Bone Involvement in Neuroblastoma

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Neuroblastic tumors (ie, neuroblastoma, ganglioneuroblastoma, ganglioneuroma) are the most common extracranial solid tumors in children.\(^1\) Neuroblastoma (NB) accounts for almost 8% of childhood malignancies. Its prognosis is extensively variable, ranging from spontaneous regression to fatal disease in spite of receiving multimodality therapy.\(^1\) Screening programs of infants show that many cases escape detection because of spontaneous regression or maturation into benign lesions. Derivation from precursors of the sympathetic nervous system accounts for (a) primary sites in adrenal glands and in paraspinal locations from neck to pelvis and (b) high urinary levels of catecholamines in 90% of cases.\(^2\)

This embryonal neoplasm frequently invades vascular structures and usually presents with substantial metastatic disease in bone, bone marrow, lymph nodes and liver; spread to brain is observed and lung metastasis has been reported very rarely to a maximum of 3.6%.\(^3\) Hence, defining disease extension and precise staging requires imaging studies such as computerized tomography scans (or MRI), bone scan, metaiodobenzylguanidine (MIBG) scan, bone marrow (BM) examinations and biopsy and urine catecholamine measurements.\(^4\)

Multiple imaging and clinical tests are needed to accurately assess patient risk with risk groups based on disease stage, patient age, and biological tumor markers.\(^1,4\) Around 60% of patients with NB have metastatic disease at diagnosis mostly involving bone marrow or cortical bones.\(^1,2\)

Since the spread of tumor cells to the BM is a dismal prognostic sign for patients with NB, obviously searching for BM infiltration is of the most prominence for both staging and therapeutic purposes.\(^5\)

Due to the International Neuroblastoma Staging System, the presence of metastasis in BM is assessed by morphological study of BM smears and trephine biopsies.\(^4,5\) Bone involvement is detected in 55–68% of patients who have metastatic disease at diagnosis.\(^5,6\) Bone lesions affected by metastatic tumor cells are conventionally divided into two categories; osteolytic and osteoblastic.\(^6\)

Main contributors in osteolytic lesions are osteoclast activating factors such as parathyroid hormone-related protein (PTHrP) which stimulates osteoclast maturation and in osteoblastic lesions there are factors that stimulate osteoblast proliferation, differentiation and bone formation.\(^7\) Regularly, both osteoclastic and osteoblastic processes are observed simultaneously. Hence, osteoclast inhibitors like bisphosphonate compounds have begun to be used and demonstrate encouraging results.\(^7,8\)

The mechanisms involved in the formation of bone metastasis in NB have now begun to be elucidated. It
Sohara et al. demonstrated that zoledronic acid has a dual antiosteoclast and antitumoral activity. The data emphasize that bisphosphonate in combination with cytotoxic chemotherapy in mice with established osteolytic lesions ended in preventing bone degradation and also extending survival, so could be trialed in children with neuroblastoma that has metastasized to the bone.9

**Conflict of Interest:** None declared.

**References**


