Simultaneous occurrence of osteosarcoma and osteochondroma following treatment of neuroblastoma with chemotherapy, radiotherapy, and bone marrow transplantation

Abstract Radiation-induced bone changes and second malignancies, as well as benign tumors, following bone marrow transplantation are being reported with increasing frequency. An osteosarcoma of the fourth right rib and an osteochondroma of the left scapula developed in a long-term survivor of abdominal neuroblastoma treated with chemotherapy, local radiation, and bone marrow transplantation. All these treatment modalities are known to induce neoplasia.

Introduction

The success of allogenic bone marrow transplantation (BMT) for the treatment of malignant and nonmalignant hematologic and nonhematologic diseases has increased during the past 14 years [1-3]. Prior to BMT, high-dose chemotherapy and total-body irradiation (TBI) are given to eradicate residual malignant cells and suppress the immune response to donor marrow. TBI is commonly performed in a single dose of 10 Gy or in multiple (fractionated) doses for a total of 12-14 Gy [4]. Long-term TBI-related complications in children include chronic pulmonary disease (obstructive and restrictive), cataracts, and multiple hormone dysfunction [5-7]. The effects on bone include benign conditions, such as necrosis, stunting of growth, osteitis, pathological fractures, fibrous dysplasia, and aneurysmal bone cysts, as well as bone tumors (osteochondroma, chondrosarcoma, and osteosarcoma) [5-13].

There have been only a few reports [12, 14] of osteosarcoma or chondrosarcoma following treatment of childhood neuroblastoma. These patients received localized radiation to the tumor bed and/or chemotherapy. However, there is no previous report of osteosarcoma and osteochondroma occurring in long-term survivors of a childhood neuroblastoma treated with bone marrow transplantation (BMT). We report on an 11-year-old patient who presented with an osteosarcoma and a benign osteochondroma 9.5 years after receiving radiation, chemotherapy, TBI, and BMT for abdominal neuroblastoma.

Case report

An 11-year-old boy was admitted because of sudden onset of mid-abdominal pain radiating to his back and the right side of his chest. The pain was exacerbated by coughing or sneezing. The patient's medical history was significant for neuroblastoma, stage IV, diagnosed at 13 months of age. He was treated with chemotherapy (dacarbazine, vincristine, adriamycin, cyclophosphamide) and radiation (2000 cGy to the tumor bed in the abdomen and 1000 cGy to the skull, possibly for bony metastasis). TBI with 1200 cGy and autologous bone marrow transplantation (ABMT) were performed at 21 months of age. Since then he had been in remission. His medical history was also significant for optic nerve atrophy, cataracts, and nystagmus, probably secondary to radiation. Furthermore, the patient had growth hormone neurosecretory dysfunction with central precocious puberty, with possible gonadal failure and primary hypothyroidism secondary to irradiation.

Imaging studies at the time of his present admission revealed the following: Plain film of the chest showed a soft tissue mass involving the right chest wall adjacent to the third to sixth ribs. There were punctate calcifications within the mass. The fourth rib showed a moth-eaten appearance and there was a pathologic fracture (Fig. 1). Plain film of the abdomen showed a nonspecific bowel gas pattern with scattered metallic surgery clips along the midline.
Fig. 1 Plain radiograph of the right hemithorax shows a soft tissue mass involving the right chest wall. There is associated punctate calcification in the area adjacent to the third to sixth ribs. The fourth rib shows evidence of destruction and a pathologic fracture (arrow).

Fig. 2 Enhanced CT scan (lung window) of the chest shows the rib changes as well as a pathologic fracture of the right fourth rib (black arrow), associated with a large extrapleural mass (white arrow).

Fig. 3 Enhanced CT scan (lung window) of the chest shows the rib destruction and soft tissue mass on the right (arrowhead) and osteochondroma arising from the left scapula (long arrow).

and mild flattening of the lumbar vertebrae, secondary to radiation. The contrast-enhanced CT scan of the chest showed destruction and a pathologic fracture of the fourth rib on the right, associated with a large extrapleural mass extending toward the lung parenchyma along the minor fissure (Fig. 2). The mass showed extraspineous calcification. There was no evidence of parenchymal pulmonary disease. There was also a lesion consistent with an osteochondroma of the left scapula, which had been seen incidentally also on a radiograph obtained 2 years earlier (Fig. 3).

The enhanced CT scan of the abdomen revealed retroperitoneal calcification along the aorta, indistinguishable at some points from surgical clips. The left adrenal gland was densely calcified. These findings were unchanged from those of a CT performed 5 years earlier. The left kidney appeared to be slightly smaller than the right, probably due to radiation, and showed delayed function. The technetium 99m MDP nuclear scan revealed increased uptake in the fourth and fifth ribs, suggestive of a neoplastic process.

At operation the tumor was found to be in the fourth rib at about the anterior axillary line. It appeared adherent to the lung at the junction of the middle and lower lobes. Complete tumor excision necessitated further resection of the third, fourth, and fifth ribs. On pathologic examination the resected tumor measured 8.5 x 5.5 x 3 cm in its greatest diameter. Sections of the tumor showed a malignant neoplasm with typical characteristics of an osteogenic sarcoma.

Following surgery the patient was started on a modified POG 9351, regimen B, of osteosarcoma chemotherapy, consisting of ifosfamide, adriamycin, high-dose methotrexate, and cisplatin. Ten months after surgery there is no evidence of recurrent disease or metastasis.

Discussion

Advances in diagnosis, chemotherapy, radiotherapy, and BMT have greatly improved the outlook for the child with neoplastic disease. Therefore, the percentage of long-term survivors of childhood malignancies and, consequently, the incidence of second malignant neoplasms is increasing. The predicted incidence of second malignancies ranges from 3.3 to 35% [15]. Such a wide range of incidence may be due in part to the length of long-term follow-up and does not necessarily indicate treat-