3 General Principles of Bone Pathology

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Bone tumors are among the rarest neoplasms in humans. Bone sarcomas account for 0.2% of all neoplasms arising in the human body. Considering that and the fact that more than 40 malignant histological types have been described, it is reasonable to think that only specialized centers can have enough experience in managing these neoplasms. The peculiar "multidisciplinary-team" approach is mandatory in bone tumors, in order to avoid dramatic mistakes in the diagnosis and treatment of these tumors. The pathologist dealing with bone must follow a diagnostic flowchart that starts from the accurate collection of clinical information, followed by the careful examination of the imaging, then the decision about the kind of diagnostic procedure to apply, and finally the histological diagnosis. All these steps must be shared with the other colleagues of the team, such as the orthopedic surgeons, the radiologists, and the oncologists. Examining in detail every single step of the diagnostic approach, analysis of clinical features, such as patient age, symptoms and anatomic location of the lesion, are necessary for a preliminary assessment of the lesion. Bone tumors like Ewing sarcoma and osteosarcoma usually occur in young patients. Tumors like chordoma, myeloma, and chondrosarcoma are typical of adults or elderly patients. When osteosarcomas occur in patients older than 50, they are frequently secondary to pre-existing bone conditions, such as Paget's disease, bone infarcts, or arising after radiation therapy. Symptoms and features are frequently of great clue for diagnosis. Pain during night that can be treated with salicylates is typical of osteoid osteoma; the presence of fever favors for the diagnosis of Ewing sarcoma rather than lymphoma. Laboratory tests can also be very useful; for example, the blood levels of parathormone are the key features for the diagnosis of hyperparathyroidism. The site of the tumor within the bone and the specific bone segment are very important, as some tumors occur usually in the epiphysis, such as giant cell tumor, chondroblastoma, and clear cell chondrosarcoma, while other tumors are centrally located, and others are eccentrically located in the bone cortex; others, such as adamantinoma occur almost exclusively in the tibial diaphysis. In low-grade chondroid lesions, the site of the lesion is very important for a correct interpretation of histology: if the lesion is in the small bones of the hands and feet, it is usually benign, while, with similar histological features, it is usually malignant if located in the ribs and sternum. Tumors that arise in the periostium are generally clinically less aggressive than the intramedullary counterparts. The radiographic features of the lesion are very important for the pathologists:

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they have to be considered like a negative image of the macroscopic appearance of the neoplasm. Bone lesions can cause osteolysis or reactive bone production (osteosclerosis). Combinations of these two processes give rise to three typical patterns of bone destruction:

(a) The geographic bone destruction pattern, typical of slow growing lesions
(b) The "moth-eaten" pattern, that is typical of more aggressive lesions, that usually have a faster growth rate, and for this reason the osteosclerosis in this situation is less evident
(c) The permeative growth that can be observed in the most aggressive lesions, such as lymphomas and Ewing sarcoma

Finally, periosteal reaction gives a great clue for the interpretation of biological features of a bone neoplasm. Fast-growing lesions do not cause a periosteal reaction that usually requires about 2 weeks to be detectable on radiographs. Some kinds of periosteal reactions suggest a specific diagnosis (onionskin reaction is frequently present in Ewing sarcoma). A careful examination of all these aspects helps the pathologist to achieve a correct interpretation of the histology of a given bone lesion.

In the last years, pathologists have started to collect biologic samples of fresh tumor tissue to store in biobanks, which are necessary for the study of these rare tumors, in order to perform molecular diagnostic and research tests and to share these samples with other institutions in the context of large international scientific projects.

The 2013 WHO classification of bone tumors is based on cytologic and histogenetic criteria and on the kind of matrix produced by the tumor (see previous table). It represents the classification used today. Bone producing lesions together with cartilaginous lesions and Ewing sarcoma account for about 80% of all bone tumors; the remaining entities are by far rarer. The use of ancillary techniques such as immunohistochemistry is very important for the assessment of the possible origin of a bone metastasis, but also in some primary bone tumors. Molecular techniques are widely used in the validation of the diagnosis of Ewing sarcoma and, recently, also in other situations, such as aneurysmal bone cyst, fibrous dysplasia, giant cell tumor of bone, chondroblastoma. The grading system for bone sarcomas used at the Rizzoli institute is a four grading system according to Broders (grade 1–2: low grade; grade 3–4: high grade); the grading system in WHO classification is a three grading system based on the histological type or subtype of the tumor.

The Rizzoli's syllabus is based on the study of the most numerically important series in the world, and the use of a schematic approach for every single entity gives the reader a useful diagnostic tool, very practical for such rare diseases.

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