Management with fertility preservation of an ovarian juvenile granulosa cell tumour presenting with retroperitoneal spread and bilateral ureteric obstruction

Introduction

Metastatic and recurrent ovarian juvenile granulosa cell tumours in young women are an uncommon condition.\(^1,2\) Primary management in young patients includes surgery with subsequent chemotherapy in selected cases. Fertility-preservation surgery may be possible, while still achieving appropriate cytoreduction and staging procedures. Retroperitoneal spread to lymph nodes is rare and lymphadenectomy is not routinely recommended.\(^3\) Recurrent disease or persistent disease may require further surgery and once again, it may be possible to preserve fertility without compromising oncological outcome.

Case history

An 18-year-old nulliparous patient presented with a 24-hour history of nausea and vomiting. She reported experiencing abdominal pain for a week. The pain was exacerbated with the onset of nausea and vomiting. The patient noted no change in bowel motions and reported a normal menstrual cycle since menarche at 14 years. A clinical examination showed signs of a dehydrated patient with tachycardia. An abdominal examination revealed a 28-week mass. On palpation, the mass was fixed and tender. Bowel sounds were present. A gynaecological examination disclosed a virgo intactum. An ultrasound uncovered a semi-solid abdominal mass with bilateral hydronephrosis and ascites.

Management

Management included admission, rehydration and analgesia. Blood tests showed a raised white cell count, a raised erythrocyte sedimentation rate, a raised C-reactive protein and haemoglobin of 10.1 g/dl. Beta human chorionic gonadotropin (hCG), lactate dehydrogenase (LDH) and \(\alpha\)-fetoprotein levels were normal. A computed tomography scan revealed a large abdominal tumour with solid and cystic areas. The uterus was displaced to the left and the origin of the tumour could not be documented. Bilateral hydronephrosis, more pronounced on the right, was present, and generalised ascites with enlarged lymph nodes below the level of the renal vessels were noticed. There was loss of tissue planes between the right psoas muscle and the tumour, as well as loss of plane between the tumour and the right internal iliac vessels (Figure 1).

Figure 1: Sagital section with hydronephrosis (black arrow) and mass (white arrows)
Preoperative hydronephrosis, ascites and retroperitoneal disease favoured a malignant tumour. The normal serum tumour markers made a malignant germ cell tumour unlikely. The patient was counselled and consented to cytoreductive surgery without preservation of fertility, or with preservation of fertility dependant on operative findings.

During surgery, ascites and a large omental tumour, adherent to the anterior abdominal wall and encasing the small bowel, was encountered. The omentum was freed with sharp dissection from the anterior abdominal wall, and an infracolic omentectomy was performed. Pelvic access was obtained by sharp dissection between the mass and the anterior abdominal wall. The right retroperitoneal plane was entered using the technique as described by Hudson, and the right-sided hydroureter freed to the level of the uterine artery. The right-sided obturator fossa was filled with the tumour, and it was removed with sharp dissection from the underlying blood vessels. The intact right ovary could be identified separate from the mass. A tumour, adherent to the bladder, was freed with sharp dissection. The left ovary was totally displaced by the tumour. The left retroperitoneal space was entered and the left hydroureter freed to the level of the uterine artery. The tumour displaced the entire left ovary and a left-sided salpingo-oophorectomy was performed. Further examination of the abdomen revealed a small bowel loop encased in the tumour. A resection with anastomosis was performed.

On completion of the surgery, the only residual tumour was in the subdiaphragmatic areas with small (less than 1 mm) peritoneal seedlings. The surgical result was optimal cytoreduction of a tumour arising within, displacing the left ovary and spreading intraperitoneally, retroperitoneally and to the omentum.

Histology confirmed a juvenile granulosa cell tumour (JGCT) (Figure 2). Immunohistochemistry was positive for S100, vimentin, inhibin and calretin. Epithelial membrane antigen (EMA), CD30, beta hCG, chromagranin and α-fetoprotein immunohistochemistry were negative. Submucosal small bowel involvement with tumour embolus formation was documented. The bladder’s muscularis propria was infiltrated by the tumour.

Subsequent to histological confirmation, blood levels of oestradiol and Müllerian inhibiting factor (MIF) were normal. The patient received six courses of bleomycin, etoposide, and cisplatin (BEP) chemotherapy. At six months follow-up, an asymptomatic, 35.5 mm x 34 mm right-sided pelvic solid mass was diagnosed by ultrasound. The mass was completely resected at relaparotomy. Histology confirmed a JGCT. The patient underwent six courses of paclitaxel and carboplatin (PC) and was in remission at three months follow-up. She reported a normal menstrual cycle.

**Discussion**

Granulosa cell tumours account for 2% of ovarian tumours, and can be divided into adult (95%) and juvenile (5%) histological types. JGCTs occur predominantly in women under the age of 30. A nulliparous state is seen in 30%. In up to 80% of cases, the tumours are associated with isosexual pseudopuberty. Virilising symptoms, hirsutism and oligomenorrhea occur in 3%. Oestrogen production results in endometrial hyperplasia (30%) and endometrial adenocarcinoma in 8% of cases. The majority of juvenile tumours present with unilateral localised disease. A clinical examination reveals palpable masses in up to 95% of cases and ascites in 10%. The differential diagnosis of solid ovarian masses in young women includes germ cell tumours and sex cord stromal tumours. Malignant germ cell tumours may be associated with raised tumour markers, e.g. beta hCG, LDH and α-fetoprotein.

Tumour markers can be useful in the management of primary or recurrent JGCTs. Raised inhibin distinguishes stromal ovarian tumours from other ovarian neoplasms, but is not specific to granulosa cell tumours. Raised serum oestradiol is present in approximately 70% of cases. MIF and calretin are potential serum markers. In the current case, serum oestradiol and MIF levels were normal. Initial surgery in younger women includes fertility-preservation procedures, e.g. unilateral salpingo-oophorectomy. The preservation of the uterus and right ovary in the current case represents a unique approach to preserve fertility in advanced-stage disease. Surgical staging is limited to intraperitoneal procedures and...
lymphadenectomy should be omitted. Brown et al reported 111 cases of completely and partially staged patients with no lymph node involvement. The authors reported that 67% of cases were diagnosed as stage I, and 22% as stage III disease. The current case presented with widespread disease and this is unusual. Abu-Rustum and Thrall documented similar findings with regard to pelvic and paraaortic lymphadenectomy, thus, as part of initial staging, it is not warranted. Metastatic disease requires optimal cytoreductive surgery. Prognosis links directly to a residual tumour on completion of the surgery. Lymphadenectomy may be indicated in cases of bulky lymph nodes. Features that are associated with poor prognosis include advanced-stage disease, tumours of more than 5 cm in diameter and high mitotic count (more than 10 human papillomavirus types) with nuclear atypia and the absence of Call-Exner bodies.

Chemotherapy is indicated in advanced and recurrent disease. Currently, the Gynaecology Oncology Group is performing a randomised control trial that compares BEP to PC in this scenario. In disease recurrence subsequent to primary chemotherapy, Tao et al reported antiangiogenic activity in eight cases that were treated with bevacizumab. Hormonal suppression treatment with aromatase inhibitors, megestrol and tamoxifen, and a gonadotropin-releasing hormone (GnRH) antagonist in recurrent ovarian granulosa cell tumours has been described with conflicting reports of efficacy. Chemotherapy has the potential for premature ovarian failure. Whitehead et al reported a 100% return of menstruation in patients who received BEP chemotherapy. Fertility-preservation surgery and chemotherapy with subsequent normal pregnancy has been documented.

Conclusion

The current case of ovarian JGCT illustrates that retroperitoneal spread of disease, even if uncommon, may occur. This spread resulted in hydronephrosis. The case further illustrates that lymphadenectomy was needed as a debulking procedure and that tailored surgery with chemotherapy resulted in the preservation of fertility.

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