Bone metastases in Wilms’ tumor – report of three cases and review of literature

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Abstract. Bone metastases are extremely rare in patients with classical Wilms’ tumor (WT). We describe the clinical and radiologic features, treatment and outcome of three patients with WT (one with favorable histology and two with anaplasia) in whom bone metastases were detected at diagnosis or relapse. Bone metastases were documented by skeletal radiographs, computed tomography and/or bone scintigraphy. The patient with favorable histology WT had no evidence of pulmonary metastases and is now free of disease following aggressive chemotherapy and radiotherapy.

Wilms’ tumor (WT) typically spreads to regional lymph nodes, and distant metastases involve the lungs and liver [1]. In contrast with neuroblastoma, the occurrence of bone metastases in classical WT is extremely uncommon [2]. Of 375 patients diagnosed with WT in our institution between 1962 and 1992, only three (0.8%) were found to have bone metastases (one at diagnosis and two at relapse). Here we report the radiologic findings and clinical course of these patients. In each case, the histologic material was reviewed by our institution’s pathologist and confirmed to be WT.

Case Reports

Patient 1

A 5-year-old white male was diagnosed in 1986 with stage IV anaplastic WT with pulmonary metastases, including a large right upper lobe mass. Computed tomography (CT) of the abdomen showed a large right renal mass and non-contiguous lytic lesions of the lumbar vertebrae and right sacral ala. Plain radiographs showed lytic bony lesions in both proximal humeral metaphyses. A 99mTc-methylene diphosphonate (MDP) bone scan showed focally increased radioactivity in the proximal femora, both proximal tibial metaphyses, the neck and distal metaphysis of the right femur, the occiput, left temporal bone, the third lumbar vertebra, and the right sacroiliac region. The diagnosis of WT was confirmed by needle biopsy of the primary tumor (biopsy of the bone metastases was not performed) following which the patient received chemotherapy with vincristine, cisplatin, and etoposide alternating with vincristine, actinomycin D, and doxorubicin. Four months from diagnosis and after five courses of treatment, delayed excision of the primary tumor was performed with a right nephrectomy. The patient then underwent pulmonary irradiation at a dose of 15 Gy with the field extended to include the proximal humeral metaphyses. The patient then underwent pulmonary irradiation at a dose of 15 Gy with the field extended to include the proximal humeral metaphyses. Radiographs revealed lytic bone metastases in the calvarium and the distal femoral and proximal tibial metaphyses (Fig. 1) and healing lytic lesions of the proximal humeri and right femoral neck. Bone scintigraphy showed abnormal activity in the right tarsus, the distal right tibial metaphysis and the second cervical vertebra. The patient responded poorly to further treatment and died of progressive disease 6 months after diagnosis. Autopsy was not performed.

Patient 2

A 9-year-old white male was diagnosed in 1990 with stage I favorable histology WT, and underwent chemotherapy with vincristine and actinomycin D every 2 weeks for 6 months. Eight months following diagnosis, he presented with right groin pain. Radiographs and CT of the pelvis disclosed an osteolytic lesion in the right ischium and pubis, with an associated soft tissue mass (Fig. 2). A 99mTc-MDP bone scintigram revealed increased uptake in the region of the right acetabulum. CT showed no evidence of recurrent disease in the abdomen or pulmonary metastases. Biopsy of the lesion confirmed metastatic favorable histology WT. The patient received five courses of ifosfamide, carboplatin, and etoposide, together with local radiotherapy at a dose of 27 Gy. There was evidence of healing of the metastasis on CT and bone scintigraphy. The patient remains disease-free 30 months from relapse.
Fig. 1. Patient 1: An AP radiograph of the knee shows lytic destructive lesions of the distal femoral and proximal tibial metaphyses.

Fig. 2. Patient 2: An IV contrast-enhanced CT image of the pelvis shows a lytic lesion of the right pubis and ischium with an associated soft tissue mass.

Fig. 3a, b. Patient 3: a An AP radiograph of the chest shows a sclerotic, expansile lesion of the right scapula. There are bilateral lower thoracic paraspinal masses and small bilateral pulmonary metastases. b A lateral radiograph of the lumbosacral spine shows sclerotic metastases involving the bodies of L2 and L3-S3.

Patient 3

A 11-month-old white male was diagnosed in 1977 with stage I diffuse anaplastic WT. A radiographic skeletal survey performed as part of the diagnostic evaluation was normal. The patient was initially treated with vincristine and actinomycin D. Five months after diagnosis, he presented with inability to use his right arm and palpable right axillary lymphadenopathy. Chest radiographs disclosed an expansile, diffusely sclerotic lesion of the body of the right scapula, small bilateral paraspinal masses extending from T7-9 and numerous small pulmonary nodules consistent with metastases (Fig. 3a). Biopsy of an axillary lymph node confirmed metastatic anaplastic WT. The patient was treated with cyclophosphamide and doxorubicin. One week later he developed paraplegia with urinary retention. He then received local radiotherapy to the thoracolumbar spine at a dose of 20 Gy, and further chemotherapy with di-carbazine, etoposide, and methotrexate. Response to chemotherapy was poor. Reassessment, including plain radiographs following completion of chemo- and radiotherapy, revealed persistent paraspinous masses and new sclerotic lesions involving the lumbar and sacral vertebral bodies (Fig. 3b), both proximal femurs, both ischia, and the mid-portion of the left tibial shaft. A right iliac crest bone marrow biopsy confirmed metastatic WT. The patient died of uncontrollable disease 10 months after diagnosis. Autopsy was not performed.

Discussion

Bone metastases are rare in patients with classical WT, in contrast to patients with clear cell sarcoma of the kidney (CCSK). The latter tumor has a well-known tendency to metastasize to bone; this occurs in approximately 60% of patients [2, 3]. CCSK was previously included in the category of WT, but is now classified as a histologically distinct tumor [3]. While bone metastases have been described previously in association with pediatric renal tumors, the reports have either included patients with CCSK [4], or were published before the pathology of CCSK was widely recognized [5, 6]. However, reports suggest that in patients with classical WT [2, 7-11], the true incidence of bone metastases is less than 2% [2, 8].

When they occur, bone metastases in WT are usually multiple, with the spine, pelvis, and long bones commonly affected [2]. This was the case in two of our three patients. One-half of the previously reported bone metastases in children with WT involved the spine, whereas skull involvement is prevalent in patients with CCSK [2]. Bone metastases in WT have been reported to be uncommon in the absence of pulmonary involvement [8].

In our study, skeletal radiographs, CTag 99mTc-MDP scintigraphy were all useful in identifying bone metastases. Direct extension of vertebral WT metastases into the epidural space may cause spinal cord compression [2, 7, 9, 10] which can be demonstrated by magnetic resonance imaging or post-myelogram CT [9].

While bone involvement in WT is usually a destructive process with very little bone formation [2, 7-10], sclerotic or osteoblastic lesions as seen in patients 1 and 3 have been previously described [11]. The mechanisms of bone destruction or formation in bone metastases associated with WT have not been specifically studied. As