CASE REPORT

Primitive neurectodermal tumors: A case of extraosseous Ewing’s sarcoma of the small intestine and review of the literature

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Summary

This is a review of extraosseous Ewing’s sarcoma (ES) which includes a new, extremely rare case. The literature was examined with respect to determining the locations of extraosseous ESs, the incidence per site and in total and the criteria which confirm the similarity between extraosseous and osseous ES.

ES sites were detected in several organs and tissues, mainly in the trunk, extremities and the retroperitoneal region. Studies confirmed that osseous and extraosseous ES are identical chromosomally and histologically. ES of the small intestine, described here, has not been previously documented in the literature.

Along with the other different documented sites, a new location of primary extraosseous ES is also reported here.

Key words: Ewing’s sarcoma, intestinal

Introduction

ES is a separate clinicopathological entity which is considered to be the second most common malignant bone tumor in children and adolescents [1], with most cases occurring during the second decade of life [2,3]. Classified as a peripheral primitive neuroectodermal tumor (PNET), ES, in the great majority of cases, originates in the bones but it is also seen in the soft tissues without osseous involvement. The extremities, chest wall and pelvis are the sites which are mainly involved [4].

Extraosseous ES arises exclusively in the soft tissues [2]. In light microscopy, the histology is indistinguishable from that originating in the bone.

PNETs arise from pluripotential neural crest cells and are characterized by aggressive development with a tendency to metastasize, and a high recurrence rate [5]. The soft tissue localization of peripheral neuroepithelioma or peripheral neuroblastoma and PNET expresses positive neural markers [6], whereas only rarely are they expressed in extraosseous ES. The chromosomal reciprocal translocation (11;22) (q24;q12) which is found in peripheral neuroepitheliomas has been detected in a case of extraskeletal ES [6]. These authors suggested that confirmation that this translocation is consistently present in both skeletal and extraskeletal ESs would be an indication of a common histogenesis [7]. Chromosomal abnormalities were also detected in 3 cases of extraskeletal ES which showed 48XY t (11;22) (q24;q12) karyotype as well as other abnormal chromosomal findings [8]. These researchers correlated the histologic characteristics, tumor genetic patterns in nude mice and growth in cell cultures. The characteristics appeared at both optical and electron microscopic levels [8,9].

Although there are several extensive reviews of extraosseous ES in the literature, none has documented intestinal ES. What follows is, we believe, the first reported case of ES originating in the small intestine.

Case presentation

A 66-year-old male patient with intestinal hem-
orrhage was admitted to our hospital. On surgery, a tumor from the small intestine was removed. Histology showed ES (PNET). Fifteen months later a recurrent local tumor was detected (Figures 1, 2). An abdominal CT scan showed more than one mass in the abdomen adjacent to the small as well as the large bowel. A second operation led to complete tumor excision, again located in the small intestine and adjacent to the large bowel. Part of the small intestine was removed and a left hemicolectomy was performed. The size of the larger mass was 10 cm. Histology was identical to the first one and showed a malignant mesenchymal neoplasm consisting of dense rosette-like unified cells and round or oval light-dyed nuclei. Mitoses were moderate (mitotic index). The periodic acid-Schiff (PAS) histochemical dye was positive in a small percentage of cells. Immunohistochemistry was positive for Vim, S100 and neuron specific enolase (NSE) in a small number of cells. No metastatic disease was found. The patient underwent 4 cycles of chemotherapy (doxorubicin, cisplatin and ifosfamide) and has been well for 48 months.

The location of ES in this case is extremely rare. Although extrasosseous ES has been described in the retroperitoneal region, in the pelvis, urothelial and gynecological organs, the literature seems to lack data on Ewing’s intestinal sarcoma.

Discussion and review of the literature

Reviewing the literature on extrasosseous ES, a number of cases locating the primary disease in several organs or tissues all over the body has been reported. The appearance of ES in children at early age at these diverse sites, justifies the embryonal origin of the tumor.

In an extensive review, 42 cases (19 males, 23 females) of extrasosseous ES were analyzed. The age distribution ranged from 2-months-old to 70 years, with a median age 22 years. The sites of involvement were: 22 (52.38%) cases in the limbs, 8 (19.05%) in the pelvis, 5 (11.90%) in the paravertebral region, 3 (7.14%) in chest wall, 2 (4.76%) in the shoulder and 2 (4.76%) in the head and neck. Although in previous studies the prognosis had been very poor, in this study, 38.5% of the patients had a 5-year survival. No chromosomal analysis was described. Apart from surgery, chemotherapy and radiation therapy were administered in most cases [10]. Successful combined modality treatment has been described by others [11].

A report reviewing 83 cases of histologically confirmed ES defined the extrasosseous cases as 3% [12], while another report described 3 cases out of 46 (6.52%) [13].

In 84 cases of extrasosseous ES during or after

![Figure 1. Histology showing dense rosette-like unified cells and round or oval light-dyed nuclei (H&E ×340).](image1)

![Figure 2. Histological picture with the surrounding tissue of the small intestine (H&E ×120).](image2)
adolescence it was reported that the most common primary sites included the trunk, extremities and retroperitoneum. Males were more frequently affected but the difference from females was small [14]. Pathological characteristics were the rosette formation (18 cases) and glycogen deposition (21 cases), while less common were NSE (8 cases), S-100 protein (6 cases) and neurosecretory-type granules (9 cases).

Primary retroperitoneal sarcomas in children was the subject of another study in which the great majority were undifferentiated embryonal or botryoid rhabdomyosarcomas. Four cases (3.96%) were described as extraskeletal ES. Two- and 3-year survival was 44% and 42%, respectively [15].

A reported cutaneous case represents a very unusual site for extraskeletal ES. Although ES in deep soft tissues has been well documented, the cutaneous type is considered to be a rare occurrence: it involved a 12-year-old girl who presented with a dermal and subcutaneous tumor of the third toe, without osseous involvement [16].

Cutaneous extraskeletal sarcoma was described many years ago in an 18-year-old female patient: located in the left paravertebral region, it was considered to be non-Hodgkin's lymphoma which spread rapidly. At autopsy the histopathologic features classified it as extraskeletal ES [17].

A rather recent report describes the occurrence of extraskeletal ES in deep soft tissues and makes the distinction of a superficial variant. The latter has been characterized as less aggressive than the osseous and deep soft tissue counterparts, with an apparently favorable outcome. These researchers reviewed 14 cases (7-21-year-old, median age 16 years) of cutaneous and subcutaneous ES. The anatomic locations included the trunk and pelvis, upper or lower extremities and the head and neck. Surgery was performed and radiation therapy and chemotherapy (doxorubicin, ifosfamide, vincristine cyclophosphamide, etoposide and dactinomycin) were administered in the majority of the cases. It was concluded that these cases of ES are associated with an indolent course and a favorable prognosis when treated with combined modality therapy [18].

The good prognosis of cutaneous ES has been also pointed out by another report of 5 cases where local excision was followed by chemotherapy. Three cases showed no recurrent disease after a median of 33 months [19].

The histological appearance of extracutaneous and osseous ES is considered to be identical. Remarkable ultrastructural uniformity was found in ES of the bone as described in a review which also reported that soft tissue sarcomas can be divided into two distinct groups on the basis of the ultrastructural criteria: “those closely resembling primitive areas of otherwise differentiated rhabdomyosarcomas” and “those indistinguishable from ES of the bone [20].” It was supported that on the basis of MIC2 expression and of specific chromosome aberration, ES and peripheral primitive neuroectodermal tumors are of common histogenesis [21].

Extraskeletal ES in the spinal epidural space was documented in 2 cases 25 years ago. In their review of 43 extraskeletal ES, these authors reported that 7 were epidural in location [22]. Primitive neuroectodermal tumor - extraskeletal ES, has also been reported as originating in the ureter and presenting with right flank pain and hematuria in a 17-year-old girl [23]. Another case developed 8 years post allogeneic bone marrow transplantation performed for beta-thalassemia major. The authors discussed the possible contribution of the transplantation procedure as well as of the genetic factor [24].

In 123 soft tissue tumors and 65 bone tumors, the cytomorphicologic features of ES were reviewed. Of the 14 cases classified as ES, 3 were extraskeletal. The age of patients ranged from 8 to 30 years. The cells of ES had finer nuclear chromatin compared to other neoplasms such as PPNET and Askin tumor [25].

Two cases of extraskeletal ES in another unusual location have been described. One tumor involved the vaginal wall of a 35-year-old woman and the other neoplasm arose in the dermis of the vulva in a 28-year-old woman. Nodular monotonous proliferations of undifferentiated, small, round, hyperchromatic cells with a low mitotic index and rare rosette-like formations were apparent only in the vulvar neoplasm. The tumor displayed intense immunoreactivity in a membranous pattern for CD99, the cell surface glycoprotein encoded by the MIC2 gene. Genetically, the tumor expressed the EWS/FLI-1 chimeric transcript, derived from t(11; 22) (q24; q12), chromosomal translocation [26]. The Ewing tumor family of peripheral neuroectodermal tumors expresses human gastrin-releasing peptide [27].

A case of extracutaneous sarcoma has also been reported in the uterus, a cystic mass involving the uterine cervix, as well as two other cases in the cervix [28,29]. A case of PNET in the kidney which showed the characteristic microscopic and immunohistochemical appearances of a small, round, dark-blue cell tumor with local rosette formation and strong membrane positivity for the MIC2 gene product, has also been described [30].

The Intergroup Rhabdomyosarcoma study (1972-1991) reported that out of 2,792 cases, 130 (4.66%) aged under 21 years had extraskeletal ES. Fifty-four percent were males [31]. The primary tumor sites were: trunk (41), extremities (34), head and neck (23), retroperitoneum/pelvis (21) and other sites (11). Over 60%
of these patients were alive after 10 years [32]. A review of ESs in childhood and their epidemiology has been documented [33].

The literature reports other cases of extraosseous ES either as case reports or reviews of a number of patients [9,13]. Our case included here describes another extremely unusual site of extraosseous ES: the small intestine. We believe that to date, there have been no reports of such a case in the literature.

References