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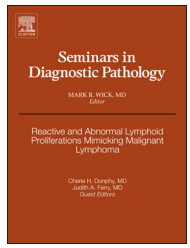

Metastases to bones

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ABSTRACT

Metastatic tumors involving the bones may derive from a number of visceral primary sites, and they can assume several histological appearances. In selected instances, diagnostic confusion with some primary bone tumors may eventuate, necessitating the use of adjunctive pathologic studies to reach a final interpretation. This review considers metastatic osseous neoplasms in the small-cell, large-polygonal-cell, and spindle-cell-pleomorphic microscopic categories. The use of immunohistology and molecular analysis to study such tumors is discussed.

Metastatic tumors in the bone usually pose little or no diagnostic difficulty for pathologists because their clinical attributes have already been recognized by radiologists or orthopedists as those of secondary malignancies at the time a biopsy is done. However, there are selected instances where that rule does not hold true, and those typically involve solitary "herald" or "messenger" metastases of visceral carcinomas. Metastatic tumors with small-cell, large-polygonal-cell, or spindle-cell attributes are those that are most likely to be confused with selected primary osseous neoplasms because both of those groups of lesions may be similar to each other histologically. Another pertinent problem is the determination of the anatomic origin of an obvious metastatic carcinoma in the bone.

Misinterpreted lesions are usually represented by metastases of visceral carcinomas that have been missed in the excitement of making the morphological interpretation of a primary osseous malignancy. Native bone tumors that enter consideration in that context include neoplasms such as Ewing sarcoma, non-Hodgkin lymphoma, adamantinoma, clear-cell chondrosarcoma, variants of osteosarcoma, fibrosarcoma, and pleomorphic sarcoma.

In the enthusiasm of diagnosing those entities, the admonition may be forgotten that the identification of bone tumors requires careful correlation of clinical, radiographic, and histologic findings. That error is potentially substantial because of the significantly different treatment approaches for primary and metastatic malignant osseous lesions. Most patients with metastatic bone tumors die within 5 years of diagnosis.[1–4] In addition, unfamiliarity with a primary intraosseous epithelial neoplasm—adamantinoma[5]—may account for another diagnostic misadventure in which that lesion is mistaken for a metastasis.

Clinical considerations

Many visceral carcinomas are capable of dissemination to secondary bony sites. At autopsy, up to 50% of patients with selected malignant epithelial neoplasms have metastatic osseous involvement.[6] In that context, cancers of the prostate, breast, lung, kidney, and thyroid are most commonly implicated.[7] Accordingly, adenocarcinomas are more frequently observed as bony metastases than are epithelial neoplasms with other lineages. In surgical pathology practice, recent studies have reported that metastases account for up to 18% of all tumors seen in bone biopsies.[8] Metastatic bone lesions primarily occur at sites of persistent red marrow and brisk intraosseous blood flow, such as the skull, ribs, vertebrae, pelvis, humerus, and femur[7] (Fig. 1). Radiographically, some specific secondary tumors reproducibly produce lytic defects in the bone in plain films (e.g., lung and renal carcinomas), whereas others are consistently osteoblastic

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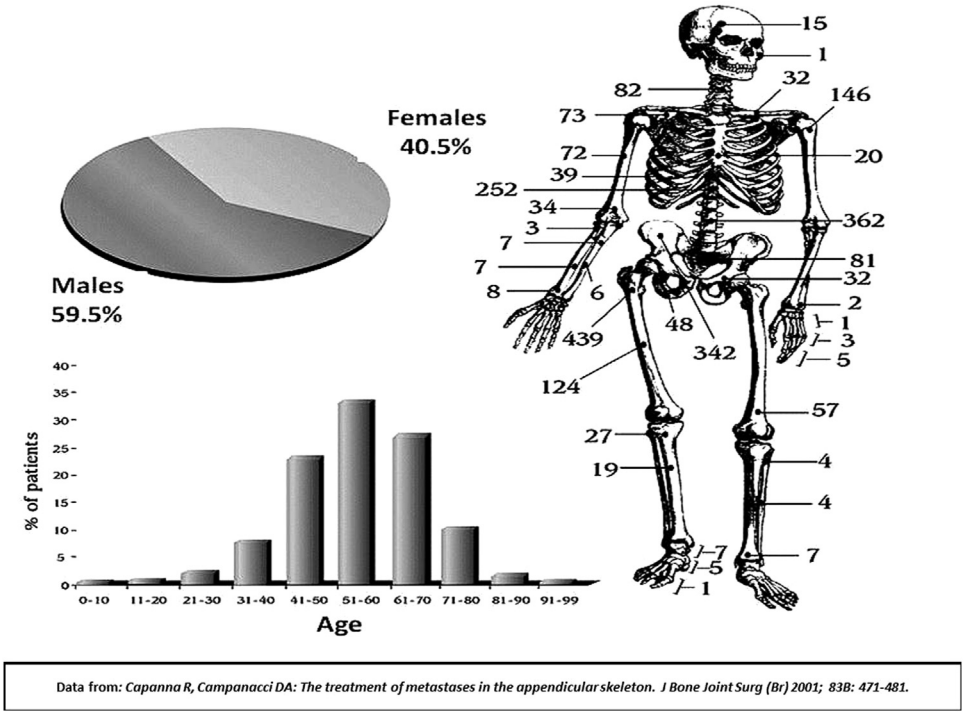

Fig. 1 – A diagram of anatomic locations, patient ages, and patient genders pertaining to metastatic tumors in the skeleton.

(e.g., prostatic and pancreatic adenocarcinomas and low-grade neuroendocrine carcinomas) (Fig. 2). However, a sizable group of lesions can yield either of those patterns.[9–11]

Bone metastases are usually observed in the context of widespread disease, when the primary site of growth has already been well documented. A sizable proportion of such patients develop osseous lesions within 6 months after diagnosis of their internal malignancies.[8] However, metastatic tumors are also capable of remaining latent in the bones for prolonged periods of time, and these are represented principally by breast and thyroid carcinomas.[7]

One must analyze this topic from another perspective to gain insights on metastatic neoplasms that can truly simulate primary bone tumors. Toma et al.[8] found that the most frequent anatomic sites of origin for bone metastases were the breasts (23%) and kidneys (21%). These were followed by

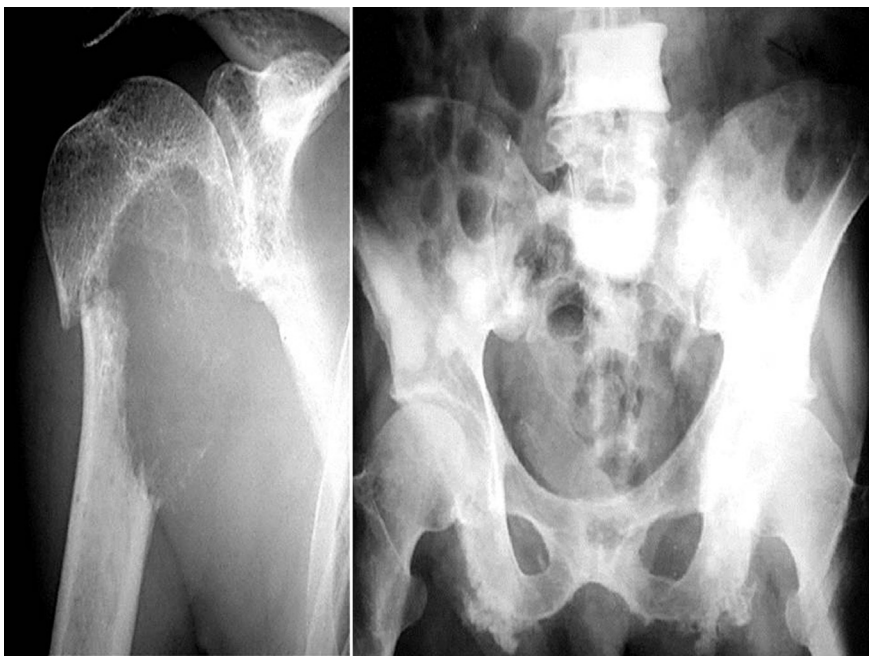

Fig. 2 – Representative plain-film radiographs of a lytic metastasis of renal cell carcinoma in the humerus (left) and blastic metastases of prostatic adenocarcinoma in the vertebrae and pelvic bones (right).