

## CONTINUING MEDICAL EDUCATION ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

### Hematology Quiz – Case 33

A 62-year-old woman was admitted in the Orthopedics Department, due to a recent right hip injury. The X-ray revealed a subtrochanteric fracture of the right femur.

Her medical history was remarkable for an episode of mastitis of right breast four years ago, regular consumption of non-steroidal anti-inflammatory drugs (NSAIDs) due to lumbar pain for the last three years, and treatment with oral bisphosphonates during the last year. Multiple osteolytic lesions and few osteosclerotic lesions were prominent in pelvic and spine X-rays (figures 1–3).



Figure 1



Figure 2

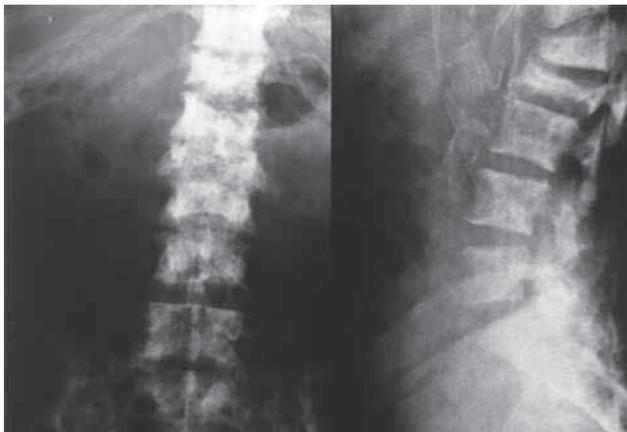


Figure 3

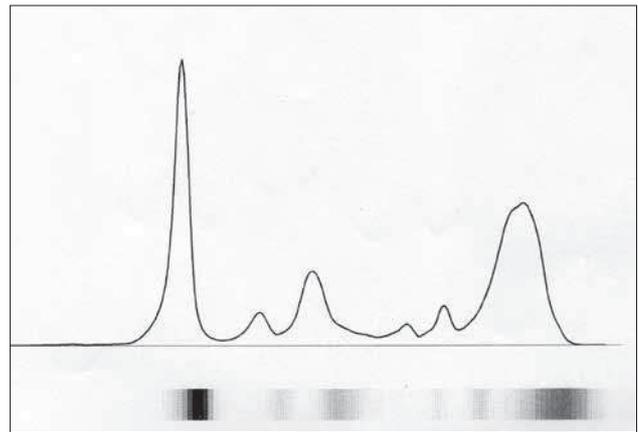


Figure 4

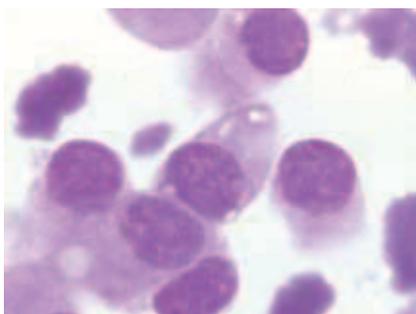


Figure 5



Figure 6

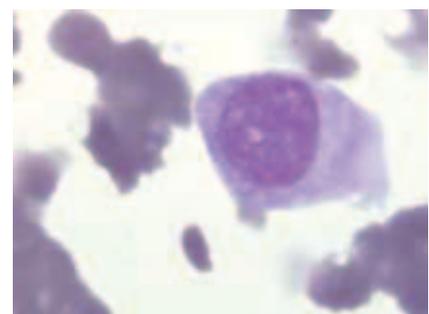


Figure 7

ARCHIVES OF HELLENIC MEDICINE 2013, 30(2):246–247  
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2013, 30(2):246–247

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Peripheral blood smear revealed a mild leukoerythroblastic reaction and complete blood counts were as follows: Ht 24.5%, Hb 7.9 g/dL, WBC  $8.59 \times 10^9/L$  (differential count: neutrophils 86%, myelocytes 2%, metamyelocytes 3%, lymphocytes 7%, monocytes 2%; few circulating erythroblasts) and platelets  $209 \times 10^9/L$ .

The remaining laboratory findings revealed a highly elevated erythrocyte sedimentation rate of 120 mm/h, marked hypergammaglobulinemia (7.3 g/dL; fig. 4), and hypercalcemia (10.6 g/dL). C-reactive protein (CRP) was also elevated (95 mg/L) along with mild elevations in serum alkaline phosphatase (188 U/L versus upper normal limit of 106 U/L), and lactate dehydrogenase (LDH; 273 U/L versus upper normal limit of 220 U/L).

Regarding the complete blood count and the blood smear, there was prominent mild leukoerythroblastic reaction. A bone marrow aspiration and biopsy was diagnostic (figures 5–7).

### Comment

*Lumbar pain, anemia, elevated ESR and hypergammaglobulinemia in an elderly patient are mostly consistent with the diagnosis of multiple myeloma. In this case however, the details of the morphology of the electrophoretic diagram, the pattern of bone disease, and serum alkaline phosphatase elevation questioned the diagnosis of multiple myeloma.*

*Marked hypergammaglobulinemia in serum protein electrophoresis resembled to a monoclonal component (fig. 4), but in fact it was polyclonal as clearly shown in the electrophoretic gel. The polyclonal nature of the process was definitely proved by a negative immunofixation.*

*The pattern of bone disease was mixed, osteolytic and osteosclerotic, a feature which is not also expected in multiple myeloma. Myeloma-associated bone disease is typically characterized by increased bone resorption and impaired osteoblast activity. In this setting, lytic lesions and osteopenia constitute the usual forms of bone disease. Sclerotic lesions are extremely rare in malignant monoclonal gammopathies, although they are occasionally associated with POEMS syndrome.*

*Serum alkaline phosphatase was elevated in this case in contrast to what expected in multiple myeloma. Serum alkaline phosphatase is a marker of bone formation and, based on the above considerations, is not increased in myeloma, unless the patient has an active fracture undergoing repair.*

*In this case, bone marrow aspiration and biopsy, an easily performed, minimally invasive diagnostic technique, immediately excluded bone marrow infiltration by plasma cells and revealed the presence of atypical cells of non-hematopoietic origin. Bone marrow biopsy and immunohistochemistry revealed that metastatic disease was due to breast cancer.*

*Bone is the third most common site of metastatic disease in solid tumors. Breast, lung, prostate, thyroid and kidney cancer are most likely to be associated with bone metastases. In women, the most common tumor that metastasizes to bones is breast cancer,*

*which can be morphologically manifested with lytic, sclerotic or mixed type bone lesions.*

*Skeletal metastases are often multifocal; however, renal and thyroid carcinomas are notorious for producing solitary lesions. By far, the most common location for osseous metastases is the axial skeleton, followed by the proximal femur and proximal humerus.*

*Patients with metastatic bone disease have different presentations. Lesions may vary from extremely painful and or disabling to completely asymptomatic. Most metastases present with a destructive bone lesion detected on bone imaging. Metastases from lung, renal, and thyroid tumors tend to be entirely lytic. As already reported, breast metastases may be lytic or show a mixed lytic-blastic appearance.*

*In contrast to multiple myeloma, solid tumor metastases are frequently associated with serum alkaline phosphatase elevations, as was the case in this patient.*

*Finally, marked polyclonal hypergammaglobulinemia is an unusual finding, which can be typically attributed to distinct causes, such as chronic infections (leishmaniasis, tuberculosis etc.), liver cirrhosis, HIV infection, multicentric Castleman's disease, malignant lymphomas (especially angioimmunoblastic T-cell lymphoma), chronic myelomonocytic leukemia etc. In this case, the extremely marked polyclonal hypergammaglobulinemia was attributed to the very extensive metastatic disease, although such pictures are very unusual.*

### References

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**Diagnosis: Breast cancer, bone and marrow metastases**