CASE REPORT

Congenital Ewing’s Sarcoma/Peripheral Primitive Neuroectodermal Tumor: A Case Report and Review of the Literature

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Ewing’s sarcoma (EWS) and peripheral primitive neuroectodermal tumor (pPNET) are small round cell malignancies that develop in soft tissue and bone. They very rarely affect newborns. A diagnosis of EWS/pPNET depends mainly on immunohistochemistry and molecular/genetic assays. Since these tumors are highly aggressive, patient prognosis is typically very poor, and treatment remains a challenge. Here, we report a 13-day-old newborn diagnosed with congenital EWS/pPNET and describe its treatment.

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1. Introduction

Ewing’s sarcoma (EWS) and peripheral primitive neuroectodermal tumor (pPNET) are two types of malignant tumor that are histologically characterized by the presence of small, round cells in soft tissues and bone. This rare malignancy occurs primarily in children and adolescents, but it is extremely rare in newborns. Here, we describe a 13-day-old newborn diagnosed with EWS/pPNET in her upper left arm.

2. Case report

A 13-day-old newborn female was admitted due to a swollen mass on her upper-left arm after birth. She was a full-term cesarean neonate without a family history of genetic diseases. A physical examination revealed a round, soft, dark mass with clear boundaries, measuring about 5 cm x 5 cm x 4 cm, in her upper left arm. There was no increase in local skin temperature or any detectable fluctuation. An ultrasound showed a well-defined isoechoic mass close to the brachial artery with point-like blood flow within the mass, and rich blood flow surrounding the mass. Computed tomography (CT) detected an isodense soft tissue mass measuring 4.6 cm x 3.7 cm in the coronal maximum of her upper left arm, which was attached to the biceps and triceps (Figure 1). Enhanced scanning further showed a heterogeneously enhanced mass pressing onto the
left brachial artery, with branches of the brachial artery extending within the mass. The bone in the left humerus did not appear to be affected.

The mass was completely resected and, upon gross inspection, had the appearance of a fish-like cut surface. A pathologic examination found histological evidence of malignant, small round tumor cells that were not accompanied by a margin of residual tumor cells (Figure 2). The tumor cells were immunohistochemically positive for CD99 (Figure 2) and Ki67 (40%; Figure 2), and negative for desmin, myogenin, synaptophysin, leukocyte common antigen, S-100 protein, P63 protein, smooth muscle antibody, and epithelial membrane antigen. To detect chromosome 22q12 translocation, fluorescence in situ hybridization (FISH) was employed using LSI EWSR1 (22q12) Dual Color, Break Apart Rearrangement Probe (Vysis; Abbott Molecular, Des Plaines, IL, USA). Fluorescence was detected using a microscope with a Y-Fl Epi-Fluorescence Attachment (Nikon, Tokyo, Japan). Tumor cell nuclei that exhibited a split of signal pair were scored as positive for translocation and rearrangement of chromosome 22q12 (Figure 2).

After surgery, enhanced chest CT and abdominal ultrasound were performed. No evidence of abnormality or metastasis was detected. However, it was recommended that the upper left limb be amputated. The patient’s parents refused, and the infant was transferred to the oncology department for further treatment 7 days after surgery. Due to the infant’s young age and the immaturity of her organs, she received four courses of chemotherapy with cisplatin (20 mg/m².day, quaque die × 4 days, once every 3 weeks) and cyclophosphamide (0.2/ m².d, qd × 4 days, once every 3 weeks). However, 3 months later, distant metastasis involving the lung and liver were detected without local recurrence. Gradually, the infant became emaciated and infirm, and eventually she died of dyscrasia.

Figure 1  Computed tomography detects a mass present in the upper left arm.

Figure 2  (A) A uniform population of small round cells with minimal cytoplasm and fine granular chromatin nuclei stained with hematoxylin and eosin (magnification, 300×). (B) Neoplastic cells with strong expression of CD99 (En Vision; magnification, 300×). (C): Expression of Ki67 (40%; En Vision; magnification, 300×). (D) Fluorescence in situ hybridization reveals that tumor cells are characterized by one fused, one red, and one green signal pattern (labeled with lines), and chromosome translocations of the EWSR1 region have occurred in 22/50 nuclei.
3. Discussion

EWS and PNET are both small round cell malignancies that develop in soft tissue and bone. These tumors originate from the neuroectoderm and are composed of undifferentiated, or poorly differentiated, neuroepithelial cells that have the capacity to differentiate into neuronal, neuroglial, or other mesenchymal cell types. PNET and EWS exhibit differences in their level of cell differentiation. Accordingly, PNET and EWS are considered two distinct tumor types. However, immunohistochemistry, electron microscopy, and genetic pathology have demonstrated that EWS of bone and extraskeletal tissue, PNET, and Askin’s tumor are all EWS/PNET tumors. Furthermore, the treatment and prognosis for each of these diseases is essentially identical. In addition, based on the site of origination, PNETs are classified as central or peripheral.

Four percent of EWS/pPNET cases involve soft tissue sarcomas. Moreover, although 70–80% of patients experience tumor onset prior to the age of 20 years, 14% of EWS/pPNET cases involve children younger than 5 years. The most common symptoms are local pain and a swollen mass, accompanied by fever or a deteriorating condition. Elevated leukocyte counts and erythrocyte sedimentation rate are also frequently observed. Imaging methods typically show no specific signs, leaving EWS/pPNET to be diagnosed based on histopathological and immunohistochemical characteristics. In addition, 90% of patients show reciprocal chromosomal translocations and fused genes (e.g., the fusion of the EWS gene on chromosome 22q12 with the FLI-1 gene on chromosome 11). The presence of this chromosome translocation combined with positive immunostaining of CD99 represent the sensitive and specific assays that are currently available for establishing a diagnosis of EWS/pPNET.

At present, the treatment of choice for patients with EWS/pPNET consists of radical surgical resection followed by chemoradiotherapy. However, due to the highly malignant and aggressive phenotype of these tumors, approximately 25% of patients present with distant metastasis at the time of diagnosis, making it difficult to completely resect all of the tumor tissue present.

EWS/pPNET tumors are extremely rare in newborns. To date, only 13 newborns (<28 days) with congenital EWS/pPNET of soft tissue have been reported in the English literature (Table 1). In all of these reports, the prognosis was very poor, and most of the infants did not survive more than 2 years. Consequently, judicious fetal screening is extremely important. Furthermore, when a fetal soft tissue mass is revealed by prenatal ultrasound, EWS/pPNET should be suspected. A mass puncture is necessary and will allow an immunohistochemistry examination to be performed in combination with assays to detect chromosome translocations. These results will be useful for a diagnosis of EWS/pPNET, and they can differentiate it from other conditions. If screening is performed as needed, there should be a reasonable intervention timely involving radical resection in the fetal period.

Conflicts of interest

All contributing authors declare no conflicts of interest.

References


