

Double Primary Presentation of Liposarcoma and Ewing's Sarcoma: A Case Report

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The development of different entities of soft tissue sarcoma in one patient is rare. It usually affects head and neck or abdominal region, whereas those affecting the extremities are much rarer. We describe a patient with double primary presentation of liposarcoma and Ewing's sarcoma in extremity. This case implies that sarcoma patients are at increased risk of a second malignancy, and this implies a need to search for occult tumors during follow up.

색인단어: liposarcoma, metachronous, Ewing's sarcoma, primitive neuroectodermal tumor

Soft tissue sarcoma (STS) patients are at increased risk of a secondary primary malignancy, particularly another primary soft tissue sarcoma. The incidence of a secondary primary STS occurring in a previously diagnosed adult STS patient is 12.5-fold risk of a normal health individual.¹⁾ Most reported synchronous or metachronous STS affect the head and neck or abdominal region, whereas those affecting the extremities are much rarer.²⁾ The probability of primary STS with metachronous bone tumor occurring in same patient at different location is a rare occurrence indeed. In addition, the metachronous presentation of liposarcoma and Ewing's sarcoma/primitive neuroectodermal tumor (ES/PNET) has not reported so far. Therefore, we report a patient who presented with different types of sarcoma, a liposarcoma of left proximal thigh, and an ES/PNET of contralateral proximal tibia.

Case Report

A 48-year-old man presented with left proximal thigh swelling for 6 months. There was no history of trauma or any obvious initiating event. He had no constitutional, endocrinologic, or neurologic symptoms. There was no history of soft tissue tumors. Examination revealed a large mass in the medial aspect of left proximal thigh and

there was no lymphadenopathy.

Magnetic resonance imaging (MRI) showed 8×6×11 cm sized lobulated mass. T1-weighted images showed similar signal intensity with surrounding muscle, T2-weighted images showed heterogeneously high signal intensity, and the lesion was peripherally enhanced with contrast (Fig. 1). Additional workups were performed to evaluate metastasis, however there was no evidence of disease elsewhere (Fig. 2).

We performed wide margin excision. The mass was relatively well circumscribed whitish mass with necrosis. Pathologic diagnosis was compatible with round cell type of liposarcoma (Fig. 3). The patient was recommended 5 cycles of sequential high dose chemotherapy with vinblastine, ifosfamide, and cisplatin, and had radiation therapy of 6,000 cGy for 30 times. However, patient did not receive full cycles of sequential high dose chemotherapy because of cardiomyopathy, but received only radiation therapy.

Two years and 6 months after excision, the patient returned to the clinic with a left knee pain and swelling of proximal tibia. Plain radiographs showed osteolysis in proximal tibia (Fig. 4), MRI demonstrated a heterogeneous mass tibia and ilium (Fig. 5), and bone scan showed hot uptake at same site. We performed open bone biopsy with prophylactic plate fixation to prevent pathologic fracture because we considered this lesion as metastasis from primary site. Histopathological study of the specimens revealed small round cell sarcoma. Immunohistochemically, the tumor cells were positive for CD99 and FLI-1. Based on the histological features and the immunostain results, a diagnosis of ES/PNET was favored. Fluorescence

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Figure 1. (A) Axial T2-weighted fat-saturated image, (B) Axial T1-weighted image, and (C) gadolinium enhancing image showing mass in proximal thigh.

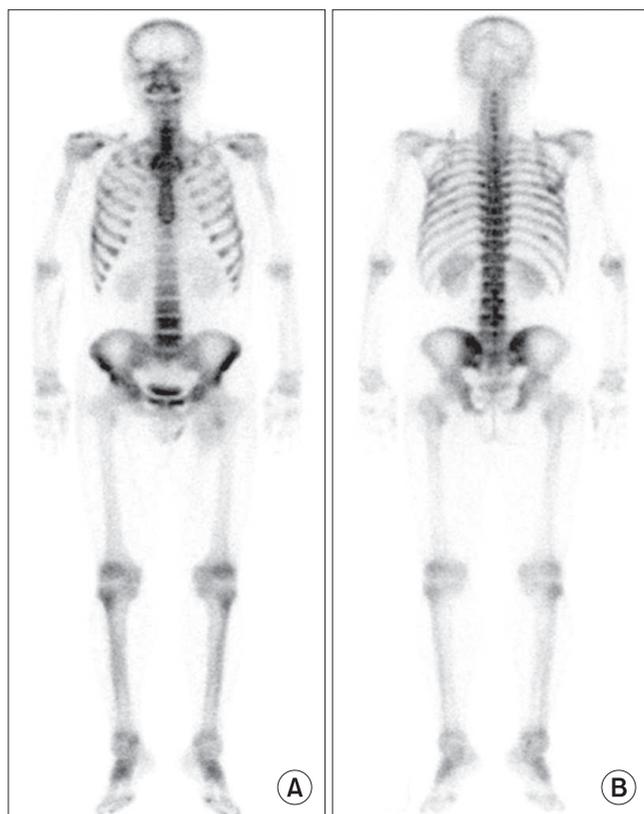


Figure 2. Tc99-bone scans showing diffuse uptake left proximal thigh and no other site of disease. (A) Anteroposterior, and (B) posteroanterior bone scan view.

in situ hybridization (FISH) analysis confirmed an Ewing sarcoma region 1 (*EWSR 1*) gene rearrangement at chromosome 22q12, establishing the diagnosis of ES/PNET (Fig. 6), and he was referred for receiving chemotherapy and radiation therapy of 3,250 cGy for

13 times.

Discussion

Soft tissue sarcomas have been associated with the development of other malignancies in the genetic conditions neurofibromatosis, familial adenomatous polyposis (FAP), retinoblastoma, and Li-Fraumeni syndrome.³⁻⁶ In addition, there are possible explanations for multiple primary tumors in one individual; a genetic predisposition to malignant disease, an increased risk of secondary primary tumors in patients who were treated previously for breast carcinoma, Hodgkin disease, osteosarcoma, lung carcinoma, and an immunocompromised state and increased age. The rate of synchronous/metachronous neoplasm is 7.5% in STS patients compared with 1% in the general cancer population. Patient was evaluated for family history of genetic condition of multiple STS; however there were no specific findings. In this case, patient did not receive full cycles of sequential high dose chemotherapy because of cardiomyopathy, and had only radiation therapy to the operation site. ES/PNET may be resulted from increased risk of a secondary primary malignancy after primary liposarcoma resection and/or inadequate chemotherapy because of patient condition.

Liposarcoma is the most common histology of STS and accounts for 20% to 30% of all sarcoma in adults. Myxoid liposarcoma and round cell liposarcoma were formerly classified as distinct entities but are now recognized as a continuum of the same entity on the basis of a common chromosomal translocation found in up to 90% of cases.⁷ Patients with myxoid liposarcoma containing areas of round cells exceeding 5% reportedly have a worse prognosis than those

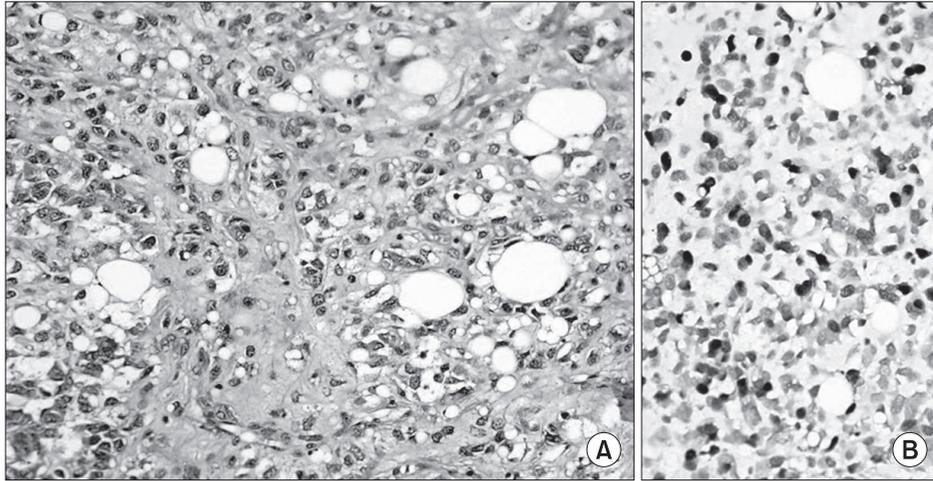


Figure 3. (A) A high-power photomicrograph of the specimen shows findings compatible with liposarcoma (Stain, hematoxylin & eosin; magnification, $\times 200$) and (B) positive S-100 immunohistochemical analysis stain.

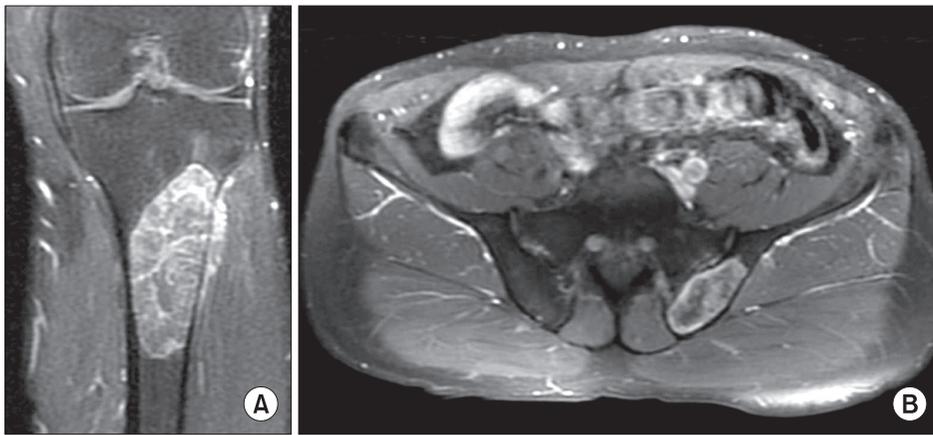


Figure 5. Magnetic resonance imaging showing heterogenous enhancing mass. (A) proximal tibia and (B) left ilium.

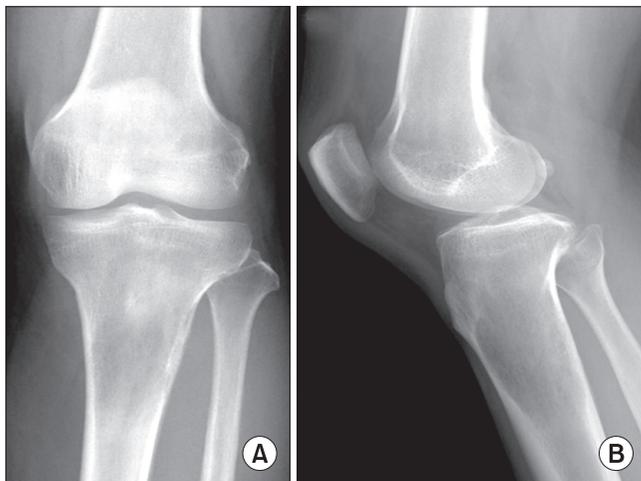


Figure 4. 2 years and 6 months follow up radiographs showing a new osteolytic lesion in proximal tibia. Anteroposterior (A) and lateral view (B).

containing no round cell components.⁸ Most metastases occurred in extrapulmonary sites, including the retroperitoneum, pericardium, subcutaneous tissues, and bone, which is a typical feature of myxoid

liposarcoma. Metastasis to ilium and tibia like this patient was considered as very rare condition, when they metastasize, in contrast to other liposarcoma variants they tend to metastasize to unusual locations with worse prognosis.^{9,10} In this case, areas of round cells exceed 5% and therefore, we performed palliative surgery which was open bone biopsy at ilium and tibia and prophylactic plate fixation to prevent pathologic fracture.

ES/PNET are more common in adolescents with a peak incidence between 10 and 15 years of age, can rarely occur in old age and, have a slight male predominance, and typically involve the extremities and the axial skeleton. The diagnosis of ES/PNET based on identifying, in the majority of aberrant interphase cells examined, the presence of a rearranged EWS gene locus. The $t(11;22)(q24;q12)$ trans-location, a chromosomal abnormality specific to the Ewing's sarcoma, is detected in $\sim 90\%$ of cases. This translocation results in the formation of the EWS-FLI1 fusion gene. Another 10% of cases have a variant translocation fusing EWS to closely related EWS genes such as ERG, ETV1, EIAF, and FEV. The presentation of ES/PNET at this age is rare, in addition, metachronous occurrence after

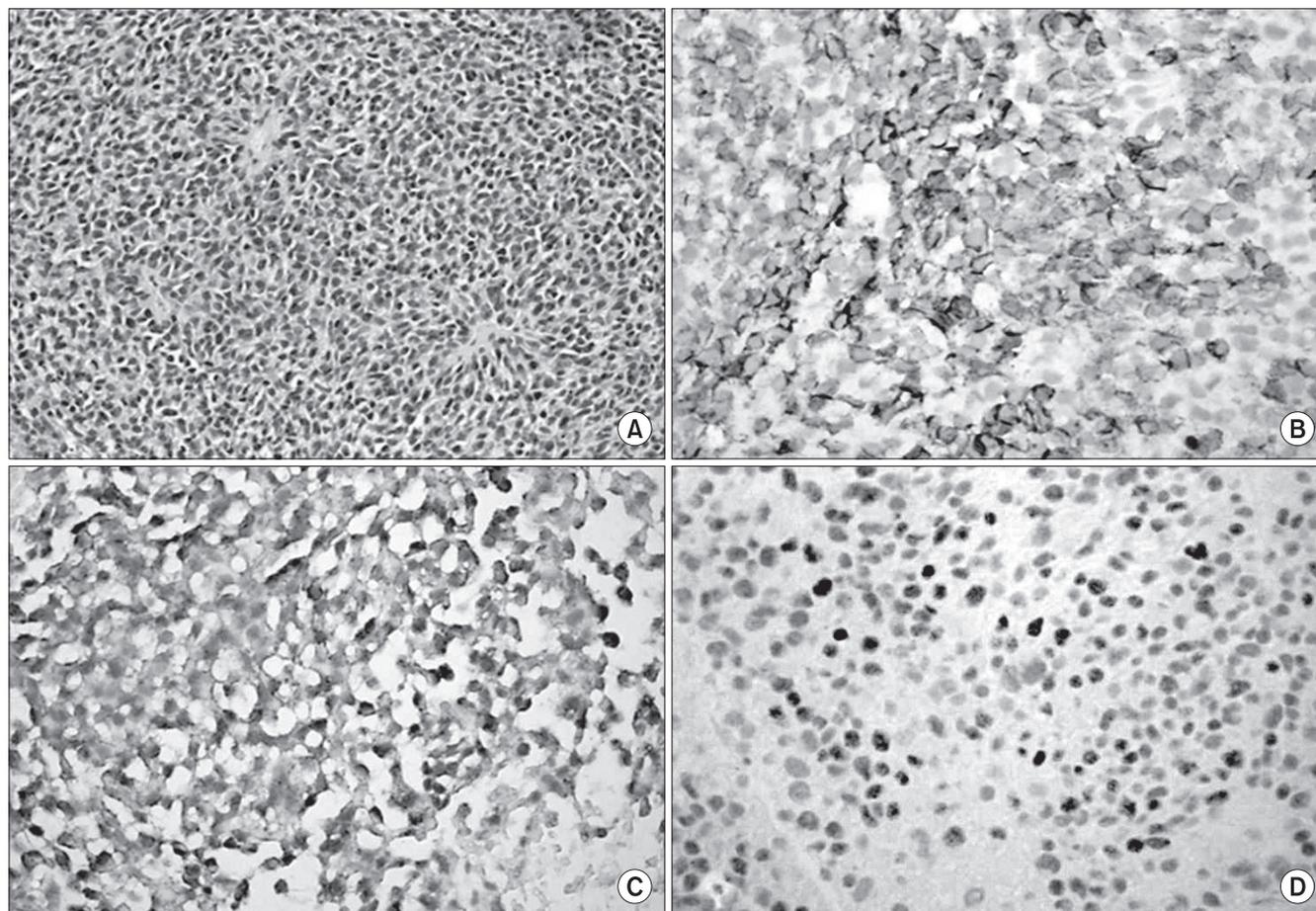


Figure 6. Pathology revealing ES/PNET. (A) photomicrograph (Stain, hematoxylin & eosin; magnification, $\times 200$), (B) CD56, (C) CD99, and (D) FLI-1 of immunohistochemical analysis.

liposarcoma is considered as a very unusual finding.

In conclusion, this case report establishes metachronous presentation of liposarcoma and Ewing's ES/PNET can occur. To the best of our knowledge, this is the first report of this metachronous presentation of two different presentations. Sarcoma patients are at increased risk of a second malignancy, and this implies a need to search for occult tumors during follow up.

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대퇴부 지방육종 수술 후 발생한 반대측 근위 경골의 유잉육종/원시 신경 외배엽 세포종

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악성 연부조직 종양 수술 후 이시성(metachronous)으로 발생하는 악성 골종양은 매우 드물다. 이시성 종양은 두 · 경부 또는 복부에 주로 발생하며, 사지에 발생하는 경우는 더욱더 드물다. 저자들은 48세 남자환자에서 근위 대퇴부 악성 지방 육종의 광범위 변연 절제술 후 발생한 근위 경골 유잉육종/원시 신경 외배엽 세포종 1예를 경험하여 문헌 고찰과 함께 보고하는 바이다. 육종 환자들에게서는 이와 같이 이차적으로 악성 종양이 발생할 확률이 높아지기 때문에 추시 기간 동안 잠복 종양(occult tumor)에 대한 검사가 필요하겠다.

색인단어: 지방육종, 이시성, 유잉육종, 원시 신경 외배엽 세포종

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