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ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 20

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2010, 27(5):856–857

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A 66-year-old man was admitted to the hospital due to afternoon fever up to 38.5 °C, fatigue, blurred vision and diplopia, which was started the day before admission. His medical history was unremarkable and included only mild hypertension and hypercholesterolemia under treatment with atorvastatin.

The physical examination revealed limited motility of the right eye in all directions. Pupil reflexes were normal. Ophthalmologic examination confirmed the diplopia. The laboratory profile revealed anemia (Hb 9.8 g/dL) with normal white blood cell and platelet counts, hypoalbuminemia (2.8 g/dL), high β_2-microglobulin (4.6 mg/L), IgAκ paraprotein (2.370 mg/L), and increased serum free κ-light chain (6.820 mg/L). ESR was 82 mm/1 hour and CRP was negative. There was anosoparesis but renal function and LDH levels were normal. Common or opportunistic infections were excluded by blood and urine cultures and CT scans of the thorax and abdomen.

Due to the presence of IgAκ paraproteinemia, a bone marrow aspiration was performed and the trephine biopsy showed the presence of plasma cell infiltration of the bone marrow at a proportion of 55%. Many of them were atypical, with large multilobulated nucleus (figures 1, 2). Both conventional cytogenetics and FISH analysis revealed no abnormalities. Magnetic resonance imaging (MRI) of the spinal cord and plain radiography of the skeleton were also normal. An MRI of the orbits revealed a soft-tissue mass infiltrating the left carvenous sinus. A mass biopsy was performed and the initial pathologic evaluation revealed a high grade pleomorphic neoplasm that failed to express multiple epithelial, mesenchymal, lymphoid and melanoma immunohistochemical markers. Subsequent fresh tissue evaluation with touch imprints and immunophenotypic characterization confirmed the plasma cell origin of the tumor.

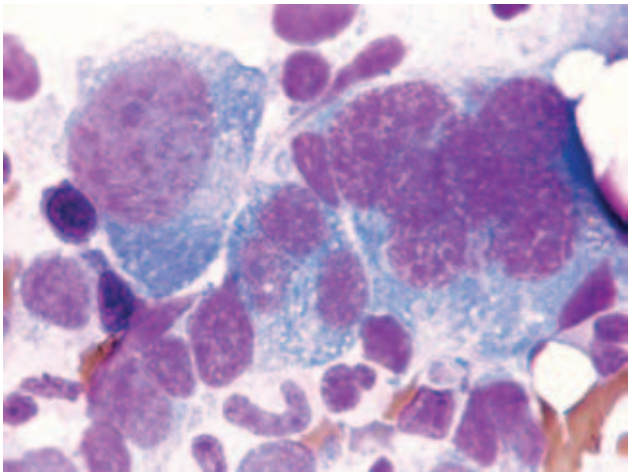

Figure 1

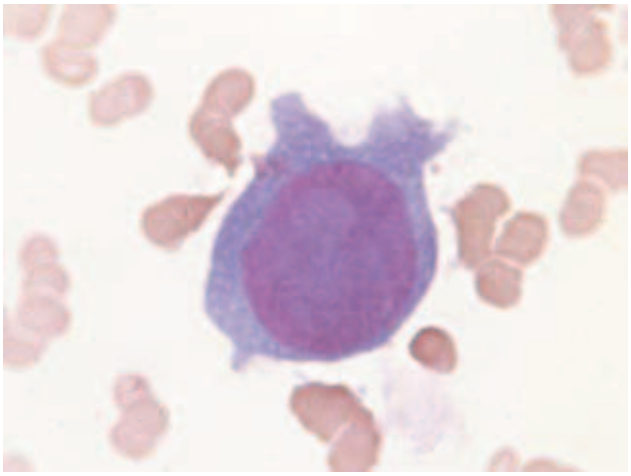

Figure 2

Thorough retrospective review of the touch imprint smears clearly showed the plasmacytic cytologic features. The diagnosis was established and the patient was treated with systemic therapy and also local radiotherapy in the mass of the nervous system. After two cycles of treatment, there was a dramatic deterioration of the disease with leukemic phase which could not respond to every therapy that was used. The patient was died within 4 months from initial diagnosis.

Comment

The term "anaplastic morphology" has been applied in multiple myeloma (MM) cells with atypical morphological features resembling high-grade or anaplastic lymphomas. This aggressive type of myeloma is accompanied by the development of rapidly enlarging extramedullary soft tissue masses and or of bone marrow transformation. The median age of these patients seems to be lower that of "classical" myeloma. A disproportionate percentage of these patients have an IgA gammopathy. Following the onset of the aggressive phase, these patients have a rapidly fatal course, refractory to therapy, with a mean survival of less than 3.5 months. It is hypothesized that this aggressive phase represents part of the natural history of multiple myeloma, analogous to the terminal transformations associated with other relatively indolent myeloproliferative and lymphoproliferative disorders. Several studies support the proposition that the clinical and morphological changes associated with the aggressive phase result from a clonal evolution of the original malignant cell line and do not represent the development of an independent new neoplasm.

Extramedullary plasmacytoma (EMP) is a plasma cell tumor that arises outside the bone marrow. The upper respiratory tract, including the nasal cavity and sinuses, nasopharynx and larynx, is the most frequent location of lesions. EMPs may also occur in virtually any organ including the gastrointestinal tract, CNS, urinary bladder, thyroid, breasts, testes, parotid gland or lymph nodes. The diagnosis is made on the basis of finding a monoclonal plasma cell tumor in an extramedullary site and the absence of multiple myeloma on the basis of bone marrow, radiography, and appropriate studies of blood and urine. Symptomatic MM occurs in only 15% of patients with EMP. The pathogenesis of EMP has not been fully clarified yet. It is very well documented that the interactions between bone marrow microenvironment and myeloma cells are crucial for the myeloma cell growth and survival. Myeloma cells that lose their stroma-dependency may result in extramedullary tumor growth. The EMP of the CNS does not exceed 1% of the EMP and is associated with poor outcome. In the present case, the patient had a very aggressive form of MM with extramedullary disease of the CNS. Although, he was treated with combinations including novel agents, such as bortezomib, the patient did not respond and died very early, just 4 months after diagnosis.

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Diagnosis: *IgAκ multiple myeloma with anaplastic morphology and extramedullary plasmacytoma of the right cavernous sinus*