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Case Report

Intestinal Ewing Sarcoma Misdiagnosed as an Adnexal Mass in a Young Woman

Genç Kadında Adneksiyal Kitle ile Karışabilen İntestinal Ewing Sarkomu

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ABSTRACT

Extraosseous Ewing's sarcoma is an extremely rare tumor. In the literature, intestinal Ewing's sarcoma was reported in 20 cases, and omental Ewing's sarcoma was reported in only two cases. In this case report, we report a 23-year-old female who presented with the complaint of diffuse abdominal pain. Abdominal ultrasound and whole-body computed tomography revealed a mass starting from the adnexal area and extending between the intestinal loops. Serum levels of tumor markers were high. The serum levels of carbohydrate antigen-125 (CA-125) and carcinoembryonic antigen-19.9 (CA-19.9) were high (427.5 U/mL and 67.9 U/mL, respectively). Laparotomic exploration was performed with the preliminary diagnosis of an adnexal mass, and a mass originating from the small intestine meso and completely covered by the omentum was excised. Histological evaluation reported intestinal and omental origin of Ewing's sarcoma. This case highlights the importance of rare extraosseous Ewing's sarcoma, which should be included in the differential diagnosis of a young female with intra-abdominal mass.

Keywords: Ewing sarcoma, immunohistochemistry, omentum, fluorescence *in situ* hybridization, primitive neuroectodermal tumor

ÖZ

İskelet dışı Ewing sarkomu, oldukça nadir görülür ve intestinal Ewing sarkomu literatürde sırasıyla 20 kez ve omental Ewing sarkomu 2 kez bildirilmiştir. Bu olgu sunumu, yaygın karın ağrısı şikayeti ile başvuran ve ovaryan kitle ön tanısı ile opere edilen 23 yaşında kadın hastaya aittir. Hastaya yapılan abdominal ultrasonografi ve intravenöz kontrastlı batın tomografide adneksiyal alandan başlayarak bağırsak ansları arasına doğru uzanım gösteren kitle saptandı. Tümör markerları yükselmişti [karbonhidrat antijen-125 (CA-125): 427,5; karsinoembriyojenik antijen (CA-19.9): 67,9]. Laparotomide ince bağırsak mezosundan köken alan ve tümü ile omentum ile kaplanmış kitle total olarak eksize edildi ve histolojik olarak Ewing sarkomu tanısı kondu. Bu olgu intraabdominal kitle ile başvuran genç kadın hastada nadir görülen iskelet dışı Ewing sarkomunun ayırıcı tanılarda yer alması gerektiğinin önemini vurgulamaktadır.

Anahtar Kelimeler: Ewing sarkomu, immünohistokimya, omentum, floresan *in situ* hibridizasyon, primitif nöroektodermal tümör

INTRODUCTION

Ewing's sarcoma (EWS) is a small round blue cell tumor characterized by the pathognomonic EWSR 1 gene fusion to a member of the ETS family of transcription factors, creating a novel fusion oncogene crucial to its pathogenesis. EWS is the second most common primary malignant neoplasm of bone after osteosarcoma in the second decade of life. Extraosseous EWS is very rare, and out of 38 reported cases (22 cases in men and 15 cases in women); 3 originated in the esophagus, 9 in the stomach, 5 in the colorectal region, and 20 in the small intestine. EWS, which included the primary omentum, was reported in only 2 cases. The reported cases were in a wide age range from 9 to 68 years.

Here, we present a case of primary intestinal (including omental tissue) EWS that was operated with a prediagnosis of an adnexal mass.

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CASE REPORT

A 23-year-old gravida 0-parity 0 female patient was consulted by the department of general surgery with a complaint of widespread abdominal pain that had been intermittent for about a month and had been getting worse over the last week. The patient's personal and family histories were unremarkable for malignancy and systemic diseases. A 7-8 cm semimobile mass located in the midline of the abdomen was palpated during physical examination. A 90x60x65 mm mass was observed in the midline of the abdomen, at the level of the epigastrium, whose relationship with the intestinal loops could not be distinguished. Both ovaries had a normal appearance, but the potential relationship with the mass could not be excluded because of the close relationship with the mass. The patient was prediagnosed with an ovarian tumor or retroperitoneal Castleman disease. Laboratory tests were unremarkable except for the high tumor marker values: the concentration of carbohydrate antigen-125 (CA-125) was 427.5 U/mL and that of carcinoembryonic antigen-19.9 (CA-19.9) was 67.9 U/mL. In contrasted abdominal computed tomography (CT), the internal genital organs were normal and a 7.5x7.7 cm lobulated solid mass with contrast enhancement, which was connected with the right adnexal lodge and extended upwards between the intestinal loops in the mesentery fatty tissue at the level of the iliac arteries, was observed. The mass continued up to the front of the aorta and vena cava and was pushing the intestines. The origin of the mass could not be clearly determined, and there was an extension toward the right adnexal site and intraperitoneal fluid component, which was more prominent on the right and continued into the pelvis through the cecum, appendix, and peritoneum. No significant retroperitoneal pathological lymph nodes were observed. The other abdominal and retroperitoneal organs were normal (Figure 1).

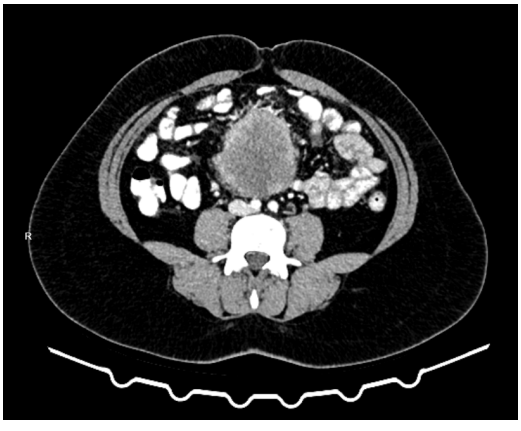

Figure 1. Preoperative appearance of the tumor on pelvic CT
CT: Computed tomography

Laporatomy by superior-inferior median incision was performed. An approximately 8x8 cm necrotic heterogeneous tumoral mass involving the mesos of the small intestine loop starting from approximately 110 cm from Trietz and continuing up to 80 cm distally and omentum was fixed on the tumor. The genital organs had a normal appearance. The omentum covering the mass was partially excised. The frozen section results were reported as lymphoma or neuroendocrine tumor. The intestinal loop with the mass was cut using a TCR55 linear stapler and closed by the general surgery team. The mass with the related small intestinal loop and meso was removed as a block, and end-to-end double-layer isoperistaltic anastomosis was performed. The early postoperative course was uneventful. The patient was discharged on the 6th day following the operation.

Histopathological evaluation revealed extraosseous EWS. The tumor measured 12x10x3 cm and consisted of a nodular mass. On the cut surface, the tumor was composed of solid areas. The solid areas were cream and white, with brown areas representing necrosis and hemorrhage (Figure 2a). Microscopic examination of the tumor revealed cellular areas showing diffuse growth. The

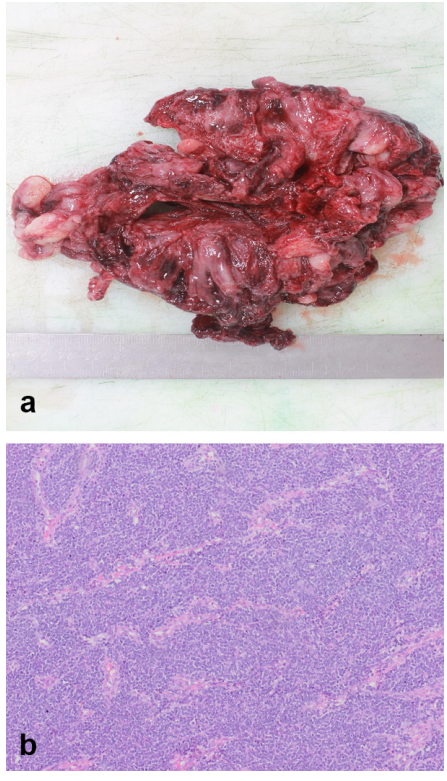

Figure 2. **(a)** Macroscopic appearance of the cut surface of the tumor (8x9 cm in size) composing of white solid, brown necrotic, and hemorrhagic tissue. **(b)** Microscopic appearance of the tumor which is composed of uniform, small, round cells with round nuclei containing fine chromatin, scanty cytoplasm (H& Ex100)

neoplastic cells were uniform, small, and round in shape and had scanty cytoplasm (Figure 2b). Vast areas of necrosis were also observed. Immunohistochemically, tumor cells showed strong and diffuse immunoreaction with CD99 and vimentin, weak immunoreaction with synaptophysin, and focal immunoreaction with CD56.Other neuroendocrine markers such as chromogranin and INSM1 were absent. Other neuroendocrine markers, such as chromogranin and INSM1, were absent. CD45 (LCA) (leukocyte common antigen), CD3, CD20 and TdT (Terminal deoxynucleotidyl transferase) immunohistochemical stains applied to differentiate from lymphoid neoplasms were negative. No immunostaining was detected with desmin, and myogenin was applied to differentiate it from rhabdomyosarcoma. Immunostaining with WT-1 was absent for distinction from desmoplastic small round cell tumor. No immunoexpression was observed with cytokeratin AE1-AE3 and S100. Ki-67 immunohistochemistry revealed a proliferative index of 95 percent. EWRS1 FISH test was performed for tumor-specific diagnosis of undifferentiated small cell sarcoma morphology, and *EWRS1* gene rearrangement was detected. The case was evaluated as an extraskeletal Ewing sarcoma. While the wall of the small bowel resection material was intact, a similar tumor was observed in the meso- and omentectomy material. Widespread lymphovascular invasion was noted in the sections. Metastasis was detected in 8 of 22 lymph nodes extracted from the material (Figure 2).

At the first postoperative month, the patient presented with complaints of fatigue, diffuse free fluid in the abdomen, and diffuse abdominal pain. Laboratory tests were in the normal range except for elevated C-reactive protein (10.15 mg/dL) and decreased albumin (3.2 g/dL) levels. Paracentesis was performed, and 3000 cc of acid fluid was evacuated. Multiple diffuse lesions in the liver and 70x60 mm in size in the right adnexal lodge and 40x40 mm in size in the left adnexal lodge were detected on CT evaluation. Multiple implants were observed in the peritoneum and omentum (Figure 3a). Thorax CT was normal. Magnetic resonance imaging showed results similar to CT. Multiple metastatic masses were observed in the liver parenchyma, most of which were capsular and some were 4-5 cm in size. Peritoneal masses with diffuse intraperitoneal fluid and peritoneal involvement findings not exceeding 1 cm were observed in the upper abdomen. Identified masses were evaluated as liver metastases. In addition, several metastatic implants were observed in the Morrison pouch on the right. An 8x10 cm mass with possible metastatic solid and occasionally cystic areas was observed in the posterior part of the uterus, adhering to the peritoneum toward both adnexal sites and continuing into the Douglas space. Multiple peritoneal, mesenteric, and metastatic masses were noted (Figure 3b).

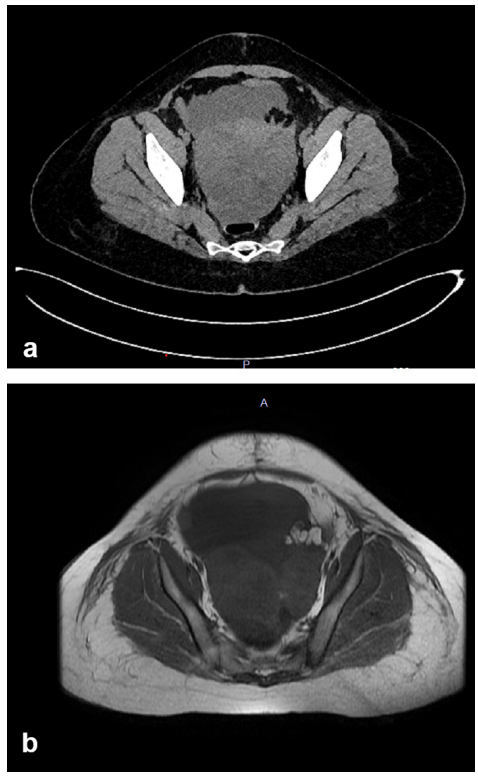

Figure 3. Postoperative 1st-month imaging of the patient at CT **(a)** and MRI **(b)**
CT: Computed tomography, MRI: Magnetic resonance imaging

Ifosfamide, etoposide, vincristine, actinomycin-D, and cyclophosphamide regimen was applied to the patient. Granulocyte colony-stimulating factor was added to the treatment because of neutropenia. Our case progressed rapidly after the first diagnosis, and chemotherapy continued in the 2nd postoperative month.

The authors certify that they have obtained all appropriate patient consent forms.

DISCUSSION

EWS/primitive neuroectodermal tumor (PNET) was described by Stout in 1918 and usually occurs as a sporadic aggressive malignant small round cell tumor in the soft tissues, bones, or central nervous system (1). It is examined under two main headings: central EWS/PNET, which develops from the central nervous system, and peripheral EWS/PNET, which grows out of the central nervous system (2). In this study, the tumor was of the peripheral type. This aggressive and unusual tumor has been seen in the esophagus, liver, pancreas, adrenal gland, kidneys,

prostate, bladder, and gynecological organs (3). Intestinal EWS may occur asymptomatically or present with fatigue and weakness due to the mass, as in our case, as well as symptoms such as intussusception (4), perforation (5,6), intestinal obstruction (7,8) and rupture.

The clinical presentation mainly depends on the affected area of the gastrointestinal tract. It may be misdiagnosed as a gynecological pathology, especially in young women, as the literature indicates that pain could often occur in the lower abdomen (9). Out of 38 reported cases, 3 originated in the esophagus, 9 in the stomach, 5 in the colorectal, and 20 in the small intestine. EWS, which included the primary omentum, was reported in only 2 cases. Twenty-two cases were observed in men, 15 cases were observed in women. Ewing sarcoma occurs in a wide age range from 9 to 68 years. There is no established treatment for intestinal PNET. Once diagnosed, surgical excision offers the best chance for survival, and adjuvant radiotherapy may reduce local recurrance (10). Combination chemotherapy traditionally includes vincristine, doxorubicin, cyclophosphamide, and dactinomycin. Adding ifosfamide and etoposide to a standard regimen significantly improves outcomes in patients with non-metastatic EWS (11). We chose multiagent chemotherapy because of the aggressive behavior of the tumor. Mesenteric PNET has a better prognosis than other regions independent of tumor size. In patients without metastasis, disease-free 5-year survival rate (>60%) is considerably higher than that in patients with metastatic disease (35%) (4). The reported causes of mortality were recurrent tumors in two patients, acute respiratory failure in one patient, and survival of the other two patients without any signs of disease. The reported follow-up period ranged from 6 to 20 months, with a median survival of 12 months.

Young women presenting with atypical clinical and imaging findings should be evaluated by a multidisciplinary approach during pre-, intra-, and post-operative periods for proper management of the disease.

ETHICS

Informed Consent: The authors certify that they have obtained all appropriate patient consent forms.

Authorship Contributions

Surgical and Medical Practices: P.S.H., S.M., G.G., Concept: A.A., Design: G.G., Data Collection or Processing: G.G., Analysis or Interpretation: P.S.H., S.M., Literature Search: A.A., Writing: A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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