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Case Report

Rare Malignant Pediatric Ovarian Tumors; Two Case Reports and Literature Review, 2022

[1]Okbu Frezgi, [1]Berhe Tesfai*, [2]Malede Birara

[1]MD, Obstetrics and Gynecology Resident, Orotta College of Medicine and Health Science, Ministry of Health, Asmara, Eritrea
[2]MD, MPH, Obstetrician and Gynecologist, Associate Professor, Orotta college of Medicine and Health Science, Ministry of Health, Asmara, Eritrea

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***Corresponding author:** Berhe Tesfai
MD, Obstetrics and Gynecology Resident, Orotta College of Medicine and Health Science, Ministry of Health, Asmara, Eritrea

Abstract

Background: Ovarian tumors are uncommon in childhood and the teenage years. About one-fourth of all ovarian tumors in females younger than 16 years are described to be malignant.

Case report: The first case was an 8 years old child, presented with abdominal pain, distention, easy fatigability and weight loss of 3 months duration. The abdomen was asymmetric with 8x7 cm, firm, mobile, non-tender mass originating from deep pelvis. Alpha fetoprotein level was >1000ng/mL and CA 125 level was 16.4 U/mL. Laparotomy with left salpingo-oophorectomy was done and histo-pathologic result revealed a high grade malignant serous carcinoma of the ovary. Finally, she was sent abroad for chemotherapy. The second case was a 13 years old adolecent, had lower abdominal pain, distention, shortness of breath and dry cough for two months accompained by profound weight loss. Left supraclavicular lymph node was enlarged and there was decreased air entry on right side chest. Abdomen was grossly distended with 20x14cm, firm, non-tender mass with rough surface and irregular boarder. Tumor markers showed high level of CA 125 (305.6 U/mL) and was positive for β-hCG on urine dipstick. Peritoneal cytology and FNA of supraclavicular lymph node revealed malignant metastasis. Right salpingo-oophorectomy and omentectomy was done and the histopathologic result revealed Small cell carcinoma of the ovary. Patient was sent abroad for chemotherapy management.

Conclusion: The clinical presentation, being unilateral ovarian involvement, malignant pathologic evidence was seen in both cases. But, they had different serum tumor markers and rare, which was highly malignant type of ovarian cancer. As pediatric ovarian tumors are rare and highly malignant, health professionals' awareness and high index of suspicion is crucial. Introducing pediatric chemotherapy treatment and monitoring center in our country is vital.

Keywords: malignant, pediatric, ovarian cancers, Eritrea

INTRODUCTION

Gynecological malignancy accounts for 1–2 % of all pediatric cancer, age 1–15 years. The diagnosis is challenging due to varied histologic features. The incidence of ovarian masses in childhood is 2.6 cases per 100,000 girls per year, and 50 % are malignant; 85 % are germ cell tumors (GCT), 8 % epithelial cell carcinoma and 5 % sex cord stromal tumors.[1, 2, 3]

The incidence, histologic distribution, and clinical manifestations of ovarian tumors in the pediatric population are distinct from those in adults. Although ovarian neoplasms in childhood and adolescence are rare, the diagnosis should be considered in young girls with abdominal pain and a palpable mass.[4]

Abdominal pain is the commonest symptom (50–75 %). Most of the patients have clinically palpable non-tender mass and absence of ascites. The diagnosis of ovarian tumors is based on pelvic ultrasound, abdominal-pelvic MRI, Pathology and tumor markers.[1]

Elevated levels of serum tumor markers, including α-fetoprotein, the beta subunit of human chorionic gonadotropin and CA-125 raise concern for ovarian malignancies.[4] The useful tumor markers for the diagnosis of adnexal masses in children are: CA-125 for epithelial tumors, α-FP and β-HCG for germ cell tumors in newborns, CA-125, β-HCG, inhibin for granulosa cell tumors, LDH for dysgerminomas, and CA 19-9 for immature teratoma.[1]

The most important immunohistochemical finding in Yolk Sac Tumor is positivity for AFP. Germ Cell Tumors (GCTs) are cytokeratin positive but epithelial membrane antigen (EMA) negative. Lack of staining for EMA and positive staining for AFP differentiate GCT from clear cell carcinoma.[1, 3]

Ovarian small cell carcinoma is a rare, aggressive neoplasm that occurs in young women and has a poor long-term prognosis. Treatment involves surgical resection and chemotherapy. Various chemotherapy regimens are utilized due to confusion regarding the neoplasm's lineage.[8]

Small-cell carcinoma of the ovary, hypercalcemic type (SCCOHT) is a rare and aggressive cancer which mainly occurs in adolescents and young women.[9, 10]

Multiple groups discovered that SCCOHT is characterized by both germline and somatic deleterious mutations.[9] Because of the wide range of differential diagnoses of the various neoplasms in this broad group, pathologists commonly struggle with these tumors due to overlapping morphology and immunohistochemistry (IHC). In diagnosing the various tumor types, IHC and molecular studies are of value.[9, 10] We are reporting rare cases of malignant ovarian cancers in two pediatric patients.

Case Reports

Case: 1

This is an 8 years old child, from Barentu subzone of Gash-barka, Eritrea; presented with abdominal swelling associated with easy fatigability, decreased appetite, weight loss and dizziness of 3 months duration. She had history of vomiting and low grade fever which makes her to seek medical attention in her nearby clinic. She had no history of any chronic illness and vaccinated for her age with the locally available vaccines. She had no diarrhea, constipation, urinary complaints or vaginal discharge. She visited her nearby hospital and referred to Orotta National Referral Maternity Hospital on 21/09/2022. On her arrival to this hospital, she was having similar compliant.

On physical examination, she was chronically sick looking not in respiratory distress. Her vital signs revealed: blood pressure 80/60mmHg, left arm sitting position; pulse rate 92 beats/minute, right radial; respiratory rate 29 breaths/minute and temperature 37.1^0C. She had pale conjunctiva and chest was clear to auscultation. Abdomen was grossly distended, asymmetric with 8x7 cm mass which was firm, mobile, non-tender and regular in the left lower quadrant of the abdomen.

She was investigated with complete blood count, pelvic ultrasound, renal function test, liver function test, serum electrolytes and tumor markers. Her hemoglobin was 9.98g/dL and MRI shown an 8x7cm pelvic mass. Tumor markers revealed Alpha-fetoprotein of >1000ng/mL, CA 125 of 16.4 U/mL and calcium of 8.9mg/dL. (Table: 1)

She was transfused with 03 units of blood and laparotomy under general anesthesia was done. A regular 8x7x5cm cystic, non-adherent mass was found in the left adnexa which involved the left ovary and left salpingo-oophorectomy was done. Sample was sent for histopathology and revealed high grade malignant serous carcinoma of the ovary. Post operatively the patient was improving clinically and was sent abroad for chemotherapy management.

Case: 2

This is a 13 years old pre-menarche adolescent come with the complaint of lower abdominal pain and distention of two months. The abdominal distension was followed by shortness of breath and occasional dry cough. The pain was ill-defined, more in right lower quadrant radiating to back. It was not accompanied by vomiting, fever or alteration in bowel habit. Her care giver (father) reported that she lost profound weight which they couldn't quantify. She had no history of exposure to radio-chemotherapy for any disease entity. They also informed that they had no similar problems in their family.

On examination, she was chronically sick looking with mild respiratory distress. Vital signs revealed blood pressure of 90/50mmHg, respiratory rate 28 breaths/min, pulse rate 108 beats/min in right radial artery, temperature 36.4^0c in left axillae, random blood sugar 122mg/dl and SPO_2 of 92% at room air. She had left supraclavicular enlarged lymph node of 2×2cm, non-tender. There was decreased air entry on the right side of the chest with dullness to percussion from mid to lower lung field. Abdomen was grossly distended, shiny without collateral veins, with asymmetry more bulged on right side without tenderness. On deep palpation, there was a firm about 20x14cm pelvic mass not attached to superficial and

deep structures. The mass had rough surface and irregular boarder. Both fluid thrill and shifting dullness were positive. On per-rectal digital examination, right adnexal mass was appreciated.

Her laboratory results indicated with hemoglobin of 11.38g/dl and platelet 986.1 x10^3/µL. She was also investigated with liver function test, renal function test and electrolyte which were within the normal range (calcium level of 9.7mg/dL). She was further investigated with serum tumor markers (Table: 1) and was positive for β-hCG on urine dipstick. Peritoneal fluid analysis and FNA of supraclavicular lymph node revealed metastatic evidence. Besides, MRI of the pelvis and abdomen revealed gross ascites with right ovarian mass.

After thorough assessment and investigation, fertility preserving surgery was planned and family was counseled for possible hysterectomy and bilateral oophorectomy based on the distant metastasis to the cervical lymph nodes. Under spinal anesthesia, midline incision was done and around 3000ml of serosanguinos fluid was sucked and greater omentum was found adherent to the right ovary. Left ovary and uterus were checked and found to be healthy. Right salpingo-oophorectomy and omentectomy was done and tissue sample was sent for histo-pathology assessment which revealed Small cell carcinoma of the ovary. She was showing some improvement and discharged after 10 post-operative days and sent abroad for chemotherapy management.

Table: 1 Tumor markers, investigations and procedures done for both cases

Investigations	**Case 1**	**Case 2**	**Reference values**
Serum tumor markers			
CA-125	16.4 U/mL	305.6 U/mL	0.0 - 34 U/mL
CA19-9	26.97 U/mL	10.9 U/mL	0.0 - 39 U/mL
Carcinoembrionic Ag	1.14 ng/mL	0.54 ng/mL	0 - 3.0 ng/mL
Alpha-fetoprotein	>1000 ng/mL	1.33 ng/mL	0.0 - 8.1 ng/mL
β-hCG on urine dipstic	Negative	Positive	_____
Hematology			
WBC	9.26 x10^3/µL	7.3 x10^3/µL	3.71 - 10.67 x10^3
Hemoglobin	9.98 g/dL	11.38 g/dL	12.00 - 16.75
Hematocrit	30.7%	37.8%	35.1 - 48.7
Platelets	454.7 x10^3/µL	986.1 x10^3/µL	150.5-366.8 x10^3
Renal, liver function test and serum electrolytes			
BUN	13 mg/dL	12 mg/dL	6 - 20mg/dL
Creatinine	0.8 mg/dL	0.6 mg/dL	0.5 - 1.1mg/dL
AST	33 U/L	40 U/L	0 - 31U/L
ALT	21 U/L	13 U/L	0 - 31U/L
Albumin	3.2 m/dL	2.4m/dL	3.4 - 4.8m/dL
Sodium (Na)	1398m/dL	1378m/dL	135 - 145mmol/L
Chlorine (Cl)	1068m/dL	1038m/dL	101 - 111mmol/L
Calcium	8.9 mg/dL	9.7 mg/dL	8.8-10.2mg/dL
Imaging, Histo-pathology and Intervention			
MRI result	Left adnexal mass	Right adnexal mass with ascites	
Histo-pathology	High grade malignant serous carcinoma of ovary	Small cell carcinoma of the ovary	
Interventions	Left salpingo-oophorectomy	Right salpingo-oophorectomy, Omentectomy	

Figure: 1 Pre-operative and intra-operative findings of case 2

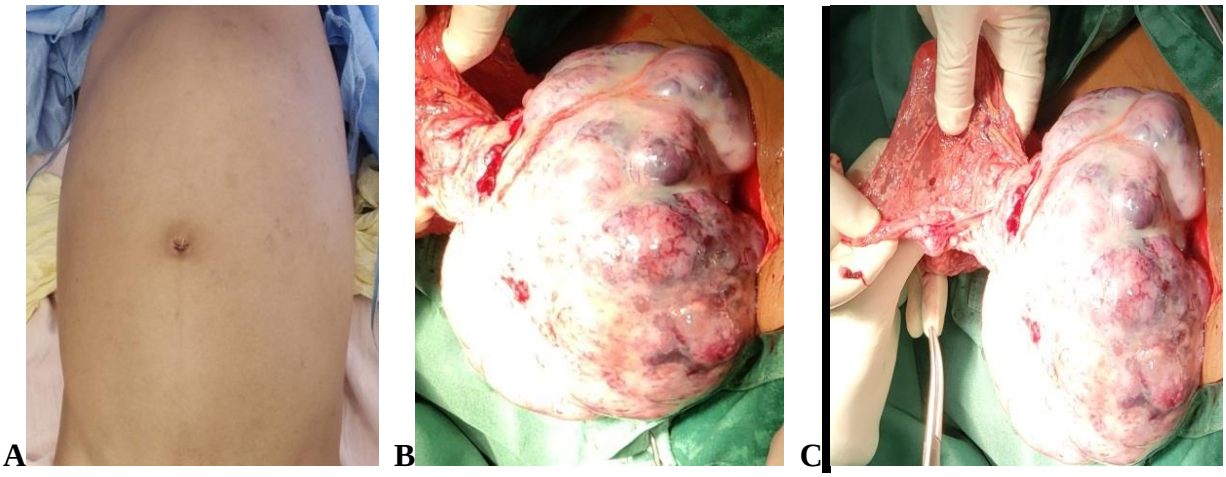
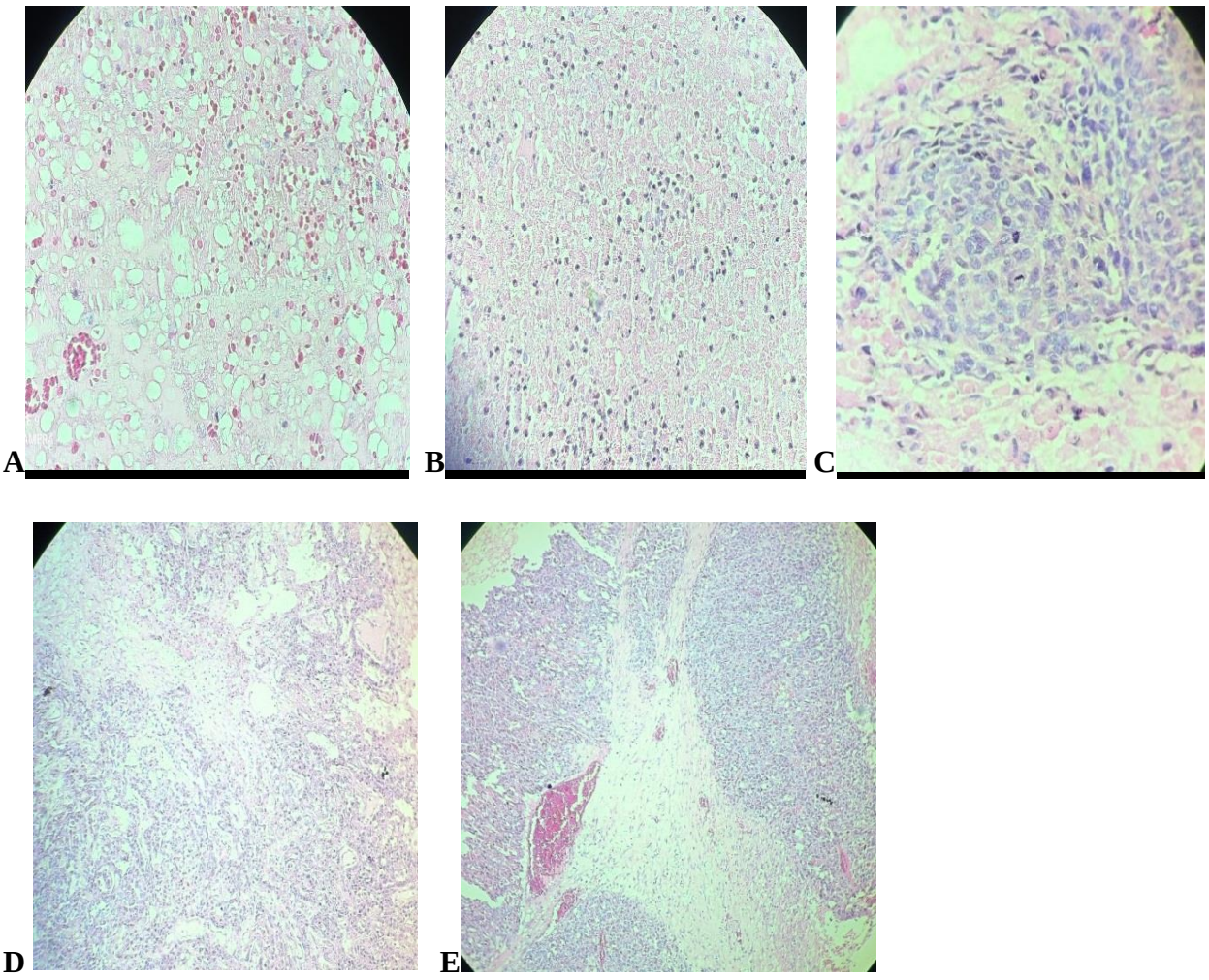


Figure_1: (A) - distended abdomen preoperatively, (B) - irregular right ovarian tumor, (C) - omentum adhered with ovarian tumor with omental kicks

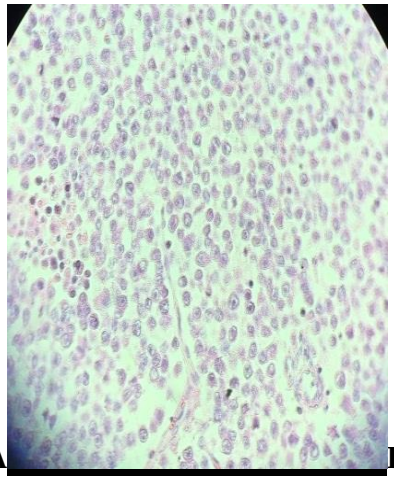
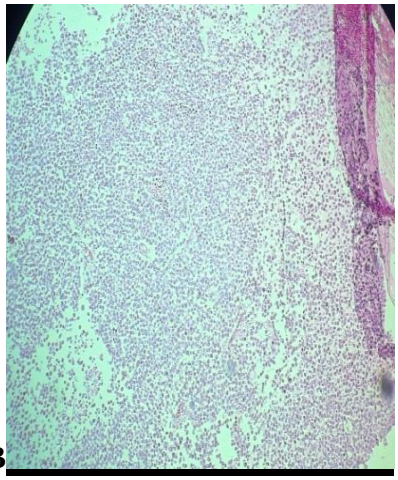
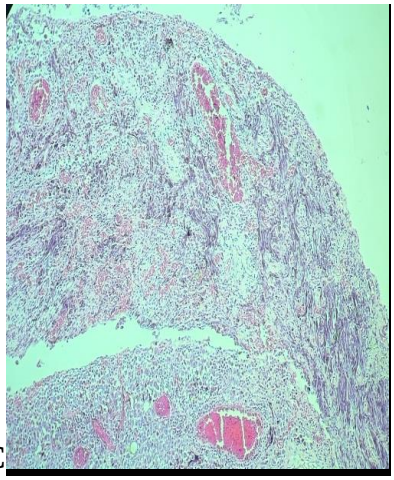
Histo-pathologic slides of case 1 on Hematoxin and Eosin staining



Macroscopic description: Ovarian mass measuring 8x7x5cm, firm and necrotic area with hemorrhage and cystic dilatations and the mass is well encapsulated.

Microscopic description: Sections show high grade malignant tumor forming sheets of highly pleomorphic hyperchromatic cells featuring brisk mitotic activities (>50 figures per 10 HPF). The tumor infiltrating the fat (omentum) and also vascular invasion was seen mutifocally. Wide area of necrosis noted in the background. **Diagnosis: High Grade Malignant Tumor, Serous Carcinoma of the ovary**

Histo-pathologic slides of case 2 on Hematoxin and Eosin staining

A  B  C 

Macroscopic Description: A semi cystic with smooth and nodular outer surface measure 20x14x9cm and a fragmented tissue (omentum) measure on aggregate 11x11x4cm.

Microscopic Description: Sections show malignant tumor forming sheets composed of pleomorphic cells with prominent nucleoli and featuring brisk mitotic activity >30 mitotic figures in HPF. The tumor was infiltrating the fatty tissue (omentum). **Diagnosis: Small Cell Carcinoma of the Ovary**

DISCUSSION

Pediatric ovarian tumors are rare and highly malignant with poor prognosis, diagnostic and treatment dilemmas throughout the world. Since there is no specific screening method for ovarian tumors, they are diagnosed in late stage with distant metastasis and poor treatment outcomes. Based on the reviewed literature, there are no reported published cases of pediatric ovarian tumors in Eritrea.

Even though they had almost similar MRI result which indicated adnexal tumor, the histo-pathologic and serum tumor markers result was different. Both of them had high grade malignant epithelial ovarian tumor. Other study showed that 50 % are malignant; 85 % are germ cell tumors and 8 % epithelial cell carcinoma.[3] Malignant epithelial tumors are rare in females younger than 14.[2] This displayed that these cases had a highly aggressive and rare ovarian tumor.

Both cases had almost similar clinical presentation and duration of illness. This was similar to other study that abdominal pain and swelling was the commonest symptom (50–75 %).[1] This is mainly due to that it's the most common presentation and easily noticeable symptom by the family members that make them to seek medical attention.

The first case had high level of Alpha feto protein (>1000 ng/ml) and normal level of CA 125. This was not consistent with the histo-pathologic type of the tumor (high grade malignant serous carcinoma of the ovary). Other study reported that the diagnosis of a mixed ovarian germ cell tumor showed elevated αFP with normal level of β-hCG.[6] Based on the histo-pathologic result (epithelial ovarian cancer), the CA 125 level was mostly expected to be higher, but, she had high level of αFP, which was a characteristic of most germ cell tumors. Thus she could have a mixed component of ovarian malignancies.

The second case had high level of CA-125 and was positive for β-hCG, consistent with the histo-pathologic result (Small cell carcinoma of the ovary). This is a very rare and highly malignant ovarian cancer which has a poor prognosis and shows high level of CA 125.[7] This was consistent with the clinical finding that she had clinical signs of metastasis to the peritoneum, pleura and lymph nodes. But, as she was positive for β-hCG urine dipstick with high CA 125; she has

serum tumor markers consistent with granulosa cell tumor. In around 10% of ovarian tumors, histopathology results showed mixed ovarian tumors.[2] similarly, other studies reported that, Small cell carcinoma of the ovary is an undifferentiated neoplasm and the origin of tumor cells is epithelial, germinal, or mesenchymal, which is not clearly determined.[11] The exact histogenesis of the tumor is unclear and it may present as an undifferentiated tumor.[10] In both cases the serum tumor markers and histopathology results didn't coincides for specific ovarian tumor, which would be clarified by immunohistochemistry analysis which was not available in our country. In diagnosing the various tumor types, immunohistochemistry and molecular studies are of value.[9, 10]

Both cases had normal level of calcium level and they had no clinical signs of hypercalcemia, similar to other study.[10] But, most literatures reported that, in two-thirds of the cases, Small cell carcinoma of the ovary is associated with hypercalcemia.[11] Both cases had unilateral ovarian mass similar to other studies that, it is usually unilateral (99%), but bilateral familial cases are reported.[10]

The second case had clinical sigs of ascites, pleural effusion and supraclavicular lymphadenopathy with cyto-pathological evidence of metastasis. She was also positive for β-hCG on urine dipstick and had tumor size > 12cm that shows malignant ovarian tumor with poor prognosis. The first case had high level of Alpha feto protein (>1000 ng/ml) and children with αFP > 1000 ng/ml had poor prognosis.[3] Similarly, other studies revealed that predictive factors for malignancy were abdominal distension, palpable mass, increased β-hCG and/or AFP levels, tumors larger than 12 cm and ascites.[5] The histo-pathologic results was also consistent with malignant clinical presentation. Thus, both of them may reveal poor prognosis. The diagnosis delay is mainly due to that most ovarian malignancies are at their advanced stage at diagnosis and also its rare presentation, vague clinical manifestation and low level of health professionals and community awareness about the disease in this age group. The outcome is not known on these cases as their chemotherapy treatment is to be given abroad.

Based on their age and clinical status, a fertility preserving surgery and omentectomy was done. Most literatures also reported that, it's universally agreed that uterus and contralateral adnexa are preserved. Even though the surgical debalcking was done for both patients, the chemotherapy was supposed to be started within 4 weeks postoperatively. Because of the rarity of the disease, there are no evidence-based treatment recommendations and these cases have poor prognosis even when diagnosed at early stage.[10] various chemotherapy regimens are utilized due to confusion regarding the neoplasm's lineage.[8] Due to the challenge of pediatric age oncology treatment in our country, they were sent abroad for continuation of management with chemotherapy.

CONCLUSION

This is reported on the rarity of the disease in the pediatric population. These two cases had similar acute clinical presentation but they had different serum tumor markers and histo-pathological finding. The second case had clinical signs of metastasis at the time of diagnosis that indicates poor prognosis. Both of them had rare and highly malignant type of ovarian cancer and fertility preserving unilateral salpingo-oopheroctomy was done, which the outcome can't be determined as their chemotherapy is to be given abroad.

As pediatric ovarian tumors are rare and highly malignant, health professionals' awareness and high index of suspicion about the diseases presentation for early initiation of investigations is crucial to get at early stage of the disease. Besides, drafting treatment protocols and introducing pediatric chemotherapy treatment and monitoring center are vital as they are highly responsive.

Declarations

Acknowledgment: Authors' acknowledges the patients for using their data for this case report and for the pathology department for facilitating the processing of the pathology analysis

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Author contribution: All authors had contributed in analysis, discussion and case report writing

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