube-like structure and aberrant epididymal tissue in a male patient. ***Hum Pathol*** 2005; 36: 927-931.
5. Isse K, Harada K, Suzuki Y, Ishiguro K, Sasaki M, Kajiura S, et al. Retroperitoneal mucinous cystadenoma: report of two cases and review of the literature. ***Pathol Int*** 2004; 54: 132-138.
6. Erdemoglu E, Aydogdu T, Tokyol C. Primary retro peritoneal mucinous cystadenoma. ***Acta Obstet Gynecol Scand*** 2003; 82: 486-487.
7. Gutsu E, Mishin I, Gagauz I. Primary retroperitoneal mucinous cystadenoma. A case report and brief review of the literature. ***Zentralbl Chir*** 2003; 128: 691-693.
8. Tamura T, Yamataka A, Murakami T, Okada Y, Kobayashi H, Ohshiro K, et al. Primary mucinous cystadenoma arising from behind the posterior peritoneum of the descending colon in a child: a case report. ***Asian J Surg*** 2003; 26: 237-239.
9. Talwar A, Bell NJ, Nicholas D. Mucinous cystadenoma of colonic mesentery: report of a case. ***Dis Colon Rectum*** 2004; 47: 1412-1414.
10. Min BW, Kim JM, Um JW, Lee ES, Son GS, Kim SJ, Moon HY: The first case of primary retroperitoneal mucinous cystadenoma in Korea: a case report. Korean J Intern Med 19: 282-284, 2004
11. Lai EC, Chung KM, Lau WY. Primary retroperitoneal mucinous cystadenoma. ***ANZ J Surg*** 2006; 76: 537.
12. Chen JS, Lee WJ, Chang YJ, Wu MZ, Chiu KM. Laparoscopic resection of a primary retroperitoneal mucinous cystadenoma: report of a case. ***Surg Today*** 1998; 28: 343-345.
13. Yang DM, Jung DH, Kim H, Kang JH, Kim SH, Kim JH, et al. Retroperitoneal cystic masses: CT, clinical, and pathologic findings and literature review. ***Radiographics*** 2004; 24: 1353-1365.
14. Vang R, Gown AM, Barry TS, Wheeler DT, Yemelyanova A, Seidman JD, et al. Cytokeratins 7 and 20 in primary and secondary mucinous tumors of the ovary: analysis of coordinate immunohistochemical expression profiles and staining distribution in 179 cases. ***Am J Surg Pathol*** 2006; 30: 1130-1139.