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Mucinous borderline ovarian tumour with torsion and micro-invasion and associated with high serum level of carbohydrate antigen 19-9: a case report

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Carbohydrate antigen 19-9 (CA19-9) is a tumour marker elevated in many gastrointestinal malignancies as well as in mucinous tumours of ovary, mature cystic teratomas and various other benign lesions. We present a case of mucinous borderline ovarian tumour with multifocal micro-invasion and torsion and associated with very high levels of serum CA19-9 in a 41-year-old woman. This report highlights that tumour markers and radiological findings may not be accurate in diagnosing the histological sub-type of ovarian tumour.

Keywords: Antigens, tumor-associated, carbohydrate; Necrosis; Ovarian neoplasms; Ovarian torsion

Introduction

Carbohydrate antigen 19-9 (CA19-9) is a tumour marker that is often elevated in gastrointestinal tract neoplasms of pancreatic, colorectal, and biliary origin as well as in ovarian mucinous neoplasms and many benign pathologies[1]. We present a case of mucinous borderline ovarian tumour with multifocal micro-invasion and torsion and associated with very high levels of serum CA19-9 in a 41-year-old woman. Tumour markers must be taken into consideration together with clinical presentation and findings of blood tests and imaging[2]. Careful clinical judgement is important when dealing with emergency admission to manage emergency complications such as torsion.

Case presentation

In November 2020, a 41-year-old woman was admitted to a gynaecological ward with a 2-day history of sudden onset abdominal pain and vomiting. She was severely obese (body mass index, 40 kg/m^2) and had regular monthly periods. She was para 3 with all normal vaginal deliveries. All her previous cervical smears were unremarkable. She had had an open appendicectomy. On examination, a solid mass was palpable in the left lower abdomen with associated rebound tenderness. Her pulse rate was 78/minute, systolic/diastolic blood pressure were 106/60, body temperature was 37.1°C, respiratory rate was 17/minute, and oxygen saturation was 98%. All were within normal ranges.

Computed tomography showed a 15-cm solid cystic mass arising from the left ovary highly suspicious of malignancy. There was no evidence of omental or peritoneal disease, and the abdominopelvic viscera were unremarkable, with no malignant ascites or pelvic, inguinal, or para-aortic lymphadenopathy (Figure 1). Serum level of CA125 was 179 U/mL (reference range, 0-35 U/mL) and serum level of CA19-9 was 17 350 U/mL (reference range, 0-37 U/mL). Haemoglobin levels had decreased from 124 g/L to 94 g/L over 2 days. The remaining blood test results and serum tumour markers were within normal limits: white blood cell count, 8 × 10^9/L; C-reactive protein, 2.60 mg/L; β-human chorionic gonadotropin, <5 IU/L; lactate dehydrogenase, 185 U/L; carcinoembryonic antigen, 2.9 ng/ml; and α-fetoprotein, <1.7 KIU/L.

With a clinical suspicion of ovarian torsion, the patient was taken to the emergency theatre for laparoscopy and potential laparotomy. A twisted large necrotic left ovarian cyst was noted on the left abdominal cavity,

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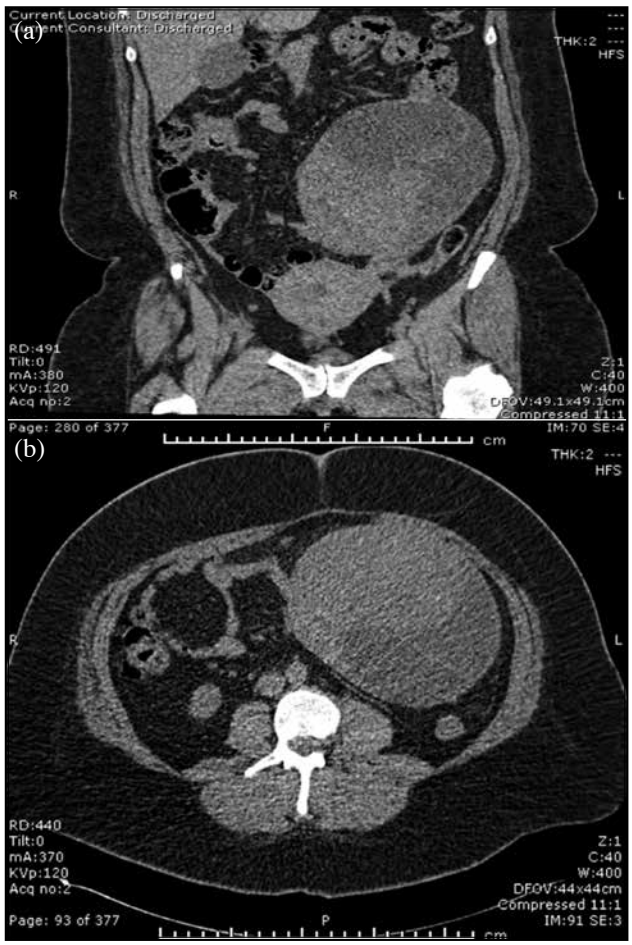

Figure 1. Computed tomography of the abdominopelvic area showing the left ovarian mass in (a) sagittal and (b) transverse view.

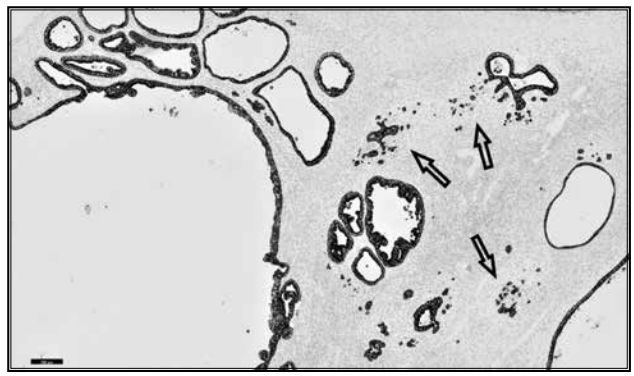

Figure 2. Cytokeratin 7 immunohistochemistry of the mucinous borderline tumour with multifocal micro-invasion: non-invasive borderline tumour is on the left and multiple foci of stromal invasion are on the right (arrows).

with spontaneous rupture resulting in about 200 mL of free haemorrhagic fluid in the pelvis. Fluid was aspirated laparoscopically and sent for cytology, followed by left salpingo-oophorectomy and omental biopsy through a transverse incision laparotomy. The right ovary and fallopian tube, omentum, peritoneum, liver, and diaphragm appeared to be unremarkable, with no signs of metastatic disease.

At 10 days after surgery, the CA125 level decreased to 91.7 U/mL and the CA19-9 level decreased to 289.5 U/mL, with a haemoglobin level of 107 g/L. Histology revealed a mucinous borderline tumour of the ovary with multifocal micro-invasion (Figure 2). Immunohistochemically, the tumour was strongly positive for CA19-9 and showed patchy ischaemic changes and infarction consistent with torsion. None of the invasive foci was >5 mm in linear extent. No tumour was identified in the omental biopsy or peritoneal fluid. The tumour was regarded as FIGO stage 1C2. The patient underwent total abdominal hysterectomy and right salpingo-oophorectomy with omental biopsy at a tertiary oncology centre. Biopsy result was unremarkable with no evidence of neoplasia.

Discussion

Epithelial ovarian cancers are considered the most common type of ovarian cancer, accounting for about 90% of cases. More than 75% of epithelial ovarian cancers are of the serous type, whereas mucinous, endometrioid, clear cell, Brenner, and undifferentiated lineage types are less common[3]. Failure in early detection can lead to high mortality rate[3].

Mucinous epithelial ovarian tumours are formed by cells that resemble those of the endocervical epithelium or, more frequently, those of the intestinal epithelium. Benign mucinous tumours are multiloculated cysts that are filled with opaque, dense, mucoid material and account for up to 25% of all benign ovarian neoplasms and 75% to 85% of all mucinous ovarian tumours[4]. Borderline mucinous tumours account for 10% to 15% of all ovarian mucinous tumours and are similar to benign mucinous tumours on gross pathological examination, but they may have solid regions and papillae projecting into the cyst locules[4]. These tumours are atypically proliferating and are intermediate in their nature with a low possibility of invasive transformation; they can occur in patients across a wide age range including paediatric patients and are the most common subtype of borderline tumour in Asia[4]. After surgical treatment, tumour recurrence and metastasis are rare, unless the tumours arise in a teratoma or are associated with pseudomyxoma peritonei; the prognosis is generally favourable[4]. Compared with borderline tumours, mucinous

carcinomas account for 5% to 10% of all malignant ovarian neoplasms and tend to contain more papillary projections within the cyst cavities, larger solid areas, and larger areas of necrosis and haemorrhage[4]. In contrast to serous tumours, for mucinous tumours, diagnosing benign type from borderline or malignant type is more challenging because of their typical large size and great variation in the degree of differentiation within individual tumours[5].

Mucinous borderline tumours with microinvasion are defined by stromal invasion measuring <5 mm in the greatest linear dimension and consisting of single cells, clusters, or small foci of confluent glandular or cribriform growth, regardless of the number of microinvasive foci[6]. Microinvasion has been reported in 4% to 18% of mucinous borderline tumours and has no adverse effect on prognosis[6]. Nonetheless, additional sampling and immunohistochemical testing are recommended to exclude frankly invasive adenocarcinoma[6]. Borderline ovarian tumours with microinvasion may lead to earlier relapses, but the overall incidence of relapses and overall survival do not differ significantly from those without microinvasion[7]. Fertility-sparing surgery is feasible, but strict follow-up is suggested[7].

Tumour markers have been used widely to determine therapeutic efficacy, detect recurrence, and predict prognosis in known cancers. Markers for ovarian cancer include CA125, CA15-3, CEA, and CA19-9[3]. CA125 contributes to early diagnosis of epithelial ovarian cancers by detecting an antigenic site on MUC16. However, CA125 is not frequently elevated in most primary ovarian mucinous neoplasms, and thus CA19-9 should be used instead[1,8]. In mucinous tumours, CA19-9 is more frequently elevated than CA125 or CEA (57% vs 15% vs 11%) and should be used for follow-up[9]. CA19-9 is a monosialoganglioside glycoprotein antigen related to Lewis blood group protein and is present in epithelial tissues of the pancreas and hepatobiliary tree and is often secreted by mucinous tumours of gastrointestinal tract including those of pancreas and biliary tree[1,2]. The reference range for CA19-9 is 0 to 37 U/mL. CA19-9 can be elevated in many conditions (Table)[10].

Compared with CA125 alone, CA19-9 and CA125 combined do not significantly improve detection of malignant adnexal masses[11]. Nonetheless, higher CA19-9 levels are helpful in differentiating metastatic tumours from primary ovarian malignancy[11]. Markedly raised CA19-9 levels of >10000 U/mL are almost exclusively seen in advanced stages of malignancy[12]. One study showed no correlation between serum CA19-9 levels and subtypes of primary ovarian mucinous tumours but a weak correlation between tumour size and serum CA19-9 levels[13]. In contrast, another study reported that CA19-9 was more frequently elevated in mucinous borderline and malignant tumours than in benign tumours, and therefore tumour pathology was the only independent factor for serum CA19-9 level elevation, regardless of tumour size or CA125 level elevation[8]. Nonetheless, there are case reports of high CA19-9 levels associated with benign mucinous cystadenoma[1].

In mature cystic teratomas, CA19-9 levels are also elevated[14], and this is correlated with larger tumour size and higher rate of ovarian torsion[15,16] but not with bilateral tumour involvement[16]. Nonetheless, one study reported correlation between tumour diameter and bilaterality and the highest CA19-9 level of 25590 U/mL in a case[17].

Table. Differential diagnoses in carbohydrate antigen 19-9 level elevation

Differential diagnosis
Hepatopancreaticobiliary malignancies
Cholangiocarcinoma
Pancreatic adenocarcinoma
Hepatocellular carcinoma
Other malignancies
Colorectal carcinoma
Gastric carcinoma
Bronchogenic carcinoma
Ovarian carcinoma
Non-malignant hepatopancreaticobiliary conditions
Acute and chronic pancreatitis
Cholecystitis
Cirrhosis
Chronic and alcoholic hepatitis
Acute hepatic necrosis
Gallstones
Non-malignant obstructive jaundice
Non-hepatobiliary conditions
Lung disorders (pneumonia, tuberculosis, cystic fibrosis)
Pelvic inflammatory disease
Hashimoto thyroiditis
Rheumatoid arthritis
Renal failure
Systemic lupus erythematosus

In dermoid cysts, elevated CA19-9 levels may be caused by rupture and leakage from the cyst wall into the blood stream or a weakened cyst wall in a larger diameter cyst[18], may be related to torsion of the ovary and to the extent of the necrosis[14], and may be an indicator for early surgical intervention owing to higher risks of torsion and larger cyst size[19].

In our patient, such high levels of CA19-9 raised suspicion of malignancy although it turned out to be a borderline mucinous tumour (rather than a frank mucinous adenocarcinoma) with torsion and multifocal micro-invasion. Immunohistochemistry revealed that the cyst epithelium was strongly positive for CA19-9. The cyst was quite large with a weakened cyst wall leading to rupture and had torsion and necrosis. We hypothesise that these could be the causes of extremely high levels of serum CA19-9. Clinically, ovarian torsion was not suspected initially owing to the abnormally high levels of serum CA19-9.

Serum tumour markers are helpful in initial diagnosis of cancer and can be used to flag further investigation of neoplasia. Nonetheless, the whole clinical picture should be taken into account, including symptoms and clinical and imaging findings, for accurate diagnoses and appropriate management.

Declaration

The authors have no conflicts of interest to disclose.

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