A BONAFIDE RARITY:

A CASE OF A MIXED MALIGNANT GERM CELL TUMOR OF THE OVARY IN AN 8-YEAR-OLD CHILD

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INTRODUCTION

The term used to describe malignant cancers of germline cells in patients aged 0–18 years old is "Pediatric germ cell tumor". It makes up about 3% of malignancies in children aged 0–18 and nearly 15% of cancers in adolescents. It may present as a pure form with only one histology or a combination of two or more types of germ cell components, known as mixed malignant germ cell tumor (MMGCT)[1].

Under this umbrella includes yolk sac tumors and high-grade immature teratomas, which are usually associated with a more aggressive behavior[1]. A yolk sac histologic type is an indicator of poor prognosis and a nondysgerminoma or immature teratoma histologic type are associated with a high risk for treatment failure.

We report a case of MMGCT in an 8-year old girl who responded well to the fertility-preserving surgery and post-operative chemotherapy.

THE CASE

An 8-year-old female was admitted at our institution due to abdominal pain. Past medical and family history are unremarkable. Patient does not have her monthly menstrual period yet. The history of present illness started 5 days prior to admission when the patient experienced abdominal pain, colicky in character, intermittent, with no other associated signs and symptoms. No consult was done and no medications were taken.

Four days prior to admission, there was persistence of abdominal pain, now associated with one episode of vomiting and fever. She sought consult at a private clinic where she was diagnosed with urinary tract infection and was given Domperidone 10 mL three times a day which afforded temporary relief.

Two days prior to admission, her mother noted a palpable hypogastric mass with pain upon light palpation. No consult was done but prescribed medications were still taken which afforded temporary relief. Two hours prior to admission, there was persistence of the above symptoms, now with increasing severity of pain, 1 episode of vomiting, and pain upon urination. This prompted consult at the Pediatrics department of our institution and was referred to our service for gynecologic clearance. Further evaluation was done and the patient was subsequently admitted.

On admission patient was awake, alert, ambulatory, in pain, in mild cardiorespiratory distress, with the following vital signs: blood pressure was noted to be 90/60 mmHg, with a heart rate of 122 beats per minute, respiratory rate of 20 cycles per minute, with a temperature of 38 degrees Celsius. Abdominal examination showed a slightly distended abdomen, with a palpable hypogastric mass, cystic in character, moveable, measuring 9x9 centimeters from the hypogastrium extending up to the level of the umbilicus with generalized tenderness upon light palpation. Digital rectal examination revealed a tight sphincteric tone, no rectal mass, with fullness and slight tenderness on the cul-de-sac.

Transabdominal ultrasound was done revealing a solid mass with posterior acoustic enhancement possibly cystic (Teratoma? Germ cell? Dysgerminoma?). No fluid in the cul-de-sac noted (Figure 1). She underwent Exploratory Laparotomy with Peritoneal Fluid Collection and Left Salpingoophorectomy.

Intraoperatively, there was no hemoperitoneum with note of minimal reddish brown serous fluid. The left ovary was described to have a cream to tan nodular external surface, measuring 9cms x 8cms x 6cms (Figure 2) with point of rupture on its anterior border adherent to the posterior aspect of the uterus measuring 3cms x 3cms with brain like tissues, friable extruding from within the left ovary. The left fallopian tube was elongated and slightly dilated and hugged to the Left Ovary. The uterus is small with smooth serosal surface. The Right Ovary and Fallopian tube were grossly normal. The Liver, subdiaphragmatic surface, Gall bladder, stomach, spleen, kidneys, omentum, intestinal surfaces and appendix were grossly normal on inspection and palpation.

The cut section of the Left Ovary revealed pinkish-brown soft to friable tissues with areas of hemorrhage **(**Figure 3**)**. The Left Fallopian tube is grayish and with smooth surface. The histology report revealed Mixed Malignant Germ Cell Tumor (Yolk Sac tumor 59%, Dysgerminoma 40%, Immature teratoma 1%) limited to the Left Ovary with capsule rupture. There was presence of ovarian surface involvement without fallopian tube surface involvement. The Peritoneal Fluid was negative for malignancy. No diagnostic abnormality was recognized on the Left Fallopian tube.

The patient was referred to another institution for further management. Chemotherapy in the form of carboplatin, bleomycin and etoposide was given. Twenty-one months after the surgery and chemotherapy, CT Scan showed no recurrence of the disease.

DISCUSSION

Germ cell tumors (GCTs) are heterogenous tumors which are thought to originate from the primitive germ cell of the developing embryonic gonad. They migrate along the midline of the body to the gonadal ridges and gradually differentiate to mimic tissues of embryonic origin (ectoderm, mesoderm, or endoderm) and extraembryonic tissues (yolk sac and trophoblast).[1] Germ Cell Tumors occur in both gonadal locations such as the testis or ovary, or in extragonadal sites such as the sacrococcygeal area and the mediastinum. The tumors in extragonadal locations are believed to originate from germ cells that failed to migrate to the gonads.[2]

Germ cell tumors comprise about 20-25% of all ovarian neoplasms, with 95% being benign mature cystic teratomas and 5% considered as malignant.[1]

Rare and malignant cancers of germline cells seen in about 3% of cancers in patients aged 0-18 years old are called Pediatric Germ Cell Tumors (GCTs).[1,2] Evidence shows that GCTs can be classified and compared differently in different age groups. Specific tumor types and locations may depend on the age of the child and there are well documented evidences in the difference in their pathology and prognosis. However, despite these differences, GCTs in all groups are usually treated with platinum-based multiagent regimens.[2]

In a study done by Kaatsch, the incidence rate of GCTs are predominantly seen in females.[2] The incidence of GCTs show that there are two peaks or bimodal – one in children aged 0-4 years old and another at the beginning of puberty or during the adolescent period.[2,3] In Europe, the United States, and Australia, the incidence rates of GCTSs have increased, however causes of the increase is unknown.

The risk factors for GCTs are poorly understood with several factors being linked to the increased incidence of GCTS. These include having a familial predilection, diet, genetics, having a history of pyloric stenosis, hernia or cryptorchidism, having disorders of sex development and chromosomal abnormalities.[4]

Patients with malignant GCTs may present with abdominal pain (in 87% of patients), an abdominal mass (in 85% of patients), an acute abdomen (10%), and tend to be large at the time of diagnosis and progress rapidly. Other symptoms include fever, abdominal distension, and vaginal bleeding. Symptoms have a median of 2-4 weeks.[4] As in the case of our patient, her condition progressed 5 days from the onset of abdominal pain. She also presented with a palpable hypogastric mass, had fever, and abdominal tenderness.

Malignant germ cell tumors maybe in pure form with only one histology or a combination of two or more types of germ cell components, known as mixed malignant germ cell tumor. They are mostly unilateral but may be bilateral if dysgerminoma elements are included. Presence of high-grade immature teratoma and yolk sac tumor is associated with more aggressive behavior.[1] Our patient had a mix of predominantly yolk sac tumor (59%), followed by dysgerminoma (40%) and an element of immature teratoma (1%).

Yolk Sac Tumors comprise about 10% of malignant germ cell tumors. Gross pathologic features include large encapsulated masses with mixed solid and cystic components. The presence of Schiller-Duval bodies is the most characteristic feature. The gold standard for the diagnosis of Yolk Sac Tumor is the presence of alpha-fetoprotein. A unilateral enhancing mixed solid and cystic mass with a hemorrhagic portion and smooth outer contour can be seen on imaging.[5]

Dysgerminomas are the most common type of ovarian malignant germ cell tumors. They account for 1%-2% of primary ovarian neoplasms and 32.8%-37% of all malignant GCTs. Most patients present with pain, bloating, and menstrual disorders. Grossly, they are seen as solid and well encapsulated. Histologic findings primarily consist of primitive germ cells with stroma infiltrated by lymphocytes. On imaging, dysgerminoma can be seen as purely solid and is richly vascularized at color and power Doppler ultrasound. Areas of cystic change and enhancing septa representing hemorrhage or necrosis and a lobular pattern may be seen at computed tomography. During MRI, the most characteristic appearance is that of a solid mass divided into lobules by fibrovascular septa.[5]

The second most common malignant GCT is immature teratoma which accounts for 35.6%-36.2% of all the ovarian malignancies. They are associated with a poorer prognosis and present with a malignant behavior. Grossly, immature teratomas are larger (14-25cm) and may be described as a predominantly encapsulated mass which is solid, soft, and fleshy. Microscopically, they consist of immature embryonic structures derived from the three germ cell layers: ectoderm, mesoderm, and endoderm.[5]

Treatment may vary depending on the clinical factors present. It may be treated both medically and surgically. Treatment for Malignant Germ Cell tumors include fertility-sparing surgery consisting of Unilateral salpingo-oophorectomy with preservation of the contralateral ovary with frozen section examination unilateral tumors in young patients.[1] Standard chemotherapy regimen for both adults and children include cisplatin, etoposide, and bleomycin (BEP). Chemotherapy with conservative surgery can result in the cure of the majority of children with GCTs. [1,2,6]

Since the 1980s, GCT survival improved dramatically. Data shows that more than 90% of those treated with platinum-based chemotherapy have increased the five-year survival rates. [2]

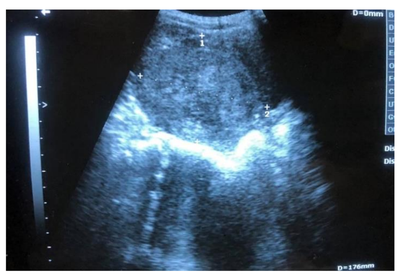

Figure 1. Transabdominal Ultrasound revealing a solid mass with posterior acoustic enhancement

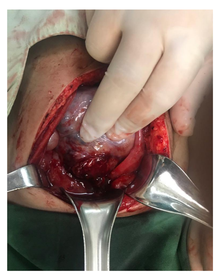

Figure 2 Intraoperatively, the ovary is described to have a cream to tan nodular external surface

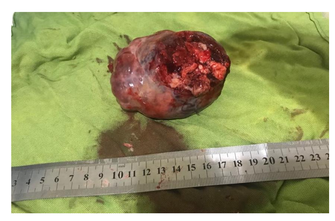

Figure 3a Gross specimen of the left ovary

Figure 4 The cut section of the Left Ovary revealed pinkish-brown soft to friable tissues with areas of hemorrhage

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