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Monocyte Subsets and Serum Inflammatory and Bone-Associated Markers in Monoclonal Gammopathy of Undetermined Significance and Multiple Myeloma

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Abstract

Monocyte/macrophages are shown to be altered in monoclonal gammopathy of undetermined significance (MGUS), smouldering (SMM) and active myeloma (MM), with an impression on the disruption of the homeostasis of the traditional bone marrow (BM) microenvironment. We investigated the distribution of various subsets of monocytes (Mo) in blood and BM of newly-diagnosed untreated MGUS (n=23), SMM (n=14) and MM (n=99) patients vs. healthy donors (HD; n=107), in parallel to an outsized panel of cytokines and bone-associated serum biomarkers. Our results showed normal production of monocyte precursors and classical Mo (cMo) in MGUS, while decreased in SMM and MM (p≤0.02), in association with lower blood counts of recently-produced CD62L+ cMo in SMM (p=0.004) and of all subsets of (CD62L+, CD62L− and FcεRI+) cMo in MM (p≤0.02). In contrast, intermediate and end-stage non-classical Mo were increased in BM of MGUS (p≤0.03), SMM (p≤0.03) and MM (p≤0.002), while normal (MGUS and SMM) or decreased (MM; p=0.01) in blood. In parallel, increased serum levels of interleukin (IL)1β were observed in MGUS (p=0.007) and SMM (p=0.01), higher concentrations of serum IL8 were found in SMM (p=0.01) and MM (p=0.002), and better serum IL6 (p=0.002), RANKL (p=0.01) and bone alkaline phosphatase (BALP) levels (p=0.01) with decreased counts of FcεRI+ cMo, were restricted to MM presenting with osteolytic lesions. This translated into three distinct immune/bone profiles: (1) normal (typical of HD and most MGUS cases); (2) senescent-like (increased IL1β and/or IL8, found during a minority of MGUS, most SMM and few MM cases with no bone lesions); and (3) pro-inflammatory-high serum IL6, RANKL and BALP with significantly (p=0.01) decreased blood counts of immunomodulatory FcεRI+ cMo-, typical of MM presenting with bone lesions. These results provide new insight into the pathogenesis of plasmacyte neoplasms and therefore the potential role of FcεRI+ cMo in normal bone homeostasis.

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