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Serum Periostin Levels in Newly Diagnosed Multiple Myeloma: Preliminary Observations and Treatment-related Changes

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ABSTRACT

Aim: This study aimed to perform a descriptive evaluation of serum periostin levels in newly diagnosed, treatment-naive multiple myeloma (MM) patients and to explore short-term changes following induction therapy.

Methods: Between May 2020 and May 2021, patients diagnosed with MM and healthy volunteers were recruited from the Hematology Unit of the Faculty of Medicine, Necmettin Erbakan University. Demographic characteristics, MM-related clinical findings, and treatment response data of the patients were documented. Serum periostin levels in MM patients before treatment were compared with those in healthy controls. Additionally, baseline periostin levels in the patient group were compared with post-treatment values.

Results: Thirty-six MM patientswere included in our study (17 females, 47.2%; 19 males, 52.8%), with an average age of 63.11±12.13 years. The control group consisted of 18 males (50%) and 18 females (50%), with a mean age of 61.94±10.53 years. Serum periostin levels were significantly elevated in the MM group compared with controls healthy (25.25 ng/mL vs. 14.84 ng/mL, p<0.001). No statistically significant associations were observed between baseline periostin levels and disease stage, cytogenetic risk groups, survival, or treatment response. In the 28 patients who completed induction chemotherapy, the median periostin value decreased from 24.96 (11.21-94.87) ng/mL at diagnosis to 17.97 (3.16-47.7) ng/mL after three courses of treatment (p<0.001).

Conclusion: In MM patients, serum periostin levels were elevated at diagnosis and decreased significantly following induction therapy. This study is the first to demonstrate a significant reduction in periostin levels after induction therapy in MM. These findings should be considered preliminary and hypothesis-generating. Larger, well-designed studies are required to clarify the clinical relevance of periostin in MM.

Keywords: Biomarkers, multiple myeloma, inflammation, periostin.

Introduction

Multiple myeloma (MM) is a clonal plasma cell malignancy characterized by bone marrow infiltration, monoclonal protein production, and end-organ damage, including anemia, renal failure, hypercalcemia, and osteolytic bone disease. Despite advances in therapy, MM remains a heterogeneous disease with variable clinical outcomes, highlighting the importance of understanding disease-related biological markers and microenvironmental factors [1]. Periostin, an extracellular matrix protein, was first isolated as an adhesion molecule from mouse osteoblastic cells. Although initially described as an osteoblast- specific factor, it was last renamed following the discovery of its predominant expression in the periosteum [2]. Periostin has been implicated in various pathological processes, including fibrosis, atherosclerosis, tumor progression, and ultimately metastatic spread. When produced by fibroblasts, periostin contributes to tissue

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remodeling by influencing collagen deposition, modifying the biomechanical properties of connective tissue, and modulating chronic inflammatory responses [3]. Beyond inflammatory disorders, periostin has been investigated in numerous malignancies. Elevated periostin levels have been reported in cancers of the gastrointestinal tract, bladder, and breast, and increased expression is often associated with unfavorable clinical outcomes. Additionally, a study involving patients with non-small-cell lung cancer found that elevated periostin levels increased the likelihood of developing bone metastases [4]. Uncontrolled monoclonal proliferation in the bone marrow contributes to the pathogenesis of MM [5]. MM accounts for approximately 10% of hematological cancers and 1% of all cancers. Although its pathogenesis is multifactorial, chromosomal abnormalities are recognized as key contributors. In MM, prognosis is influenced by cytogenetic risk factors and laboratory markers, such as serum albumin, lactate dehydrogenase (LDH), and β2-microglobulin (β2-MG); these parameters also form the basis of current staging systems [6]. Abnormal changes in the bone marrow microenvironment play an important role in MM progression. Stromal cells, along with osteoblasts and osteoclasts, promote plasma cell survival and drive the formation of MM-related bone lesions through the secretion of cytokines including vascular endothelial growth factor, insulin-like growth factor-1, tumor necrosis factor-alpha and interleukin-6 [7]. Bone complications—especially lytic lesions—are present in nearly 90% of patients with MM [8]. Given the established involvement of periostin in tissue remodeling, inflammation, and malignancy-related bone dynamics, our study aimed to explore the relationship between serum periostin levels and clinical parameters in patients with newly diagnosed MM.

Methods

The study was prospective and observational. Power analysis indicated that with an effect size of 0.5, 80% power, and a type I error rate of 5% ($p<0.05$), a minimum sample size of 34 individuals per group was required , yielding a 1:1 ratio. Ethical approval for the study was obtained from the Necmettin Erbakan University Ethics Committee (approval no: 2020/2467, date: 08.05.2020). Patients newly diagnosed with MM at the Adult Hematology Department of Necmettin Erbakan University between May 2020 and May 2021 were screened.

Inclusion criteria for the study were newly diagnosed MM and age over 18 years.

Exclusion criteria were; a pathology affecting heart or lung function, an active infection, a chronic systemic disease, and a chronic bone disease.

The control group consisted of healthy volunteers over 18 years of age who reported no systemic illness, were not taking regular medications, and had normal blood counts and biochemical parameters during the same period. Informed consent was obtained from all participants. Following informed consent, serum samples were collected from both groups prior to treatment initiation to determine periostin concentrations. Demographic information, complete blood count results, standard biochemical analyses, MM subtype, disease stage, cytogenetic risk category, clinical characteristics, and treatment response after three chemotherapy cycles were documented for all participants. The primary aim of the study was to compare serum periostin levels in patients with MM to those in healthy individuals. For this purpose, baseline periostin concentrations in the patient group were compared with those in the healthy controls. The secondary objective was to investigate the clinical associations between periostin and MM and to evaluate changes in serum periostin levels following three cycles of therapy.

Periostin Measurement

After collection, Blood samples from patients and healthy individuals were centrifuged at 4000 rpm for 10 minutes at 37 °C. The collected samples were kept at -80 °C until analyzed. Periostin levels were measured in the central biochemistry laboratory using an ELISA-based assay (Human Periostin, POSTN ELISA kit, BTLAB, Atlas Biotechnology Ltd.).

Statistical Analysis

IBM SPSS Statistics for Windows, version 22.0 (USA), was used to analyze the study's statistical data. The distribution of continuous numerical variables was assessed using the Kolmogorov-Smirnov test. Descriptive statistics were presented as median (minimum-maximum) for variables that were not normally distributed and as mean ± standard deviation for variables that were normally distributed. To compare two independent groups, the Mann-Whitney U test was used for variables that were not normally distributed, and the independent samples t-test was used for variables that were normally distributed. The Wilcoxon signed-rank test was applied for comparisons of dependent (paired) data. Categorical variables were expressed as percentages (%) and compared using chi-square test. In the correlation analyses, the Spearman correlation coefficient (rho) was used, and correlation strength was interpreted as follows: weak (0.2-0.4), moderate (0.4-0.6), strong (0.6-0.8), and very strong (0.8-1.0). A p value <0.05 was considered statistically significant.

Results

Our study included 36 participants in two groups. The mean age was 63.11±12.13 years and 61.94±10.53 years in the patient and healthy groups, respectively. The median periostin level was significantly higher in the group of patients (14.84 ng/mL vs. 25.25 ng/mL, $p<0.001$). Baseline laboratory and demographic data for the patient and healthy groups are shown in Table 1.

Eight (22.2%) of the MM patients died during remission-induction treatment. The remaining 28 (77.8%) patients reached the response evaluation stage. Although initial periostin levels were higher in the 8 patients who died than in the 28 surviving patients, the difference was not statistically significant (25.1 ng/mL vs. 21.1 ng/mL; $p=0.158$). Table 2

Table 1. Laboratory and demographic findings of the MM group and the control group

Parameters	Control (n: 36)	MM (n: 36)	p
Age	61.9±10.5	63.11±12.13	0.664
Sex (female/male)	18/18	17/19	0.815
Periostin (ng/mL)	14.84 (4.16-32.11)	25.25 (11.21-94.87)	**<0.001***
WBC (µLx10^3)	7.75±1.6	7.30±2.54	0.372
Neutrophil (µLx10^3)	4.77±1.29	4.51±1.79	0.489
Platelet (µLx10^3)	257±57.7	247.97±124.92	0.696
Hb (g/dL)	14.8 (11-17)	10.75 (5.2-16)	**<0.001***
Basophil (µLx10^3)	0.03 (0.00-0.07)	0.02 (0.01-0.1)	**0.008***
Total protein (g/dL)	74.15 (24.2-85)	78.2 (10.45-145.5)	0.110
Albumin (mg/dL)	4.5 (3.7-5.2)	3.7 (1.8-5.1)	**<0.001***
AST (U/L)	13.55 (7.5-76)	19.6 (9.8-99.6)	**0.001***
ALT (U/L)	13.15 (5.7-154)	14.4 (6.1-155.3)	0.182
CRP (mg/dL)	2.62 (0.1-130)	5.05 (0.5-193.2)	**<0.001***
Ca (mg/dL)	9.3 (8.15-10.10)	9.51 (7.3-14.7)	0.156
Ürea (mg/dL)	30.35 (12.7-68.4)	42.5 (7.7-186.6)	**<0.001***
Creatinine (mg/dL)	0.88 (0.5-1.3)	1.23 (0.66-5.18)	**<0.001***
Uric acid (mg/dL)	5.15 (3-8.7)	6.6 (3.1-15.8)	**<0.001***
Mg (mg/dL)	2.11 (1.52-2.94)	2.05 (1.51-2.4)	**<0.049***
Na (mmol/L)	139.5 (133-144)	137 (129-148)	**0.001***
K (mmol/L)	4.42 (3.55-9.3)	4.5 (3.2-5.87)	0.279
P (mg/dL)	3.42 (2.12-4.41)	4 (2.31-7.21)	**<0.001***
LDH (U/L)	190 (137-261)	241.5 (123-530)	**0.002***
IgG (g/dL)	12.05 (7.93-19)	10.8 (1.42-124)	0.702
IgM (g/dL)	0.84 (0.4-2.3)	0.17 (0.16-28.8)	**<0.001***
IgA (g/dL)	2.75 (0.71-5.5)	0.37 (0.24-72)	**<0.001***

*: The Mann-Whitney U test, WBC: White blood cell, Hb: Hemoglobin, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein, MM: Multiple myeloma, LDH: Lactate dehydrogenase, IgG: Immunoglobulin G, IgA: Immunoglobulin A, IgM: Immunoglobulin M

Table 2. Comparison of baseline periostin level between subgroups

	N (%)	Periostin level	p
Sex			
Female	17 (52.8)	23.2 (11.2-94.8)	0.176
Male	19 (47.2)	21.5 (11.4-52)	
ISS			
I-II	14 (38.9)	25.3 (11.2-94.8)	0.284
III	22 (61.1)	21.5 (11.4-46.3)	
R-ISS			
I-II	18 (50.0)	23.3 (11.2-94.8)	0.486
III	18 (50.0)	21.5 (11.4-46.3)	
Genetic risk			
Standard	22 (61.1)	22.05 (11.2-94.8)	0.673
High	14 (38.9)	22.4 (11.4-46.8)	
Survival			
Death	8 (22.2)	25.1 (12.5-46.8)	0.158
Alive	28 (77.8)	21.1 (11.2-94.8)	

Patients who could not complete their treatment were not included, ISS: International Staging System Revised, R-ISS: Revised International Staging System Revised

Table 3. Correlation of periostin value at the time of diagnosis with other parameters

Parameters	Rho (correlation coefficient)	P
WBC (μLx10^3)	-0.432	0.009
Neutrophil (μLx10^3)	-0.420	0.011
Monocytes (μLx10^3)	-0.352	0.035
Urea (mg/dL)	-0.339	0.043
B2 microglobulin (mg/L)	-0.371	0.026

WBC: White blood cell

compares periostin levels by sex, stage, genetic risk group, and patient survival.

According to the Spearman correlation analysis, serum periostin levels demonstrated a moderate negative correlation with both neutrophil count and white blood cell count (rho=-0.420, p=0.011; rho=-0.432, p=0.009, respectively). The statistically significant correlations are summarized in Table 3.

The median initial periostin level of 28 patients who underwent interim evaluation was 24.96 (11.21-94.87) ng/mL, and the serum periostin level of these patients after 3 cycles of treatment was 17.97 (3.16-47.7) ng/mL. The decrease in periostin level after treatment was statistically significant (p<0.001). Additionally, post-treatment serum periostin levels in the patient group were compared with those in the healthy control group, and no statistically significant difference was observed (p=0.457).

Discussion

MM is characterized by the uncontrolled monoclonal proliferation of plasma cells and predominantly affects older adults. The median age at diagnosis is approximately 66-70 years, and fewer than 40% of cases occur in individuals younger than 65 years. This illness is also more frequently observed in men [1]. In our study, the mean age of the patient cohort was 63.11±12.13 years, and the female-to-male ratio was 1.11; these findings are consistent with existing epidemiological data. A key result of our study was that serum periostin levels were significantly higher in MM patients than in healthy individuals. According to our information, only one study to date has evaluated the relationship between periostin and MM [9], making our research likely one of the first from Türkiye to examine this association. Periostin is known to be involved in extracellular matrix remodeling, inflammation, and bone metabolism; elevated levels of periostin have been reported in various malignant and inflammatory conditions [2-4]. Given the profound alterations in the bone marrow microenvironment in MM, increased periostin levels may reflect disease-related stromal and inflammatory changes. However, this finding should be interpreted descriptively, as the present study was not designed to establish mechanistic pathways. Despite the elevated periostin levels observed at diagnosis, no statistically significant associations were identified between serum periostin concentrations and clinical or laboratory parameters commonly used to define disease burden, including anemia, renal dysfunction, or hypercalcemia. Similarly, periostin levels did not differ significantly across the International Staging System (ISS), the Revised ISS (R-ISS), the cytogenetic risk categories, or the survival status. Although non-significant trends were observed in some subgroup analyses, these findings cannot support conclusions regarding disease severity or prognostic relevance. This lack of association may be attributable to the heterogeneity of the patient population and the relatively limited sample size. Additionally, since MM is typically diagnosed at an advanced age, age-related factors such as nutritional deficiencies or comorbid renal dysfunction may confound the interpretation of anemia-related findings [10]. In the R-ISS scoring system, elevated LDH levels and high-risk cytogenetic abnormalities contribute to upstaging [11]. Correlation analyses revealed weak to moderate negative associations between periostin levels and certain hematological and biochemical parameters, including white blood cell count, neutrophil count, monocyte count, urea, and β2-MG. These correlations were statistically significant but biologically inconsistent, particularly the inverse relationship observed with β2-MG, a well-established marker of tumor burden in MM. Given the small effect sizes and the exploratory nature of these analyses, no mechanistic or clinical inferences can be drawn. These findings should therefore be interpreted with caution. Existing studies investigating the relationship between periostin and laboratory markers, such as albumin, LDH, and C-reactive protein (CRP), have yielded inconsistent results. Massy et al. [12] reported a negative correlation between periostin and albumin and a positive association with CRP, whereas another study found no statistically significant relationships between periostin and LDH or CRP [13]. In our study, periostin levels were not significantly associated with albumin, LDH, CRP, or cytogenetic abnormalities. The role of periostin in survival outcomes has been explored in several solid tumors. Massy et al. [12], in a cohort of 133 patients with lung adenocarcinoma, demonstrated that high periostin levels were strongly associated with increased mortality in patients with bone metastases. In our study, periostin levels in the 28 patients evaluable for treatment response were lower than in the eight patients who died during follow-up; however, this difference was not statistically significant. This finding positions our study as the first to explore the prognostic implications of periostin in MM. A reduction in serum periostin levels following symptom improvement has previously been described in asthma patients treated with corticosteroids [13]. However, no prior study has compared pre- and post-treatment periostin levels in MM. In our investigation, serum periostin levels decreased significantly after three cycles of induction therapy and reached levels comparable to those of healthy controls. This appears to be the first report in the literature showing such treatment-related changes in MM. This observation suggests that periostin levels may be dynamically influenced by treatment-related changes in the disease microenvironment. However, the clinical significance of this decrease remains unclear, and

whether periostin reflects treatment response or merely secondary inflammatory changes cannot be determined from the current data.

In summary, while serum periostin levels were elevated at diagnosis and decreased following treatment, the absence of statistically significant associations with established prognostic markers limits the clinical interpretation of these findings. Larger prospectively designed studies with appropriate control groups and longer follow-up are required to clarify the potential role of periostin in the biology of MM.

Study Limitations

This study has several important limitations that should be acknowledged. First, the relatively small sample size limits the statistical power of subgroup and correlation analyses, reducing the ability to detect clinically meaningful associations. Second, multiple subgroup comparisons and correlation analyses were performed without adjustment for multiple testing, increasing the risk of type I error. Therefore, statistically significant findings should be interpreted cautiously. Another limitation relates to the control group. Healthy controls were not matched for inflammatory status, renal function, or comorbidities, all of which may influence serum periostin levels. This lack of matching may have affected the observed differences between patients and controls. In addition, periostin measurements were limited to baseline and post-induction time points; longitudinal changes during long-term follow-up were not assessed. Finally, the observational design of the study precludes causal or mechanistic interpretations. The study was not designed to evaluate the prognostic or predictive value of periostin, and survival analyses were limited by short follow-up duration.

Conclusion

Serum periostin levels were significantly higher in newly diagnosed MM patients than in healthy individuals, and decreased significantly in patients following induction therapy. However, no statistically significant associations were observed between periostin levels and disease stage, cytogenetic risk, survival, or treatment response. These findings should be regarded as preliminary and hypothesis-generating. Further studies with larger sample sizes, methodologically matched control groups, and longer follow-up are required to determine the clinical relevance of periostin in MM.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Necmettin Erbakan University Ethics Committee (approval no: 2020/2467, date: 08.05.2020).

Informed Consent: Informed consent was obtained from all participants.

Footnotes

Authorship Contributions

Concept: A.K.T., A.T., Design: A.K.T., A.T., İ.K., Data Collection or Processing: A.K.T., İ.K., S.D., Ö.Ç., Analysis or Interpretation: A.K.T., A.T., Literature Search: A.K.T., A.T., Writing: A.K.T.

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