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Evaluation of Some Serum Proteins as Markers for Myeloma Bone Disease

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Abstract : Multiple myeloma (MM) is the most frequent plasma cell (PC) dyscrasia that involves the skeleton. Myeloma bone disease (MBD) is characterized by osteolytic bone lesions as a result of increased osteoclasts activity not followed by reactive bone formation due to osteoblasts suppression. Skeletal complications cause significant adverse effects on quality of life and lead to increased morbidity and mortality. Last decade studies revealed the implication of different proteins in osteoclast activation and osteoblast inhibition. The aim of the present study was to determine serum levels of periostin, sRANKL and osteopontin and to evaluate their role as bone markers in MBD. Materials and methods. Thirty-two newly diagnosed MM patients (mean age: 62.2 ± 10.7 years) and 33 healthy controls (mean age: 58.9 ± 7.5 years) were enrolled in the study. According to IMWG criteria 28 patients were with symptomatic MM and 4 with monoclonal gammopathy of undetermined significance (MGUS). In respect to their bone involvement all symptomatic patients were divided into two groups (G): 9 patients with 0-3 osteolytic lesions (G1) and 19 patients with >3 osteolytic lesions and/or pathologic fractures (G2). Blood samples were drawn for routine laboratory analysis and for measurement of periostin, sRANKL and osteopontin serum levels by ELISA kits (Shanghai Sunred Biological Technology, China). Descriptive analysis, Mann-Whitney test for assessment the differences between groups and non-parametric correlation analysis were performed using GraphPad Prism v8.01. Results. The median serum levels of periostin, sRANKL and osteopontin of MM patients were significantly higher compared to controls (554.7pg/ml (IQR=424.0-720.6) vs 396.9pg/ml (IQR=308.6-471.9), p=0.0001; 8.9pg/ml (IQR=7.1-10.5) vs 5.6pg/ml (IQR=5.1-6.4, p<0.0001 and 514.0ng/ml (IQR=469.3-754.0) vs 387.0ng/ml (IQR=335.9-441.9), p<0.0001, respectively). for assessment of differences between groups and non-parametric correlation analysis were performed using GraphPad Prism v8.01. Statistical significance was found for all tested bone markers between symptomatic MM patients and controls: G1 vs controls (p<0.03), G2 vs controls (p<0.0001) for periostin; G1 vs controls (p<0.0001), G2 vs controls (p<0.0001) for sRANKL; G1 vs controls (p=0.002), G2 vs controls (p<0.0001) for osteopontin, as well between symptomatic MM patients and MGUS patients: G1 vs MGUS (p<0.003), G2 vs MGUS (p=0.003) for periostin; G1 vs MGUS (p<0.05), G2 vs MGUS (p<0.001) for sRANKL; G1 vs MGUS (p=0.011), G2 vs MGUS (p=0.0001) for osteopontin. No differences were detected between MGUS and controls and between patients in G1 and G2 groups. Spearman correlation analysis revealed moderate positive correlation between periostin and beta-2-microglobulin (r=0.416, p=0.018), percentage bone marrow myeloma PC (r=0.432, p=0.014), and serum total protein (r=0.427, p=0.015). Osteopontin levels were also positively related to beta-2-microglobulin (r=0.540, p=0.0014), percentage bone marrow myeloma PC (r=0.423, p=0.016), and serum total protein (r=0.413, p=0.019). Serum sRANKL was only related to beta-2-microglobulin levels (r=0.398, p=0.024). Conclusion: In the present study, serum levels of periostin, sRANKL and osteopontin in newly diagnosed MM patients were evaluated. They gradually increased from MGUS to more advanced stages of MM reflecting the severity of bone destruction. These results support the idea that some new protein markers could be used in monitoring the MBD as a most severe complication of MM.

Keywords : myeloma bone disease, periostin, sRANKL, osteopontin
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