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CASE REPORT

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Appendiceal adenocarcinoma—Two unique cases of adenocarcinoma ex-goblet cell carcinoid

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Key Clinical Message

We describe the different clinical presentations, radiology, histology and management of this unique, highly aggressive disease. Clinical presentation of appendicitis may not just be appendicitis. Appendiceal tumors must always be considered in the differential diagnosis. Dedicated radiology and histological examination in addition to aggressive surgical and oncological input improve outcome.

KEYWORDS

adenocarcinoma ex-goblet cell carcinoid, appendiceal neoplasm, appendiceal tumors, appendix

1 | INTRODUCTION

Neoplasms of the appendix are rare; the incidence is about 1% of all appendicectomy specimens and 0.5% of intestinal neoplasms.[1] Carcinoid tumors are the most common, comprising over 50% of appendiceal neoplasms, followed by benign tumors. Primary malignant tumors are less frequent, of which adenocarcinoma comprises about 8%.[2] Appendiceal adenocarcinoma is very rare. To the best of our knowledge, this is the fourth case reported in the literature.[1,3,4]

2 | CASE ONE

A 38-year-old lady presented at 14 weeks gestation to the emergency department with right upper quadrant and right iliac fossa pain. She was systemically well, vital signs unremarkable but baseline bloods showed an elevated white cell count (19) and elevated C reactive protein (150). A technically difficult ultrasound due to body mass index of 42.6 kg/m^2 demonstrated gallstones. A subsequent CT abdomen identified a ~10 cm (AP) × 10 cm (craniocaudal) × 14 cm (transverse) circumscribed abnormality in the right side of the abdomen immediately deep to the abdominal musculature inferior to the gallbladder and liver adjacent to the superolateral border of the uterine fundus with groundglass opacity in the adjacent mesenteric fat. Moderate to large volume ascites was present but no pneumoperitoneum. Differentials included hemorrhage into an ovarian cyst and ovarian torsion. The patient was reviewed by the gynecologists and discharged home on conservative management.

She re-presented at 18 weeks gestation with inability to extend the right upper arm and a size discrepancy between both upper arms of 3 cm. An ultrasound and duplex doppler identified a deep venous thrombosis involving the right upper arm basilic vein, accompanying axillary vein and the right-sided supraclavicular vein. She was treated with therapeutic low molecular weight heparin.

Intra-uterine death was diagnosed at 24 weeks and a cesarean section and hysterectomy were performed. A large right-sided mass was noted intraoperatively. It was thought to be ovarian in origin, but unable to be removed. There was an additional complex ovarian mass on the left side. Left ovary biopsies were sent for histology and peritoneal fluid for cytology.

A postoperative CT abdomen and pelvis (Figure 1) identified the right adnexal mass measuring >20 cm in maximum diameter which was heterogeneous with marked central low attenuation consistent with necrosis and also a 10-cm heterogenous left adnexal mass. There was ascites but no omental

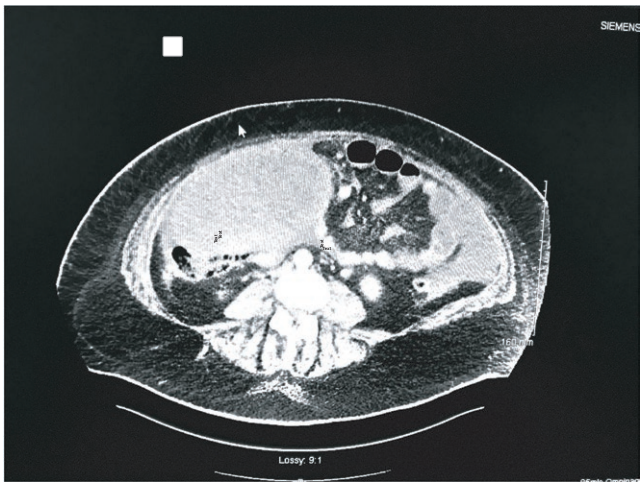

FIGURE 1 CT demonstrating ovarian metastases

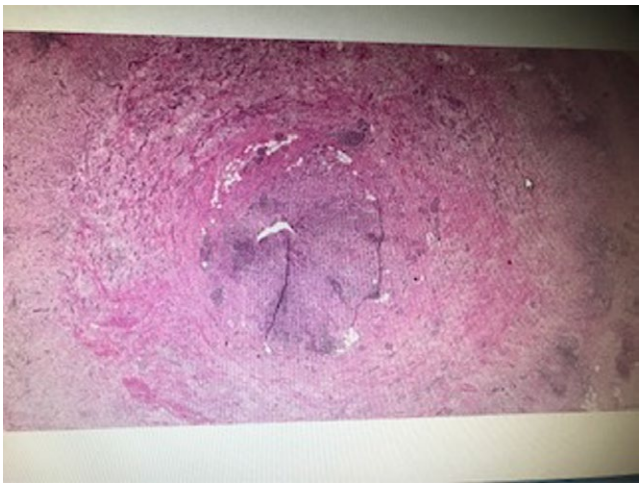

FIGURE 2 Goblet cell ex-adenocarcinoma

or peritoneal thickening were visualized. The stomach, small bowel, colon, liver, gallbladder, pancreas, spleen, kidneys, and adrenal glands appeared normal but there were shotty retroperitoneal nodes. Upper GI endoscopy and colonoscopy were noncontributory.

2.1 | Histology

No definite malignancy was seen within the peritoneal fluid. A biopsy of the left ovary metastatic moderately differentiated adenocarcinoma while an omental tissue biopsy was infiltrated by metastatic moderately differentiated adenocarcinoma. The tumor was strongly positive for CK7, CK20, CDX2 and is negative for mammoglobin, PAX8, TTF1 immunostains. Further, immunohistochemistry on the ovarian tumor confirmed that the tumor cells were positive for both Chromogranin A and Synaptophysin, supporting a neuroendocrine phenotype.

A review of the histology confirmed the presence of a goblet cell-rich tumor within the ovary. Combining the immunohistochemistry with these light morphological findings, the features suggest a metastatic mixed goblet cell carcinoid/adenocarcinoma, arising from the appendix (Figure 2).

This patient subsequently underwent total colectomy with end ileostomy, omentectomy and received HIPEC (Hot Intraperitoneal Chemotherapy) and adjuvant chemotherapy following case discussion at a multidisciplinary meeting.

3 | CASE TWO

A 58-year-old female presented to the emergency department with right iliac fossa pain and mildly elevated inflammatory markers. She underwent a CT abdomen and pelvis which identified acute appendicitis. She underwent a laparaoscopic appendicectomy.

Histological analysis of the appendix specimen confirmed goblet cell carcinoid; the tumor infiltrated through the appendiceal wall and involved the serosa.

She underwent a staging CT thorax and the case was discussed at the gastrointestinal oncology multidisciplinary meeting. By concensus, it was advised that she undergo right hemicolectomy, bilateral salpingo-oophorectomy, and omentectomy. The right hemi-colon specimen had one of sixteen lymph nodes containing metastatic goblet cell carcinoid, and the resection margin was free of malignancy. The omentum, left ovary and fallopian tube were free of malignancy. The fimbrial end of the right fallopian tube was infiltrated by metastatic goblet cell ex-adenocarcinoma. The left ovary was free of malignancy. Pathological stage TNM (8th ed): T4a N1 M1 RX. She received adjuvant chemotherapy.

4 | DISCUSSION

The first malignant tumor of the appendix was described in 1882, and the first reports about appendiceal tumors and pregnancy date from 1965.[5,6]

Adenocarcimoma ex-goblet cell carcinoid is a very rare and histologically unique appendiceal malignancy with both glandular and neuroendocrine differentiation. It represents <1% of gastrointestinal malignancies. There is a high incidence of this tumor metastasising to the gynecological tract with the mode of metastasis following peritoneal spread rather than hematogenous among female patients.

Reid et al reported 77 cases of adenocarcinoma ex-goblet cell carcinoids. Tumors occurred predominantly in females (74%), mean age 55 years (29-84), most with disseminated abdominal (77% peritoneal, 58% gynecologic tract involvement) and stage IV (65%) disease. Many presented to gynecologic oncologists, and nine had a working diagnosis of ovarian carcinoma.[7]

Malignancy is not higher in the pregnant population than in age-matched nonpregnant females, but some tumors may be hormone dependent.

The interesting features of our cases are that our index patient presented with bilateral ovarian metastases. In addition, she experienced a spontaneous upper limb deep venous thrombosis during the pregnancy. This devastating disease was advanced at diagnosis and an aggressive surgical approach was required. In the second case, again, an aggressive surgical approach was employed after confirming the appendix histology.

Lee et al demonstrated close correlation between our predefined CT pattern and the pathological classification.[8]

Most authors recommend a right hemicolectomy even for ordinary goblet cell carcinoid which would be even more applicable to this high-grade, mixed, adenocarcinoma ex-version of goblet cell carcinoid.[9]

The utility of systemic chemotherapy for metastatic appendiceal adenocarcinoma is controversial because particularly mucinous adenocarcinomas have been considered refractory to intravenous 5-fluorouracil chemotherapy, although there are studies that suggest the opposite.[10] Cytoreductive surgery with heated intraperitoneal chemotherapy may improve survival in a select few with metastatic peritoneal disease and research in this is ongoing. Collaborative multi-center studies of the molecular biology of this rare tumor type will be required to identify putative novel predictive and prognostic markers, and also identify targets for precision therapy.[11] These tumors have an unpredictable behavior even in early stages and local recurrence and delayed metastases may be seen. Lifelong surveillance is mandatory.

All clinicians, practicing obstetrics and gynecology must consider the possibility of a malignant neoplasm and should recognize the characteristic features to enable detection and treatment of this rare condition.

CONFLICT OF INTEREST

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

AUTHOR CONTRIBUTION

MMH: conceived of the idea and prepared manuscript and obtained images. II: reviewed manuscript and provided suggestions to enhance final paper.

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