Physiopathology of Schnitzler's Syndrome

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Schnitzler syndrome is a rare acquired autoinflammaory syndrome defined by the constant association of a non pruriginous urticaria with a monoclonal IgM gammopathy. The other clinical features comprise fever, bone pain, adenopathy, and hepatosplenomegaly. In addition to the monoclonal IgM, laboratory investigations usually show a major increase in sedimentation rate, C-reactive protein and fibrin levels. On the blood count, neutrophilic leukocytosis is nearly constant, inflammatory anemia and elevated platelet count are frequent. The physiopathology of this syndrome remains poorly understood. To date, neither any autoimmune activity of the monoclonal gammopathy nor secretion by the clonal cells of proinflammatory components have been clearly demonstrated. Until recently, treatment of Schnitzler syndrome was only symptomatic and unsatisfactory. We reported the efficacy of the antibiotic pefloxacin in most cases of Schnitzler. Its effect was only symptomatic and usually limited to the urticarial and febrile manifestations of the disease. We speculated on the immuno-regulatory and anti-inflammatory properties of this antibiotic that are attributed to the modulation of various cytokines. The recently demonstrated dramatic symptomatic effect of interleukine 1 receptor antagonist anakinra support the critical role of the interleukin 1 pathway at the origin of the disease manifestations. The production of interleukin 1β requires a two step process. First, pro interleukin 1β is synthesized after Toll like receptor signaling. Second, pro interleukin 1β is cleaved in an active form by a multiproteine complex named inflammasome. Based on our personal series, we will review the long term effect of anakinra in controlling the symptoms of the disease. In addition, we will discuss the potential inflammasome dysfunction that may be a key point in the physiopathology of Schnitzler syndrome.