Increased osteoclastic activity in acute Charcot’s osteoarthropathy: the role of receptor activator of nuclear factor-kappa B ligand

To the Editor,

The pathogenesis of Charcot’s osteoarthropathy is still poorly understood. We are investigating, for example, the possible involvement of genetic factor as the polymorphisms of osteoprotegerin, although other mechanism might be involved. It is possible, in fact, that autonomic diabetic neuropathy might cause a dysregulation of local immunity and inflammation that are controlled by the “inflammatory reflex”\(^1\). Inflammation may thus be the key event triggering the osteoarthropathy. In this light, the recent paper by Mabilleau et al.\(^2\) represents an important improvement, because it looks to activation of immune cells such as monocytes and their production of cytokines. Moreover, following our hypothesis that RANK/RANKL system and inflammation may be dysregulated in Charcot’s osteoarthropathy\(^3\), our preliminary data on 6 patients suggest that there is an overexpression of RANK/RANKL and a clearly raised production of cyclooxygenase 2 and prostaglandins from the monocytes extracted from the peripheral blood samples of these patients (after stimulation with 1 ng/ml of lipopolysaccharide). These findings are consistent with the results obtained by Mabilleau et al\(^2\).

However, one limitation of these works is that they are focused on peripheral blood-derived monocytes whereas more information could be obtained by the analysis of tissue infiltrating immune cells including lymphocytes. In recent years, it has became clear that tissue infiltrating lymphocytes (TIL) better represent the inflammatory microenvironment, thus contributing to get more insight into the pathogenesis of various diseases. For instance, in tumors, the demonstration that TIL have a restricted usage of their T-cell receptor rearrangements, has been instrumental in detecting tumor associated antigens as the target of the immune response\(^4,5\). Moreover, the modern concept that myocardial infarction is a disease strongly related to inflammation is getting support by the demonstration of activated TIL in coronary diseases\(^6\).

In conclusion, we propose that the study of inflammatory cells should focus on immune cells derived from the tissue and this will eventually lead to uncover the pathogenetic mechanisms of Charcot’s osteoarthropathy.

References


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