A low-grade mucinous neoplasm arising within an ovarian mature cystic teratoma: a case report

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Abstract

A 52-year old female presenting with an ovarian mass underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. Intra-operatively there was large volume ascites containing mucin and hair. Subsequent pathological examination of the ovarian mass revealed a low-grade mucinous neoplasm arising within a mature cystic teratoma (MCT). This was associated with pseudomyxoma peritonei (PMP) and is a rare entity recognized by the World Health Organisation. These tumours resemble their appendiceal counterpart and therefore diagnosis is achieved with immunohistochemistry and thorough morphological assessment to exclude a collision tumour. Additionally, the appendix should be examined to confirm ovarian origin. Identification of these neoplasms is crucial as reasonable outcomes can be achieved following appropriate referral for ongoing management which includes complete surgical cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC).

Keywords Low-grade mucinous neoplasm; ovarian mature cystic teratoma; pseudomyxoma peritonei

Case report

A 52-year old female presented with several weeks history of shortness of breath, bilateral ankle oedema and bloated abdomen. CA125 and CEA were raised (69 kU/L and 15.3 μg/L respectively). A CT scan showed moderate volume ascites and an 8 cm cystic mass rimmed by calcium, in keeping with a mature ovarian teratoma with possible features of rupture. The patient deteriorated clinically and was admitted for urgent surgical management. This involved total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, peritoneal biopsy and drainage of 4.5 litres of ascites. Intra-operative findings revealed a ruptured left ovarian mass adherent to the appendix, mesorectum and uterus and exuding mucin. The peritoneal surface was thickened, and the small and large bowel were coated with mucin, fat, and hair.

Macroscopically, a 200 × 160 × 70 mm ruptured left ovarian mass was identified containing hair, mucin, and soft, yellow material. Mucin was noted on the surface of the fallopian tube and the appendix, which otherwise appeared normal. The appendix was entirely submitted.

Microscopically the ovarian mass showed features of a mature cystic teratoma associated with a mucinous tumour (Figure 1). The mucinous tumour was of gastrointestinal phenotype with low grade cytological atypia, resembling the appendiceal counterpart (Figure 2). Dissecting pools of mucin were present however, there was no evidence of frank invasion. Mucin, focally

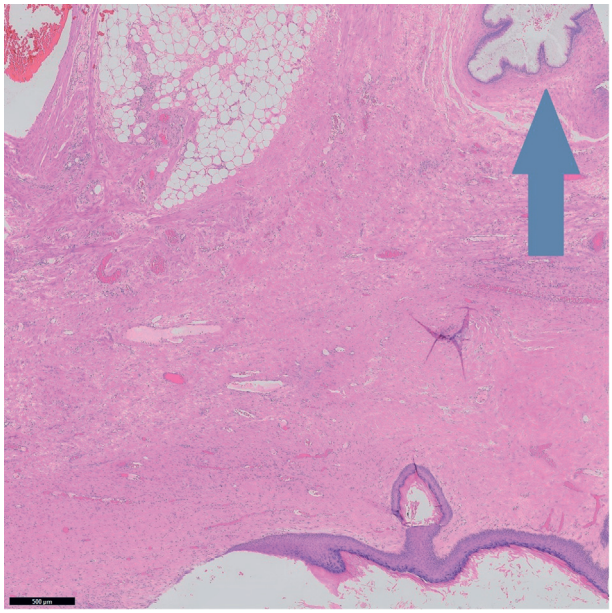

Figure 1 Representative section of the mature cystic teratoma with squamous mucosa (bottom), adipose tissue (top left), and low-grade mucinous neoplasm (top right – blue arrow). Scale bar: 500 μm.

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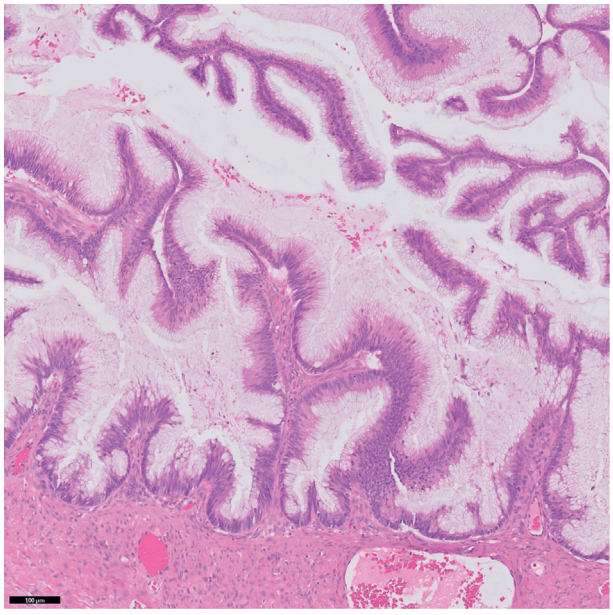

Figure 2 Low-grade mucinous neoplasm. Scale bar: 500 μm.

containing epithelium, was noted on the surface of both fallopian tubes, the right ovary, uterus, and appendix. The appendiceal epithelium was unremarkable.

Within the areas containing mucinous tumour, immunohistochemistry was positive for CK20 (Figure 3a), CDX2 (Figure 3b) and CEA. CK7, PAX8, CA125 and ER/PR were negative.

Consistent with the WHO classification, the findings were reported as low-grade mucinous neoplasm arising within a mature cystic teratoma (MCT) associated with low-grade mucinous carcinoma peritonei. This case was referred to the Pseudomyxoma centre in Basingstoke who agreed with the local diagnosis.

Follow-up imaging at 6 months showed a significant reduction in ascites however, residual disease was still noted. Subsequently, the Peritoneal Malignancy Institute in Basingstoke advised complete cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC) may be required in the future.

Discussion

Differentiating mucinous neoplasms of the ovary from a gastrointestinal metastasis can be a diagnostic challenge. However, mucinous neoplasms associated with pseudomyxoma peritonei (PMP) are nearly all appendiceal in origin.[1] In this present case, PMP occurred secondary to a mucinous neoplasm arising within an ovarian MCT. These tumours have an incidence of 1−2/1,000,000 per year and likely represent the only true cases of ovarian origin of PMP.[2,3] Although rare, it was first reported in 1988[4] and is recognized as a distinct entity by the World Health Organisation.

While teratomas commonly occur in women of reproductive age, cases of mucinous neoplasms accompanied by MCT tend to occur in post-menopausal woman. They are thought to arise either as a collision tumour (independent of the teratoma) or from intestinal epithelium within the teratoma. The morphological distinction can be achieved by identifying transition points between the MCT and that of the mucinous neoplasm − a collision tumour will not have this.

Additionally, immunohistochemistry can be helpful. Low-grade mucinous neoplasms arising within a MCT not only morphologically resemble their appendiceal counterparts but also have a similar genetic and immunohistochemical profile. They show strong positivity for CK20 and CDX2 with indeterminate CK7 positivity, indicating that they arise from the intestinal component of the teratoma and not ovarian epithelium. This is supported by studies assessing their molecular profile and identifying KRAS and GNAS pathogenic variants, like mucinous tumours of appendiceal origin. These mutations have also been shown in subsequent recurrences.[5]

Due to the diagnostic overlap with their appendiceal counterparts, the entire appendix must be examined to confirm primary origin within the ovary.

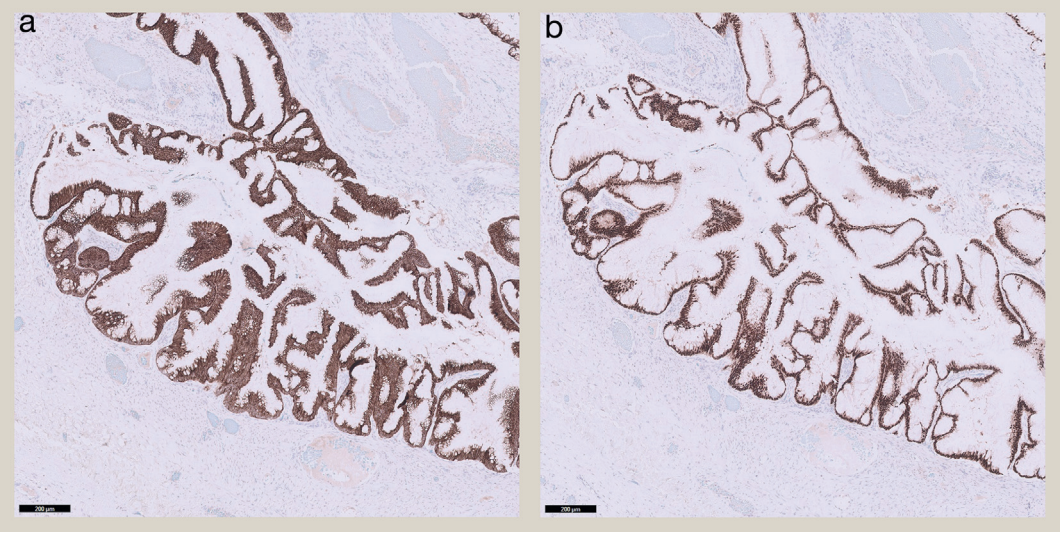

Figure 3 Immunohistochemical staining of the low-grade mucinous neoplasm shows positive staining for CK20 (**a**) and CDX2 (**b**). Scale bar: 200 μm.

Identification and characterization of these tumours is essential as they tend to recur. Poor prognosis is associated with high stage and incomplete cytoreduction. Mucinous neoplasms arising from MCT are rare with limited outcome data. However, there is evidence that complete cytoreduction and HIPEC can achieve a 68% 10-year survival rate with outcomes that are comparable for patients with appendiceal and extra-appendiceal PMP.[6]

Conclusion

Ovarian mucinous neoplasms arising within a MCT are extremely rare but can result in PMP. The diagnosis can be confirmed by immuno-morphological assessment of the tumour combined with comprehensive examination of the appendix, ensuring primary origin within the ovary. Reasonable prognostic outcomes are achievable, and further characterization of these rare tumours is essential to identify putative treatment options. ◆

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Practice points

- Ovarian mucinous neoplasms arising within a MCT are extremely rare but may be associated with pseudomyxoma peritonei
- These tumours morphologically, immunohistochemically, and genomically resemble their appendiceal counterparts
- Strong CK20 and CDX2 with indeterminate CK7 positivity indicate that they arise from the intestinal component of the teratoma and not ovarian epithelium
- The entire appendix must be examined to confirm primary origin within the ovary and exclude a metastasis

Multiple choice questions

Q1. Which immunohistochemical profile is indicative of a low-grade mucinous neoplasm arising within a MCT as opposed to an ovarian epithelial origin?

A) Positive for CK7 and CA125, negative for CK20 and CDX2
B) Positive for CK7, PAX8, and CA125; negative for CK20 and CDX2
C) Positive for CK20, CDX2, and CEA; negative for CK7, PAX8, CA125, and ER/PR
D) Positive for CK7, CDX2, and ER/PR; negative for CK20 and CEA

Answer: C

Q2. What genetic mutations are commonly associated with low-grade mucinous neoplasms arising within a MCT?

A) BRCA1 and BRCA2 mutations
B) KRAS and GNAS mutations
C) TP53 and PTEN mutations
D) APC and MLH1 mutations

Answer: B

Q3. What are the key pathological features that differentiate a low-grade mucinous neoplasm arising within a MCT from a gastrointestinal metastasis?

A) Presence of high-grade cytological atypia and extensive tissue invasion
B) Morphological transition points between MCT and mucinous neoplasm, and immunohistochemical profile resembling appendiceal neoplasms
C) Extensive mucin production and absence of teratomatous elements
D) Exclusive positivity for CK7 and PAX8 with negative CK20 and CDX2

Answer: B