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## CASE REPORT

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# Malignant Mixed Germ Cell Tumour of the Ovary in a 10-year-old Girl

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### ABSTRACT

*Ovarian neoplasm is relatively rare in the paediatric population compared with adults, but it is occasionally found in older children and adolescents presenting with abdominal distension. Germ cell tumours are the most common type of malignant ovarian neoplasms in children and adolescents. These tumours expand locally and metastasise through vascular and lymphatic invasion. Imaging is important in the initial diagnosis to assess the extent of the disease. This report describes a girl with malignant mixed germ cell tumour of the right ovary, who presented with abdominal swelling for 1 month. The preoperative radiological diagnosis was a metastatic germ cell tumour. Only partial debulking of the tumour was performed due to its extensiveness. The subsequent histological result was compatible with a mixed germ cell tumour, with components of yolk sac tumour and immature teratoma. Despite early postoperative chemotherapy, the patient developed multiple tumour-related complications and died soon after surgery. This report illustrates the aggressiveness of this tumour and emphasises the importance of early diagnosis and treatment.*

**Key Words:** Child, Endodermal sinus tumor, Neoplasms, germ cell and embryonal, Ovarian neoplasms, Teratoma

### INTRODUCTION

Germ cell tumours are the most common ovarian neoplasms affecting children and young adults. Malignant mixed germ cell tumour is a type of germ cell tumour that consists of 2 or more malignant components.<sup>1</sup> Besides being locally aggressive, these tumours commonly metastasise to the liver, lung, peritoneum, omentum, and lymph nodes. The radiological appearance of a mixed germ cell tumour varies according to its individual constituents, but is mostly a heterogeneous mass with predominantly solid components. Surgery and neoadjuvant or postoperative adjuvant chemotherapy provide cure for early disease. However, large tumours or advanced disease have a poor prognosis.

This report describes a 10-year-old girl with malignant mixed germ cell tumour who died 2 months after initial symptom presentation to illustrate the aggressive

behaviour of this tumour and the importance of early diagnosis and treatment. Radiological features that may help establish the diagnosis of this neoplasm are also highlighted.

### CASE REPORT

A 10-year-old girl with good past health was admitted to the United Christian Hospital, Hong Kong, in 2007 with constipation and abdominal swelling for 1 month. She also had a fever, poor appetite, and weight loss. Physical examination showed a large abdominal mass. Serum  $\alpha$ -foetoprotein (AFP) level was 45,812  $\mu$ g/L (normal range, <10  $\mu$ g/L), cancer antigen-125 was 473 U/mL (normal range, <35 U/mL), and haemoglobin was 61 g/L (normal range, 110-130 g/L). Serum human chorionic gonadotropin (hCG) was within normal limits.

Abdominal radiograph showed bowels loaded with faeces but no soft tissue mass. Plain and post-contrast enhanced computed tomography (CT) of the abdomen and pelvis revealed a large heterogeneous pelvic mass occupying the pouch of Douglas, displacing the urinary bladder and rectum (Figure 1). The mass was in close proximity to a large calcified fat-containing intraperitoneal tumour

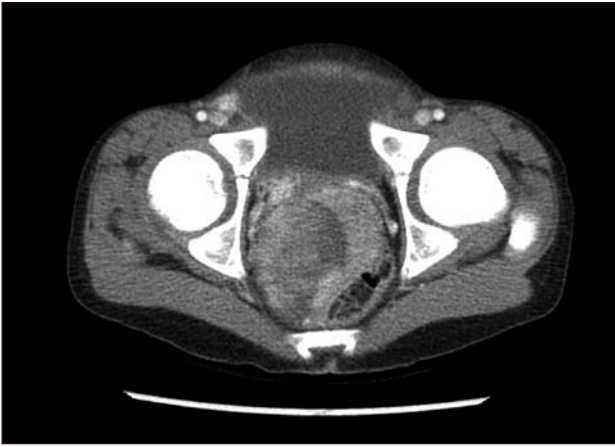
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**Figure 1.** Post-contrast computed tomography shows a large heterogeneous mass in the pouch of Douglas.



**Figure 2.** Plain computed tomography shows a large calcified fat-containing intra-abdominal mass.

occupying the abdomen and extending to the level of the origin of the coeliac trunk (Figure 2). Adjacent structures, including both ureters, were compressed resulting in hydronephrosis (Figure 3). A 2-cm hypodense lesion at the dome of the liver was compatible with metastasis. Multiple peritoneal deposits and a small amount of ascites were also evident. The ovaries did not have a normal appearance. Therefore, a clinical and radiological diagnosis of metastatic intra-abdominal neoplasm, probably germ cell tumour arising from the ovary, was made.

Laparotomy revealed a 20-cm right ovarian tumour with extension into the pouch of Douglas and extensive peritoneal deposits. Right oophorectomy, omentectomy, and debulking of the intra-abdominal tumour were performed. Due to the high surgical risk for further dissection into the pelvic region, the presacral tumour was not removed.



**Figure 3.** Post-contrast computed tomography shows mild bilateral hydronephrosis due to compression of the ureters by an intra-abdominal tumour. A small amount of ascites is also present.

Histopathological examination of the ovarian mass showed various architectural patterns with the presence of Schiller-Duval bodies, which is characteristic of yolk sac tumour. Prominent areas of haemorrhage and necrosis were also observed. Lymphovascular permeation was noted in the mucosa of the right fallopian tube. Other areas of the tumour showed a mixture of epithelium, cartilage, smooth muscle, skeletal muscle, and adipose and vascular tissues, most of which exhibited immaturity, with cellular primitive mesenchyme. Primitive neuroectoderm was not present. The overall pathological features were compatible with malignant mixed germ cell tumour with components of yolk sac tumour and immature teratoma.

Chemotherapy of carboplatin, etoposide, and bleomycin was started 2 weeks after the operation. The patient developed seizures, deterioration in consciousness, and sepsis immediately after the first course of chemotherapy. CT of the abdomen showed extensive tumour recurrence in the peritoneum. Magnetic resonance imaging of the brain showed non-enhancing asymmetrical T2 hyperintense signals over the subcortical white matter, right occipital lobe, and both parietal lobes. Chemotherapy was stopped and the patient received supportive treatment. Her condition further deteriorated. She subsequently developed cardiac tamponade and intracerebral haemorrhage, and died. Postmortem examination showed tumour deposits in the pericardium and fungal pericarditis. Intracerebral haemorrhage was confirmed but no underlying cause could be identified.

## DISCUSSION

Ovarian tumours are classified according to the cell of origin into epithelial tumours, germ cell tumours, sex cord–stromal cell tumours, and metastatic tumours.<sup>2</sup> Tumours of germ cell origin are the second most common group of ovarian neoplasms among all age groups, representing 15% to 20% of ovarian neoplasms. However, germ cell tumours are the most common ovarian neoplasms in children and young adults. Germ cell tumours are derived from the primitive germ cells of the embryonic gonad. These tumours include dysgerminoma, yolk sac tumour, embryonal carcinoma, mature teratoma, immature teratoma, choriocarcinoma, and malignant mixed germ cell tumours. All germ cell tumours are malignant except for mature teratoma.

The average age of presentation of patients with germ cell tumours is 13.8 years (range, 4 to 27 years).<sup>3</sup> The presentation includes abdominal mass, abdominal pain, and fever. Serum AFP and hCG levels may be elevated. The average tumour diameter at presentation is 15.5 cm. Germ cell tumours demonstrate variable internal consistency, ranging from completely solid to largely cystic. In children and adolescents, approximately one-third of ovarian germ cell tumours are malignant, whereas the vast majority are benign in adults.

Malignant mixed germ cell tumours are tumours that consist of more than 1 malignant germ cell component. The appearance of malignant mixed germ cell tumour varies according to the individual constituents, but is generally a complex, predominantly solid tumour.<sup>4,5</sup>

Radiological examination of a germ cell tumour shows a complex mass with solid and cystic components. Some of the imaging features can be used to establish a diagnosis, but as different types of germ cell tumours show overlapping radiological appearances, the definitive diagnosis is made by histological examination.

The calcifications present in immature teratomas are characteristically scattered throughout the lesion, as opposed to those found in mature teratomas, which are localised to mural nodules. Immature teratomas grow rapidly, and cause disseminated tumour seedings by perforating their capsules and invading the peritoneum.<sup>6</sup> Small foci of fat and fragments of cartilage and bone may be present. Such a classical appearance makes diagnosis by plain abdominal radiographs possible. However, yolk sac tumours can be difficult to diagnose radiologically because of their non-specific appearance.

Abdominal radiographs may show a soft tissue mass arising from the pelvis. Sonography is needed to demonstrate the mixed solid and cystic components. CT is used to show the complex nature of the mass, such as areas of haemorrhage and necrosis, as well as to stage the tumour. Cystic teratoma, tubo-ovarian abscess, and appendiceal abscess are common radiological differential diagnoses.

Two staging systems are used for ovarian neoplasms. The International Federation of Gynecology and Obstetrics/American Joint Committee on Cancer (FIGO/AJCC) staging system was initially developed for use for adults, and is most relevant for epithelial malignancies. The Children's Oncology Group system is germ cell tumour-specific and was developed specifically for paediatric tumours. This patient had liver parenchymal metastasis at initial diagnosis, which equated to stage IV disease by both staging systems.

This patient had mixed germ cell tumours with components of yolk sac tumour and immature teratoma, which may exhibit the biological behaviours typical of both tumour types. Ovarian yolk sac tumours are highly aggressive neoplasms. In a literature review published in 1979, when combination chemotherapy was not commonly used, only 27% of 96 patients with stage I yolk sac tumour survived at 2 years and more than 50% of patients died within 1 year of diagnosis.<sup>7</sup> More recent studies showed that, with surgery and aggressive combination chemotherapy, the 5-year survivals for patients with stage I tumours and more advanced disease were 92% and 29% to 44%, respectively.<sup>8</sup> Although mature teratomas have an excellent prognosis, survival following surgery for immature teratomas is variable. Survival depends on the tumour grading, which is determined by the quantity of immature tissue. In a series of 58 patients with immature teratoma treated before the era of combination chemotherapy, recurrence was found in 18% of patients with grade 1 disease, 37% with grade 2 disease, and 70% with grade 3 disease.<sup>4,9</sup>

Some studies have shown that size and histology were the major prognostic factors for patients with malignant mixed germ cell tumours of the ovary.<sup>9,10</sup> For large tumours, the prognosis was poor when more than one-third of the tumour was composed of endodermal sinus elements, choriocarcinoma, or grade 3 immature teratoma. For tumours smaller than 10 cm, the prognosis was good regardless of the tumour constituents.<sup>4,10</sup> A recent retrospective study has shown that elevation

of both AFP and hCG levels was a strong predictor of poor survival, based on both univariate and multivariate analysis.<sup>11</sup> Advanced stage disease at presentation was also an independent poor prognostic indicator. This patient had a poor prognosis due to the large tumour size, unfavourable histological type, and advanced stage at presentation. Unlike testicular germ cell tumour, for which a number of prognostic classification systems are in use, a standard prognostic system for ovarian germ cell tumours is currently unavailable.

Surgery is the initial treatment for the majority of patients with malignant germ cell tumour of the ovary. Procedures include unilateral oophorectomy, bilateral salpingo-oophorectomy, and intra-abdominal tumour debulking, with the goal of removing as much gross tumour as possible while preserving fertility. All patients except those with FIGO/AJCC stage I require neoadjuvant or postoperative platinum-based combination chemotherapy. Cisplatin, bleomycin, and etoposide (BEP) and vincristine, dactinomycin, and cyclophosphamide (VAC) are commonly used regimens. Cisplatin, vincristine, methotrexate, and bleomycin (POMB) and dactinomycin, cyclophosphamide, and etoposide (ACE) regimens were initially developed for treatment of testicular germ cell tumours, but have also been found to have high antitumoural activity for patients with advanced malignant ovarian germ cell tumours.<sup>11</sup>

Mixed malignant germ cell tumour of the ovary is a highly aggressive neoplasm that can present as disseminated disease at initial diagnosis. A high index of suspicion is needed and early intervention for any adolescent girl

presenting with a rapidly enlarging pelvic mass is required. Definitive diagnosis requires histological confirmation. Imaging plays an important role in the assessment of disease extent, which is of prognostic significance.

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