Primitive neuroectodermal tumor of the ovary

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ABSTRACT

نصف حالة امرأة باكستانية عمرها 31 سنة قدمت إلى مستشفى الملك عبد العزيز تشتكي من ألم في البطن وزيادة في حجم البطن، تصوير الأشعة فوق الصوتية والتصوير بالرنين المغناطيسي أظهر وجود ورم في المبيض الأيمن، أزيل الورم جراحيا، أظهر التحليل المجهري وجود ورم أولي عصبي من طبقة المضغة الظاهرة، تم إزالة الرحم والمبيضين وقناتي فالوب وغشاء الأمعاء الشحمي وبقي أقل من واحد سنتمتر من الورم تم بعد ذلك إعطائها العلاج الكيماوي وبعد أربعة أشهر عاود الورم للظهور وتم إعطائها دورة ثانية من العلاج الكيماوي ولكنها لم تستجب للعلاج وتوفيت بعد خمسة عشر شهرا من التشخيص.

A 31-year-old woman presented to King Abdulaziz University Hospital complaining of an abdominal pain and a rapid increase in abdominal girth. An ultrasound and MRI, revealed a huge cystic ovarian mass without ascites. Ovarian tumor markers were all within normal range. Exploratory laparotomy showed huge right ovarian mass with omental mass. Frozen section from the omentum showed metastatic malignant neoplasm. Total abdominal hysterectomy was carried out with bilateral salpingooophorectomy and omentectomy with residual tumor of less then one centimeter. Final pathology assessment showed primitive neuroectodermal tumor arising from the right ovary. She received post- operative chemotherapy. Four months later she had recurrence and was given second line chemotherapy, but she did not respond and died 15 months after the diagnosis due to obstructive uropathy.

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Peripheral primitive neuroectodermal tumor (PNET) is a soft tissue sarcoma of neuroectodermal origin, and is the second most common sarcoma among children and young adults.[1] It is considered one of the small round blue cell tumors. It shares many morphological features with Ewing's sarcoma (ES),[2] which arises usually in the bone, while PNET arises in soft tissue. Ovarian PNET is a very rare tumor that is associated with high mortality.[3] Few cases have been reported arising in the ovary. Previously reported cases have shown poor response to therapy in advance disease, and survival rates have been discouragingly low. We report a case of PNET arising in the right ovary with a very short survival period.

Case Report. A 31-year-old, Pakistani nulliparous woman was referred to King Abdulaziz University Hospital with complaints of abdominal pain and rapid growing abdominal girth. On physical examination pulse was 80 per minute, blood pressure was 150/90, and body temperature was 37^0C. There was no lymphadenopathy. The chest and heart were normal. Abdominal examination showed large pelviabdominal mass. There were no ascites. Ovarian tumor markers (Beta-HCG, Alpha-fetoprotein, and CA 125) were within normal limits. An MRI of the abdomen and pelvis showed a large mass that measures 15 x 12 x 10 cm with solid and cystic structure. Another mass measuring approximately 13 x 12 cm was seen in the left iliac fossa with multiple peritoneal metastases. Based on the clinical diagnosis of ovarian carcinoma, an exploratory laparotomy was performed and it showed a right ovarian mass and huge omental mass. Frozen section revealed metastatic malignant blue round cell tumor. Total abdominal hysterectomy was carried out with bilateral salpingooophorectomy, omentectomy with residual tumor of less than one cm. There were no intraoperative complications and her post-operative period was uneventful. Microscopically, the tumor was composed of solid nests and sheets of monotonous, primitive, small round cells with a few rosettes. There were focal areas of necrosis (**Figures 1a & 1b**). The tumor involved the omentum and the uterine surface.

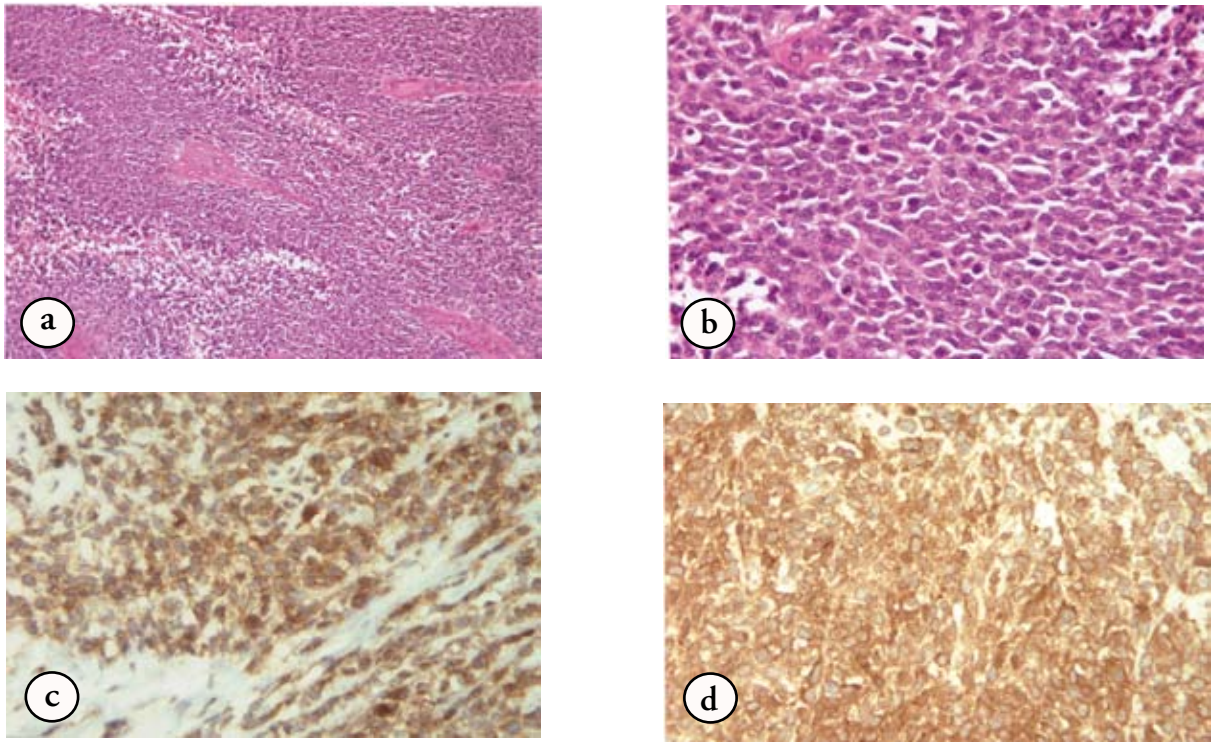

Figure 1 - Section from the tumor reveals **a**) solid nests and sheets of monotonous, primitive, small round cells associated with focal areas of necrosis (Hematoxylin and eosin stain, original power x 200), **b**) a higher power reveals frequent mitotic figures (Hematoxylin and eosin stain, original power x400), **c**) immunohistochemistry stain for CD99 reveals positive staining, and **d**) immunohistochemistry stain for neuron-specific enolase reveals positive staining.

Immunohistochemical stainings showed positive reaction for O-13 (MIC2/CD99), synaptophysin, vimentin, and neuron-specific enolase, but negative for glial fibrillary acidic protein, S-100, cytokeratin AE1/AE3, desmin, chromogranin, inhibin, CA125, and leukocyte common antigen (**Figures 1c & 1d**). The final pathological diagnosis was ovarian PNET with omental metastasis. After surgery, she received 4 cycles of Vincristine, Adriamycin, Ifosfamide alternated with Vincristine, Actinomycin D and Ifosfamide. Re-evaluation after the fourth cycle by CT scan showed recurrent tumor in the pelvis with multiple peritoneal deposits; she received second line chemotherapy in the form of 3 cycles of Taxotere and cisplatinum but did not respond. She died 15 months after diagnosis due to obstructive uropathy.

Discussion. A PNET is considered the differentiated form of tumor within the PNET/Ewing's sarcoma family.[4] Microscopically, these tumors share considerable features. Peripheral primitive neuroectodermal tumors usually have more neuroendocrine features. It is the second most common sarcoma among children and young adult,[4] it usually contains well-formed rosettes or pseudorosettes.[4] Most PNET occur in the soft tissues, however, rare cases have been reported in the ovary.[5-7] Usually these tumors behave clinically in an aggressive fashion, only a small percentage of patients with these tumors survive. The survival rate varies from 10.8 month to 3 years.[5-7] Peripheral primitive neuroectodermal tumor of the ovary with 2 successful spontaneous pregnancies has been described.[8] The oldest age reported with ovarian PNET is a case of a 78-year-old woman, and it was associated with endometrioid adenocarcinoma.[9] The occurrence of a malignant neuroectodermal tumor in a mature cystic teratoma has been reported.[10] A PNET should be considered in the differential diagnosis when examining ovarian tumors with unusual features, particularly if the patient is young.[6] Chemotherapy for PNET is the same regimen that is used for ES. In our center we use Vincristine, Adriamycin, and Ifosfamide alternated with Vincristine, Actinomycin D and Ifosfamide regimen. Apparently, she did not benefit and the tumor was also chemoresistant to Taxotere and cisplatinum therapy. Very limited cytogenetic and molecular studies have been

published on ovarian PNET. Analysis of comparative genomic hyperemization (CGH) of one ovarian PNET revealed multiple chromosomal abnormalities that includes the deletions of retinoblastoma gene (Rb), ras homologue member I (ARHI), as well as amplification of N-myc, fas ligand (FasL), glucocorticoid-induced tumor necrosis factor (TNF) receptor family related protein ligand (GITRL), and epidermal growth factor receptor (EGFR), which may be the crucial factors for tumorigenesis and the aggressive biological behavior of PNET.[11] Further studies are necessary to assess molecular biology of such tumor and different chemotherapeutic protocol should be carried out in order to improve the survival of those patients with this rare tumor. Peripheral primitive neuroectodermal tumor is very important to be considered in the differential diagnosis of ovarian malignant neoplasm, particularly in young females. It is important for this rare neoplasm to be recognized pathologically because of its very poor prognosis compared to other neoplasms.

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