Session X: Disease Related Morbidities in

Waldenström's Macroglobulinemia

Abstract 154

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Cutaneous Manifestations of Waldenström's Macroglobulinemia. JP Fermand, B Asli and JC Brouet, Immuno-Hematology unit, Hôpital Saint Louis, 75010, Paris, FRANCE.

Cutaneous manifestations of monoclonal gammopathies, whatever their isotype, may be due to 1) direct lympho and/or plasmocytoid infiltration 2) abnormal cytokine secretion by the clonal cells or their environment (POEMS syndrome) 3) peculiar physico-chemical properties of the monoclonal immunoglobulin (Ig) which may cause hyper viscosity, deposition (usually along basal membranes as in monoclonal Ig deposition disease), or aggregation of the monoclonal Ig forming fibrils (AL amyloidosis), crystals (crystal-storing histiocytosis) or microtubules (type I cryoglobulinemia) 4) auto-antibody activity of the monoclonal Ig which may result, for example, in cold agglutinin disease, type II mixed cryoglobulinemia, bullous skin diseases or xanthomatosis 5) still poorly understood mechanisms as in scleromyxoedema, neutrophilic dermatosis and Schnitzler syndrome. Schnitzler syndrome is featured by the association of chronic non pruriginous urticaria and monoclonal IgM gammopathy. Intermittent fever, asthenia, arthralgia and bone pain with imaging evidence of osteosclerosis also frequently occur. Biological findings show an increase in white blood cell count and erythrocyte sedimentation rate, which reflects both an inflammatory syndrome and the presence of the monoclonal IgM. Skin biopsies may be featured by urticarial vasculitis. Present treatment is unsatisfactory. The use of systemic corticosteroids may be effective but is hampered by cortico-dependance, with attendant well known side effects. The role of the IgM gammopathy in the pathogenesis of the various manifestations of the Schnitzler syndrome is poorly understood. In most cases, immunofluorescence studies did not document a pathogenic role of the monoclonal IgM since it rarely showed cutaneous IgM deposits. An anti-skin auto-antibody activity of the IgM could be documented by western blotting in only few patients. Conflicting data were also reported about a potential anti- interleukin-1 (IL-1)α auto-antibody activity of the monoclonal Ig. An alternative hypothesis would not implicate the monoclonal IgM by itself but the production of cytokines or chemiokines by the clonal B-cell proliferation or by its cellular environment. We reported a series of 11 patients with the Schnitzler syndrome. In most cases, the fluorinated 4-quinolone pefloxacine rapidly improved urticarial and systemic symptoms. Used as a preventive treatment, it reduced the frequency and intensity of disease flares, resulting in a significant steroid sparing effect. However, the efficacy of pefloxacine was only symptomatic, often incomplete and limited to the cutaneous and systemic symptoms of the syndrome. Pefloxacine has been shown to modulate the production of various cytokines, including IL-1. In addition, case reports documented the efficacy of interleukin-1 receptor antagonist (anakinra) in the treatment of the Schnitzler syndrome. In our patients, we confirmed that anakinra has indeed a dramatic effect on all clinical and biological manifestations of the syndrome. Although similarly symptomatic, it is more effective than pefloxacine. These therapeutic data point IL1 as the unique trigger of Schnitzler syndrome and offer new opportunities to establish the physiopathology of the disease.