Hematology Quiz – Case 14

A 68-year-old male was presented at the Outpatient Clinic of our Department because of anemia and severe lumbar pain which deteriorated during the last two weeks despite the use of paracetamol and nimesulide. The X-ray of the lumbar spine revealed diffuse osteoporosis and small lytic lesions in L2 and L4 vertebrae. Thus, the patient was admitted to the hospital for evaluation. His past medical history was unremarkable.

The physical examination revealed only pallor. Blood pressure, heart and respiratory rates were normal. The neurological examination was also normal. The diagnostic work up revealed a normochromic, normocytic anemia (Hb 10.2 g/dL, Ht 33%), hypercalcemia (13.1 mg/dL), hyperuricemia (7.6 mg/dL), low serum albumin (2.5 g/dL), and a monoclonal “M” spike in serum electrophoresis. The quantitative evaluation of immunoglobulins showed an IgG of 3.7 g/dL with diminished IgM and IgA values. CRP was normal while β2-microglobulin was 3.2 mg/L. The conventional skeletal survey revealed multiple lytic lesions in the skull, thoracic and lumbar vertebrae, ribs, pelvis and femurs. The bone marrow aspiration revealed a 45% of marrow infiltration by abnormal plasma cells, several bi-nucleated plasma cells and plasma cells containing several large vacuoles (fig. 1) or even only a large vacuole (fig. 2). Serum immunoelectrophoresis revealed an IgGκ monoclonal protein, while urinary immunoelectrophoresis was negative. The diagnosis of IgGκ multiple myeloma was established (ISS-2) and the patient was started on therapy with the combination of MPV (melphalan, prednisolone and bortezomib).

During the second line of therapy, the patient was presented with a 5-day history of cutaneous vesicles, ulcers, fever up to 38.2 °C, asthenia, and anorexia. Tense sero-hemorrhagic vesicles and multiple necrotic ulcers were observed in the skin of the
anterior thoracic and upper abdominal areas (fig. 3). Mucosal surfaces were free of lesions; there was no enlargement of lymph nodes, liver, or spleen. The skin biopsy revealed intraepidermal vesiculation with ballooning degeneration and multinucleated giant cells. Oral treatment was started and after 7 days of therapy there was an improvement of the lesions that disappeared after one month.

**Comment**

Herpes zoster is the most common infection in patients receiving immunosuppressive agents, such as corticosteroids, and undergoing bone marrow or peripheral blood stem-cell transplantation for lymphoproliferative malignancies, characterized by a localized painful vesicular rash. Herpes zoster results from reactivation of latent varicella-zoster virus (VZV). Cell-mediated immunity (CMI) is believed to play a larger role than humoral immunity in prevention of reactivation. However, because multiple myeloma (MM) is associated with defects in humoral immunity rather than CMI, patients with MM are not at increased risk for recurrent herpes and herpes zoster infections. However, in MM patients who receive bortezomib there is an increase incidence in herpes zoster events. In APEX phase III study, where bortezomib was compared to high-dose dexamethasone in patients with relapsed/refractory MM, the incidence of herpes zoster with bortezomib was 13%. In addition, other studies have shown an association of bortezomib with herpes zoster, with reactivation rates ranging from 12% to 57% of patients treated for relapsed MM. The mechanism of VZV reactivation and herpes zoster development is not fully understood. The increased incidence of VZV reactivation seen in elderly and immunocompromised patients suggests that it may be due in part to VZV-specific host immunodeficiency. Patients with decreased CMI are more likely to experience disseminated VZV infection with extensive skin lesions and risks for VZV-related organ involvement. VZV-specific T cells appear to be necessary for suppressing VZV reactivation and preventing the development of herpes zoster. Several studies have reported that patients with MM—even with previously untreated disease—present with significantly decreased numbers of activated CD4-positive T cells and natural-killer cells compared with age-matched healthy individuals. In one study, CD4-positive T-cell subsets declined substantially with each successive line of conventional chemotherapy, suggesting that the patient’s treatment status can further alter immune cell status. Importantly, that study demonstrated that both naive and activated CD4-positive T-cell subsets were significantly lower among patients with MM who developed opportunistic infections than among patients without such infections. Although data are limited, it has been suggested that bortezomib treatment may alter the number and function of specific lymphocyte subsets as well as the function of Toll-like receptors that are essential for innate immunity. Antiviral prophylaxis with acyclovir may be beneficial in reducing the incidence of herpes zoster infection and should be considered for patients with MM who receive bortezomib-based therapies.

**References**


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