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The diagnostic conundrum of chronic ectopic pregnancy: A case report

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ABSTRACT

Chronic ectopic pregnancy (CEP) is a rare condition caused by implantation of trophoblastic tissue in the fallopian tube, which causes protracted tissue destruction at the site of attachment. The process of minor rupture and bleeding results in chronic inflammation, giving rise to a haematocele which often resembles a pelvic mass. Unlike ectopic pregnancy, the level of serum human chorionic gonadotropin (hCG) in patients with CEP is usually low or undetectable as chorionic villi are generally sparse. Therefore, CEP often poses a specific diagnostic challenge for clinicians, as both biochemical markers and imaging modalities are unreliable in its diagnosis. Nevertheless, in cases where serum bhCG is significantly elevated in the presence of a large pelvic mass, the possibility of a malignant ovarian germ cell tumour (MOGCT) must be considered and investigated appropriately. Here, we present a rare case of a young woman who was referred to a gynaecological cancer centre with an acute abdomen for the treatment of MOGCT but was subsequently diagnosed with CEP following laparotomy. In our case report, we highlight the diagnostic conundrum of CEP and MOGCT and discuss the surgical challenges both these conditions pose, especially as many of these women are young and desire fertility preservation.

1. Introduction

An ectopic pregnancy is a pregnancy developing outside the uterine cavity, which, in over 95% of cases, implants in the fallopian tube, most commonly the ampullary region [1]. The incidence of ectopic pregnancy in the UK is reportedly in the range of 11 per 1000 pregnancies, with a mortality of 0.2 per 1000 cases [2]. Laparoscopy remains the gold standard modality for diagnosing and managing ectopic pregnancy; however, advances in ultrasonic imaging have significantly improved the detection rate of ectopic pregnancy, offering patients the option of non-surgical treatment.

In contrast, a chronic ectopic pregnancy (CEP) occurs when trophoblastic tissue invades the implanted structure, causing a protracted destruction at the site of attachment, resulting in repeated rupture and minor bleeding. Over time, a haematocele is formed, leading to an inflammatory reaction and the generation of chronic pelvic adhesions which resemble a complex pelvic mass [3]. Chronic ectopic pregnancy is extremely rare in developed countries, such as the UK, due to the presence of a robust early-pregnancy care service. Serum human chorionic gonadotropin (hCG) is a reliable marker used to manage ectopic pregnancy; however, in CEP the chorionic villi are usually sparse, and therefore the hCG level is typically low or negative [4], causing diagnostic confusion and delay. The prevalence of chronic ectopic pregnancy varies widely in the literature due to the different diagnostic criteria to define it [5].

To this end, we present a rare case of a young woman who was referred to a gynaecological cancer centre for the treatment of germ cell tumour but was diagnosed histologically with CEP following laparotomy.

2. Case

A 26-year-old woman presented to the Emergency Department with a gradual onset of right lower abdominal pain and distension which had rapidly worsened over the preceding four weeks. She had no past surgical or medical history and was primiparous, having had one termination six years previously. Her previous cervical smear test was normal, and she had been taking a combined oral contraceptive pill for the past ten years, stopping six weeks prior to the onset of her symptoms. A clinical examination revealed a tender 10 cm pelvic mass on the right iliac fossa with a small amount of ascites. Her urinary bhCG was positive, and the serum bhCG level was recorded as 3951 mIU/ml. An urgent pelvic ultrasound scan revealed a large right adnexal mass with a moderate amount of free fluid.

A germ cell tumour was suspected, and the patient underwent further blood tests for AFP and LDH, which were < 1 KU/L and 337 U/L, respectively. Her Ca 125 was 12 KU/L. An MRI scan of the pelvis and abdomen revealed a complex mass measuring 7.0 × 9.9 × 3.7 cm arising

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from the right adnexa with evidence of haemorrhage. No metastatic disease was detected, and a staging CT scan confirmed this.

The patient was urgently referred to a gynaecological oncology surgeon for a suspected ruptured germ cell tumour, one of the few gynaecological oncology emergencies requiring urgent laparotomy and cancer staging. The patient underwent a midline laparotomy, and there was evidence of chronic inflammation with extensive small bowel and caecal adhesions to the right adnexal mass. The appendix had adhered to the invading mass, and extensive adhesiolysis was required to release the bowel loops. Subsequently, she underwent a right salpingo-oophorectomy, omental biopsy and appendicectomy performed by K.S. and J.Y. In surgery, the mass did not resemble a malignant tumour but rather a "sterile" chronic inflammatory mass. On macroscopic examination, the mass consisted of a normal ovary and measured 60 mm × 45 mm × 50 mm. It was pale brown in colour with haemorrhagic areas and had an irregular and disrupted external surface. The cut-surface was cystic and contained blood clot and pale haemorrhagic tissue (Fig. 1). Microscopic examination showed a dilated fallopian tube containing blood clot and trophoblast along with infarcted and viable chorionic villi. There was a prominent acute-on-chronic inflammation seen within the tubal mucosa and an implantation site seen focally within the tube wall. In addition, the wall showed marked fibrosis with areas of haemorrhage and scattered inflammatory cells. Foci of mesothelial proliferation were observed on the external surface of the tube. No fetal somatic tissue or features of gestational trophoblastic disease were identified. The features were in keeping with a chronic tubal ectopic pregnancy (Fig. 2), with no evidence of gestational trophoblastic disease or fetal somatic tissue, indicating that ectopic pregnancy was unlikely. The patient had an uneventful recovery from surgery, and her subsequent post-operative serum bhCG level was undetectable.

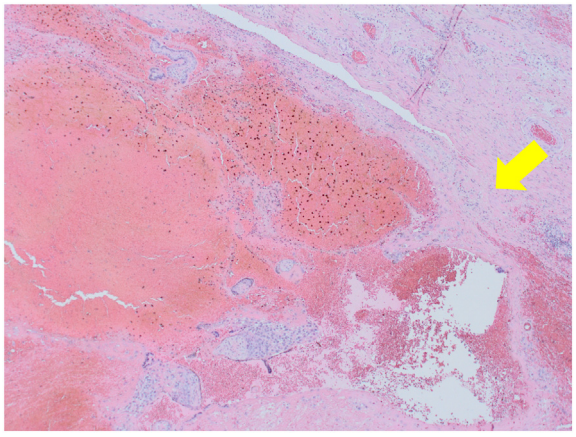

Fig. 2. Microscopic image showing dilated Fallopian tube containing blood clot, trophoblast and chorionic villi within the lumen. The implantation site is seen focally within the tube wall (arrow).

3. Discussion

Our case highlighted the diagnostic conundrum of CEP and malignant ovarian germ cell tumours (MOGCT), as the patient presented with a large pelvic mass and a positive serum bhCG (Table 1). In general, CEP is rare in developed countries and patients present with subtle and non-specific clinical signs or symptoms. In most cases, the serum bhCG level is either very low or negative. In our patient, the level of bhCG was significantly elevated which prompted the provisional diagnosis of MOGCT.

MOGCT is an umbrella term encompassing tumours derived from germ cells, and includes dysgerminomas, immature teratomas, embryonal tumours and endodermal sinus tumours. They account for only 1.5% of ovarian cancers and are sensitive to chemotherapy, with cure rates at least 80–90%, if diagnosed early [6]. The current chemotherapy regime used is etoposide, bleomycin and cisplatin [7]. MOGCTs tend to affect younger women, particularly adolescents and those in early adulthood, with 82% of cases reported before 54 years of age [6]. Investigations for MOGCT include measurements of serum tumour markers, namely alpha-fetoprotein (AFP) and hCG. These markers have been shown to correlate with disease stage, and increasing values are associated with poorer survival. Although the Royal College of Obstetrics and Gynaecology [8] advises the inclusion of the marker lactate dehydrogenase (LDH), this has not been sufficiently investigated or validated to advocate its routine use for the diagnosis of MOGCT [9].

MOGCT can present with acute abdominal pain and swelling, as observed in our patient. The primary radiological investigation is transvaginal ultrasound scan (USS), which would identify a solid pelvic mass, again, findings which resemble our case. Progression to MRI may be advised to better visualise the mass prior to surgery, and a CT scan of the chest, abdomen and pelvis would be necessary to assess metastatic spread [10].

Currently, the gold standard treatment for MOGCT is unilateral salpingo-oophorectomy, omental biopsy, peritoneal washings and lymph node assessment to remove any enlarged lymph nodes [10], an operation which was intended for this patient. The surgical aim is to adequately stage the disease whilst preserving fertility, as most of these women are young. Although most cases of pure dysgerminomas are

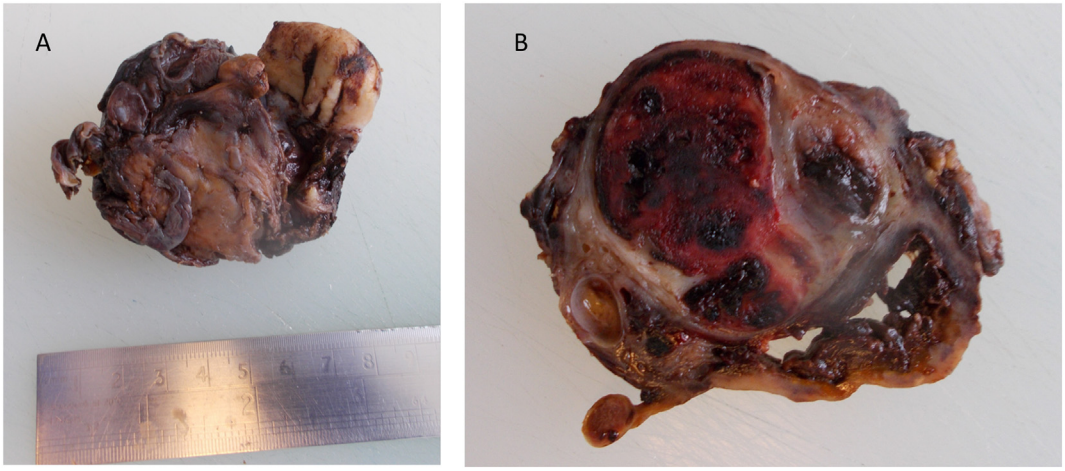

Fig. 1. Macroscopic images showing (A) mass measuring 60 × 45 × 50 mm with an irregular, pale brown and haemorrhagic external surface. (B) Cystic cut-surface with blood clot and pale haemorrhagic tissue within the cystic space. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
Comparison of presentation and clinical findings of chronic ectopic pregnancy (CEP) and malignant ovarian germ cell tumours (MOCGT).

	CEP	MOGCT
Aetiology	Women of child-bearing age	Women of child-bearing age
Symptoms	Vague abdominal/pelvic pain	Vague abdominal pain
	Vaginal bleeding	Bloating/pressure in abdomen
	Preceeding amenorrhoea	Irregular periods
	May develop pyrexia	May develop pyrexia
Signs	Palpable pelvic mass, likely fixed to pelvis	Palpable pelvic mass, likely fixed to pelvis
	Abdominal distension	Abdominal distension
Investigations	bhCG may be low or negative	bhCG raised
	Normal tumour markers including LDH and αFP	Raised tumour markers including LDH and αFP
	Ultrasound: complex pelvic mass	Ultrasound: complex pelvic mass
	CT no evidence of metastasis	CT: 70% have disease confined to pelvis at presentation, may show distant spread
Follow up	Serial bhCG	Monthly clinic follow up with serum tumour markers for first 1 year reducing to 6 month by 5 years and annually from 7 years
	Discharge when negative	Radiological follow up with MRI initially the pelvic USS and chest X-ray every 4 months for first 2 years, reducing frequency of imaging as disease-free interval increases

unilateral, occurring in 85% of cases [10], women should be adequately counselled for bilateral oophorectomy in case metastatic disease or a concurrent MOGCT is found on the contralateral ovary. Following surgery, women with MOGCT are followed up with serial alpha-fetoprotein and hCG [10], and, due to its rarity, most patients are referred to the regional specialist centre for consideration of adjuvant chemotherapy.

Another frequent diagnostic confusion with CEP is pelvic inflammatory disease (PID). Patients with CEP can present with vaginal bleeding or discharge persisting over several weeks and may give a history of preceding amenorrhoea and pyrexia. In addition, inflammatory markers in the blood are often elevated because of a chronic inflammatory process in the tissues surrounding the ectopic pregnancy. Thus, it is not surprising that these patients can easily be misdiagnosed with PID or tubo-ovarian abscess. Furthermore, radiological imaging often fails to distinguish CEP from other pelvic masses, as it is often visualised as a non-homogenous echo pattern mass with signs of recurrent bleeding. Rarely the conceptus may be seen within the mass [11], but this is extremely uncommon, for reasons described above. Currently, most cases of CEP are diagnosed incidentally with the histological finding of trophoblastic tissue within a chronic inflammatory mass.

Apart from diagnostic challenges, CEP also poses surgical challenges to gynaecologists due to extensive adhesions between the main mass to surrounding vital structures, most notably to the large and small bowel, caused by chronic inflammation. Surgical morbidity can be significant, as women are at risk of sustaining bowel injuries requiring bowel resection. It remains unclear whether CEP has been managed successfully with methotrexate, but owing to the difficulty in diagnosing the disease, the medical approach is not usually considered first. Given the underlying pathophysiology of a chronic ectopic pregnancy, one could surmise that methotrexate would not be particularly effective owing to the few viable chorionic villi, providing few rapidly dividing cells that would be susceptible to treatment such as methotrexate. Moreover, methotrexate administration for an ectopic pregnancy has been attributed to the development of CEP [12,13], reiterating the 'burnt-out' slow-growing nature of this condition. In our case, intra-operatively, we suspected that the "tumour" was not MOGCT but an inflammatory mass. However, we were not able to confidently exclude MOGCT at the time of surgery and were obliged to undertake an operation which follows the MOGCT paradigm. If the frozen histological section had been available, we might have changed the approach to our management. Nevertheless, given that the mass was bleeding and causing significant symptoms, it had to be removed as a matter of urgency. Until an accurate non-surgical diagnosis of CEP can be established, we believe that surgical management remains the gold standard treatment for this rare condition.

To our knowledge, this is one of the few CEP cases reported with a significantly elevated serum bhCG and a pelvic mass which radiologically resembles a MOGCT. The rarity of this disease, together with the diagnostic dilemma and surgical challenges which it poses, makes CEP challenging to manage. In cases where young women of child-bearing age present with a pelvic mass and an elevated bhCG, MOGCT should remain the primary differential diagnosis, and these patients should be referred promptly to a tertiary gynaecological oncology centre for management.

Contributors

Danielle O'Neill wrote the paper and performed the literature search.

Rachel Pounds helped with the literature search.

Josefa Vella was the histopathologist involved in providing the final diagnosis.

Kavita Singh was involved in the case.

Jason Yap was involved in the case.

All authors helped in editing the paper.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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Patient Consent

Obtained.

Provenance and Peer Review

This case report was peer reviewed.

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