CASE REPORT

Peritoneal mucinous cystadenocarcinoma of probable urachal origin: a challenging diagnosis

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This report describes the case of a mucinous cystadenocarcinoma of probable urachal origin that presented with mass effect, precipitating deep venous thrombosis and pulmonary embolism. The patient presented with acute symptoms of leg swelling, pain and dyspnoea, and a vague awareness of lower abdominal distension. Computer tomography showed a cystic mass closely related to the anterior abdominal wall and the superior aspect of the bladder. A 1500 cm³ cyst adherent to the dome of the urinary bladder was resected on laparotomy. Partial cystectomy was not carried out in the belief that the cyst represented a benign lesion. Subsequent imaging has shown cystic changes in the anterior bladder wall, and the patient has been referred for partial cystectomy.

A 31-year-old black man presented with sudden-onset chest pain and dyspnoea, preceded by 24 h of leg pain. Examination showed the left leg to be painful and swollen to groin level, with a diffuse hard palpable mass in the lower abdomen.

Ventilation and perfusion scan confirmed the diagnosis of pulmonary embolism, with multiple perfusion defects, which were evident bilaterally. Ultrasonography of the left leg showed a large deep vein thrombosis in the left common femoral vein. Computerised tomography showed a 10×19×15 cm cystic mass closely related to the anterior abdominal wall and superior aspect of the bladder, which was also compressing the common iliac vessels on the left (fig 1). The liver, gall bladder, kidneys, spleen, appendix and pancreas appeared normal, with no evidence of intra-abdominal lymphadenopathy. On further questioning, the patient reported 6 months of increasing abdominal distension, which he had attributed to beer consumption.

After anticoagulation, an exploratory laparotomy was carried out. The cystic mass was extensively adherent to the urinary bladder dome. Initial attempts to remove the cyst intact failed. Subsequent to aspiration of about 1500 ml of yellow mucinous contents, most of the cyst wall was resected, leaving sections stuck to the bladder.

HISTOPATHOLOGY

Macroscopic examination showed a well-encapsulated, unilocular cyst measuring 20×9 cm and 0.3 cm in thickness. The inner surface was brown, with some smooth white and smaller yellow plaque-like areas, and the outer surface showed haemorrhagic areas. The cyst contained abundant yellow gelatinous material.

The microscopic findings were a cystic neoplasm, with thick fibrous wall, mostly denuded of lining epithelium and replaced by granulation tissue, cholesterol clefts, foreign body giant cells and calcifications. Focally, small areas of the cyst wall were lined by a malignant mucin-producing columnar epithelium with small papillary formations, pleomorphic,

hyperchromatic nuclei and atypical mitoses. Foci of invasion into the underlying stroma, resembling ovarian stroma, and mucin extravasation were noted (fig 2). On immunohistochemical staining, the malignant lining cells showed strong diffuse positive staining for monoclonal carcino embryonic antigen, AE1/AE3, cytokeratin 20 and focal positivity for cytokeratin 7, cancer antigen (CA) 19.9 and caudal type homeo box transcription factor (CDX) 2. Marked heterogeneity was found with the CDX2 stain, varying from no staining to 50% nuclear staining focally (2+) (fig 3). The cells were negative for calretinin and HBME-1 mesothelial markers, inhibin A, CA125 and cluster of differential molecule (CD)34. The "ovarian-like" stroma underlying the epithelial lining was positive for CD10, vimentin and smooth muscle actin.

DISCUSSION

Urachal cysts are one of three possible sequelae of vestigial remnants of the embryological structure connecting the bladder apex to the allantois; patent fistulae between the bladder and umbilicus, and sinus tracts at either end are the other variants. Adenocarcinomatous change in such a cyst is an uncommon diagnosis accounting for 0.17–0.34% of all bladder cancers.¹ Although mucousuria is a common and relatively specific symptom of adenomas of the lower

Figure 1 Sagittal computerised tomograph showing a 10×19×15 cm low attenuating cystic mass related closely to the anterior abdominal wall and superior aspect of the bladder.

Abbreviation: CDX, caudal type homeo box transcription factor

Figure 2 Haematoxylin and eosin stain (higher magnification inset) showing foci of invasion into the stroma of mucinous cystadenocarcinoma with mucin extravasation.

urachus, patients may be asymptomatic, or may have haematuria, pain or frequency, common to many bladder disorders.¹⁻³

Although patients may become aware of a mass, our patient, to the best of our knowledge, is the first to present with such space-occupying effects as venous thrombosis, with subsequent pulmonary embolism.

A diagnosis of urachal adenocarcinoma often requires correlation of clinical and pathological findings to distinguish it from bladder or metastatic processes, criteria for which include a sharp demarcation between the tumour and an intact, normal surface urothelium; absence of cystitis cystica or glandularis; and tumour growth in the bladder wall with

extension in the bladder dome or anterior wall.⁴ Unfortunately, no bladder wall samples were taken at the time of cyst resection.

Although the tumour's close association with the bladder dome suggested urachal origin, the microscopic appearances were consistent with metastasis from primary sites such as the pancreas, appendix and gall bladder. This was excluded radiographically on the original computer tomography, and the bladder appeared normal. Immunohistochemically, no known antibody panels reliably differentiate between bladder, urachal or metastatic adenocarcinoma. Torenbeek *et al*,⁵ in a multipanel study, showed that cytokeratin 7 was expressed in 82% of adenocarcinomas of the bladder, and focally in only 40% of urachal and 38% of colonic adenocarcinomas. Cytokeratin 20 was expressed in more than 80% of adenocarcinomas of the urachus, bladder and colon. Carcinoembryonic antigen was expressed in 100% of urachal and 96% of colonic adenocarcinomas, respectively, but in only 52% of adenocarcinomas of the bladder. Vimentin was consistently negative in adenocarcinomas of the bladder, urachus and colon. A similar study reported near universal positive staining for cytokeratin 7 in adenocarcinomas of the lung, ovary and breast; however, a significant 17% of adenocarcinomas of colorectal origin were also cytokeratin 7 positive.⁶ CDX2 is a recently described immunological agent, which, when it stains uniformly, is a highly sensitive and specific marker of gastrointestinal adenocarcinomas. Variable expression in a given tumour, however, favours extraintestinal origin.⁷ The marked heterogeneity for CDX2 in our case tends to favour extraintestinal origin but by no means excludes primary gastrointestinal origin. In a recent study all colorectal adenocarcinomas showed expression of CDX2, with 74 of 75 cases showing high levels of expression (3+ in 64 cases; 2+ in 10 cases).⁷

Figure 3 Mucinous cystadenocarcinoma showing variable expression of CDX2 with no staining (A) to focal (2+) nuclear expression (B), and strong uniform expression of cytokeratin 7 (C) and cytokeratin 20 (D).

The possibility of this representing primary peritoneal origin was also considered in the light of the histological resemblance to ovarian cystic neoplasms, a resemblance first noted by Staehlin in 1915.⁸ However, given that little over 20 cases of primary peritoneal mucinous cystadenocarcinoma have been reported (none in men), it is not surprising that there is no reference to any immunohistochemical panel to differentiate it from urachal adenocarcinoma.⁹

It is, therefore, impractical, if not impossible, to use such tests to aid in the differential diagnosis, and clinicopathological correlation is as relevant as when it was first suggested by Mostofi *et al*⁸ in 1955. Our patient with mucinous cystadenocarcinoma probably represents a primary carcinoma in a urachal remnant.

Unfortunately, at no time during the preoperative management of this patient was a diagnosis of malignancy considered, although fine needle aspiration cytology and possible carcino embryonic antigen analysis of the cystic content may have assisted in this respect.¹⁰ A repeat computer tomography three months after laparotomy showed thickening of the anterior bladder wall (2.5 cm) with cystic changes. The patient has unfortunately not taken urological referral for partial cystectomy.

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REFERENCES

- 1 **Sheldon CA**, Clayman RV, Gonzalez R, *et al*. Malignant urachal lesions. *J Urol* 1984;**131**:1–8.
- 2 **Eble JN**, Hull MT, Rowland RG, *et al*. Villous adenoma of the urachus with mucusuria: a light and electron microscopic study. *J Urol* 1986;**135**:1240–4.
- 3 **Yagishita H**, Nagayama T, Zean Z, *et al*. A case of asymptomatic urachal cyst in autopsy—histopathological study of urachal cyst and review of the literature of 99 cases during a 10 year period in Japan. *Hinyokika Kiyo* 2001;**47**:849–52.
- 4 **Mostofi FK**, Thompson RV, Dean AL Jr. Mucinous adenocarcinoma of the urinary bladder. *Cancer* 1955;**8**:741–58.
- 5 **Torenbeek R**, Lagendijk JH, Van Diest PJ, *et al*. Value of a panel of antibodies to identify the primary origin of adenocarcinomas presenting as bladder carcinoma. *Histopathology* 1998;**32**:20–7.
- 6 **Wauters CC**, Smedts F, Gerrits LG, *et al*. Keratins 7 and 20 as diagnostic markers of carcinomas metastatic to the ovary. *Hum Pathol* 1995;**26**:852–5.
- 7 **Werling RW**, Yaziji H, Bacchi CE, *et al*. CDX2, a highly sensitive and specific marker of adenocarcinomas of intestinal origin: an immunohistochemical survey of 476 primary and metastatic carcinomas. *Am J Surg Pathol* 2003;**27**:303–10.
- 8 **Staehlin E**. A study of multilocular cystadenomata of retroperitoneal origin. *Ann Surg* 1915;**61**:312–23.
- 9 **Dabbs DJ**. *Diagnostic immunohistochemistry*. Philadelphia: Churchill Livingstone, 2002.
- 10 **Gulyas M**, Kaposi AD, Elek G, *et al*. Value of carcinoembryonic antigen (CEA) and cholesterol assays of ascitic fluid in cases of inconclusive cytology. *J Clin Pathol* 2001;**54**:831–35.