

CONTINUING MEDICAL EDUCATION ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 31

A 22-year-old Albanian woman presented to our department with left axillary and supraclavicular lymphadenopathy of 6-month duration. She experienced also bone pain and soft tissue swelling of left femur and knee. Swelling was insidious in onset and gradually increased in size. No constitutional symptoms (fever, weight loss, night sweats) were reported. Her medical history and family history were not contributory.

Physical examination revealed left axillary and left supraclavicular lymphadenopathy and painful, hard swelling of lower segment of the left femur. Overlying skin appeared slightly stretched. On palpation there was no local raise in temperature and the swelling was tender.

Complete blood counts, erythrocyte sedimentation rate and CRP were normal. Serum biochemistry showed slightly elevated LDH levels (230 IU/L vs the upper normal limit of 220 IU/L). CT scan of the cervix and thorax revealed enlarged axillary and supraclavicular lymph nodes (up to 2.5 cm). CT of the abdomen was negative. A left knee X-ray was performed and showed a widened metaphysis of the femur and periosteal reaction (figures 1, 2). CT of the left knee revealed a lytic lesion that caused scalloping of the cortical region of the bone. Skeletal survey was otherwise normal. Tc-99m bone scanning revealed increased uptake on the lower segment of the left femur and

the lower segment of the humerus (figures 3, 4). Bone marrow aspiration and biopsy revealed only reactive changes. A left axillary lymph node biopsy was diagnostic.

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Figure 1



Figure 2



Figure 3



Figure 4

Comment

Lymphomas are the fifth most common systemic cancer. Diffuse large B-cell lymphoma (DLBCL) is the most common lymphoma subtype, accounting for approximately 30% of all cases. DLBCL is more common in elderly. The median age of the patients is within the 7th decade, but the disease may also occur in children and young adults. It is slightly more common in males than in females.

DLBCL is a heterogeneous group of disorders, displaying a wide variability in morphology, protein expression and gene expression patterns. Since primary mediastinal large B-cell lymphoma is now recognized as a separate entity, DLBCL can be divided into two major biologically and clinically distinct groups using gene-expression profiling: The germinal-center cell (GCC) type and the activated B-cell (ABC) type. These groups of DLBCL are associated with a different clinical outcome, even if the current standard immunochemotherapy regimens (Rituximab-CHOP and equivalents) are applied. The outcome of GCC-type DLBCL is better. In contrast, ABC-type DLBCL, which display a constitutive activation of the nuclear factor κ B (NF- κ B) pathway, have inferior outcomes. However, preliminary data suggest that the addition of novel agents (such as bortezomib or lenalidomide) to standard immunochemotherapy regimens may improve the outcome of ABC-type DLBCL.

Unlike Hodgkin lymphoma, extranodal disease is much more frequent in non-Hodgkin lymphomas. In the specific setting of DLBCL, up to 40% of patients present as primary extranodal lymphomas, i.e. they are anatomically limited to (usually single) extranodal sites. Approximately 1/3 of the patients have two or more extranodal sites involved. These cases with extensive extranodal involvement (two or more sites) also carry a worse prognosis, since this variable is one of the five included in the International Prognostic Index (IPI). The most common extranodal site of involvement is the bone marrow and the gastrointestinal tract. Other, less commonly involved extranodal sites include liver, lung, bone, testis, skin, salivary glands, thyroid, kidney and adrenal glands, while central nervous system is usually involved at relapse/progression.

Bone involvement is relatively uncommon at the diagnosis of malignant lymphomas, as opposed to solid tumors. Clinical staging is not bone-oriented. Local X-rays and bone scanning is only indicated in symptomatic patients (usually local pain). Primary bone lymphomas are rare; they are DLBCL in their vast majority. However, a much more common scenario in DLBCL is the occurrence of bone involvement in the context of disseminated disease, as it was the

case in the patient described here. In this setting, bone involvement may be contiguous to a site of nodal disease (classified as stage IIE or IIIE or IVE) or may be a distant site of involvement –single or multifocal– as observed in this case. In the latter case, disease stage is by definition IV. Among stage IV patients, bone involvement does not confer a worse prognosis.

In the context of secondary bone involvement in disseminated DLBCL, multifocal lesions are more common than single ones. Spine and pelvic bones are more frequently involved than skull, long bones and ribs. The use of positron emission tomography (PET/CT) in the initial staging of DLBCL may also uncover asymptomatic bone lesions, which cannot be suspected based on clinical findings and conventional staging procedures.

Our patient received a 4-day course of dexamethasone at a daily dose of 40 mg, with rapid resolution of local pain. Due to HBsAg positivity she was started with entecavir. Prognosis was considered unfavorable due to the presence of 3/5 adverse prognostic factors (poor performance status, stage IV, elevated LDH). Subsequently, she received 6 cycles of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) and achieved a complete remission, which was verified by a negative PET/CT. Remission is sustained 4 months after the completion of immunochemotherapy.

References

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