The Correlation Between Serum Levels of Beta-2 Microglobulin and Urine Deoxypyridinoline in Patients with the Ankylosing Spondylitis

ANKİLOZAN SPONDİLİTLİ HASTALARDA SERUM BETA-2 MİKROGLOBULİN VE İDRAR DEOKSİPİRİDİNOLİN DÜZEYLERİNİN KORELASYONU

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Summary

Purpose: We performed this study to investigate a possible relationship between serum beta-2 microglobuline (B2M) levels and urinary deoxypyridinoline (DPD) in patients with ankylosing spondylitis (AS) and their relations with the disease activity.

Institution: The study was performed in University of Atatürk, School of Medicine, Department of Physical Medicine and Rehabilitation

Materials and Method: Thirty outpatients who fulfilled the modified New York criteria for AS and thirty healthy subjects were included in the study. Disease activity was assessed by laboratory parameters including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Serum B2M and urine DPD levels were measured in patients and controls

Results: The biochemical parameters (ESR, CRP, DPD and B2M) were found to be different between the patient and control groups ($p<0.001$, $p<0.001$, $p<0.001$ and $p<0.05$, respectively). In the patient group there was a statistically significant correlation between B2M and CRP ($r=-0.366$; $p<0.05$), but not ESR ($r= 0.343$; $p>0.05$). A positive correlation between ESR, CRP and urine DPD was observed ($r=-0.396$; $p<0.05$, $r= 0.466$; $p<0.01$ respectively). There was a statistically significant positive correlation between serum B2M and urinary DPD ($r= 0.381$; $p< 0.05$).

Conclusion: In patients with AS, urinary DPD and serum B2M levels may be a useful indicator for disease activity and inflammation-mediated bone loss.

Key Words: Ankylosing spondylitis, Beta-2 microglobuline, Deoxypyridinoline, Disease activity

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Özet

Amaç: Bu çalışma Ankilozan Spondilit (AS)'li hastalarda serum beta-2 mikroglobulin (B2M) ve idrar deoksipiridinolin (DPD) düzeyleri arasındaki olası ilişkiyi ve bu iki parametrenin hastalık aktivasyonu ile muhtemel değişkenliğini incelemek amacıyla yapıldı.

Çalışmanın Yapıldığı Yer: Çalışma Atatürk Üniversitesi Tıp Fakültesi Fiziksel Tıp ve Rehabilitasyon Anabilim Dalında yürütüldü.

Materyal ve Metod: Çalışmaya 30 ankilozan spondilitli (AS) hasta ve aynı sayıda sağlıklı kontrol vakası dahil edildi. Hastalık aktivasyonu eritrosit sedimantasyon hızı (ESR) ve C-reaktif protein (CRP) ile değerlendirildi. Hasta ve kontrol gruplarında serum beta-2 mikroglobulin (B2M) ve idrar deoksipiridinolin (DPD) düzeylerine bakıldı.

Bulgular: Gruplar arasında tüm biyokimyasal parametrelerde (ESR, CRP, DPD, B2M) istatistiksel olarak anlamlı fark bulundu (sırasıyla $p<0.001$, $p<0.001$, $p<0.001$ ve $p<0.05$). Hasta grubunda serum B2M, CRP ile anlamlı korelasyon gösterirken ($r=-0.366$; $p<0.05$), ESR ile korelasyonu saptanmadı ($r= 0.343$; $p>0.05$). Hasta grubunda idrarda DPD, hem ESR hem de CRP ile anlamlı korelasyon gösterdi (sırasıyla $r=-0.396$; $p<0.05$, $r= 0.466$; $p<0.01$). Serum B2M ve idrar DPD arasında da anlamlı korelasyon bulundu ($r= 0.381$; $p< 0.05$).

Sonuç: AS'li hastalarda idrar DPD düzeyleri ile serum B2M seviyeleri anlamlı korelasyon göstermekteydi. Bu iki parametre enflamasyona bağlı kemik kaybı ve hastalık aktivasyonunun takibinde yararlı parametreler olabilirler.

Anahtar Kelimeler: Ankilozan spondilit, Beta-2 mikroglobulin, Deoksipiridinolin, Hastalık aktivitesi

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Ankylosing Spondylitis (AS) is an inflammatory disease of unknown origin, first affecting the spine and adjacent structures, and commonly progressing to eventual fusion (ankylosis) of the involved joints. AS is characterized by mild or moderate flares of active spondylitis alternating

with periods of almost or totally inactive inflammation (1,2). It is well-known that the human leukocyte antigen (HLA) class I allele HLA B27 is strongly associated with a number of spondyloarthritis including AS (3,4).

Beta-2-Microglobulin (B2M), a polypeptide with a molecular weight of 11.700 Daltons, is a glycoprotein subunit of HLA class 1 protein on which occurs on surface of nucleated cells abundantly on lymphocytes and monocytes. Therefore, it is found in serum and many other biological fluids. Its function is unknown, but it may control the expression and biosynthesis of antigens on the cell surface (5). In addition, it is a regulatory factor in bone metabolism mainly stimulating the osteoclastic activity. Deoxypyridinoline (DPD), an indicator of bone resorption, is a cross-link of type 1 collagen that is released during the bone loss process and is excreted unmetabolized in urine. The DPD can be used to assess the bone resorption rate in patients with bone-related disorders (6). B2M is found at low levels in the serum and urine of normal individuals and is increased, in some viral diseases, renal dysfunction, and autoimmune diseases including rheumatoid arthritis (7). Increased urine DPD concentrations have been reported in inflammatory diseases (8).

We performed this study to investigate a possible relationship between serum B2M levels and urinary DPD in patients with AS and their relations with the disease activity.

Materials and Method

Thirty outpatients who fulfilled the modified New York criteria for AS were included in the study (9). In the patient group (n=30), there were 25 men and 5 women (mean age: 41.2 ± 7.7, range: 28–60 years). The mean disease duration was 10.2 ± 4.1 years (range 3–20 years). The control group consisted of 30 healthy donors without a history of inflammatory disease and matched age, sex and weight (23 men, 7 women; mean age 40.1 ± 7.4 range: 23-55 years). We excluded patients who had sings or symptoms of severe renal, hepatic, endocrine (Paget's disease, hyperthyroidism and hyperparathyroidism), hematological, lymphoproliferative and other malignant diseases. Twenty patients were taking a combination of sulfasalasine and NSAIDs, ten patients were only taking NSAIDs. The patients were allowed to continue their previous regimens of drugs.

Disease activity was assessed by laboratory parameters including ESR and CRP. ESR levels were determined by Westergren method. A nephelometric method was used for measuring CRP levels (Beckman Array Protein System, USA). Serum B2M was determined with a commercially available kit by nephelometric method (Beckman Coulter Immage, USA). Urine DPD levels were determined with a commercially available kit (DPD, Bayer, USA) by an automated chemiluminescence's system (ACS: 180, Bayer, USA).

Data were processed using the SPSS package programme. Laboratory results were given as mean ± standard deviation (SD). Differences between groups were performed using the Mann-Whitney U test. Spearman's rank correlation coefficient was used to assess correlations between variables. P values of < 0. 05 were regarded as significant.

Results

The clinical features and laboratory findings of the patients and control subject are shown in Table 1. In the analysis of demographic data, there was no statistically significant difference among groups (p>0.05). The biochemical parameters (ESR, CRP, DPD and B2M) were found to be different between the patient and control groups

Table 1. The clinical and laboratory features of the patients with AS and healthy controls

	Patients (M±SD) (n: 30)	Controls (M±SD) (n: 30)	P
Sex (male/female)	25/5	23/7	NS
Age (years)	41.2 ± 7.7	40.1 ± 8.4	NS
Disease duration (years)	10.1±4.2	--	
B2M (mg/dL)	0.27 ± 0.15	0.15 ± 0.2	<0.05
DPD (nMDPD/mMC)	8.99 ± 2.64	4.59 ± 1.27	<0.001
ESR (mm/h)	39.25 ± 14.46	15.36 ± 10.43	<0.001
CRP (mg/L)	2.71 ± 1.38	0.35 ± 0.23	<0.001

M±SD: mean ± standard deviation NS: not significant

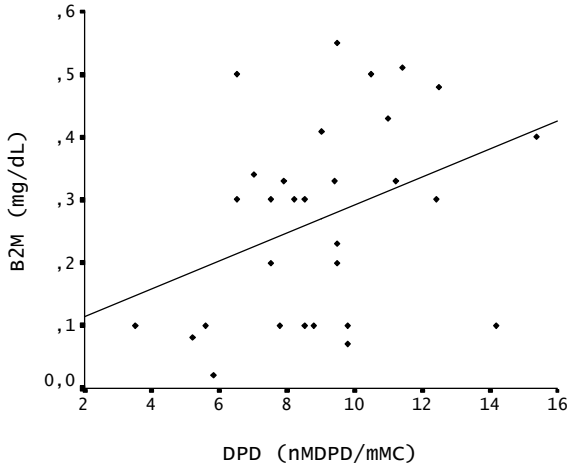

Figure 1. There was a statistically significant correlation between serum B2M levels and urinary DPD values of AS patients. Statistical analysis was performed using Spearman's rank correlation coefficient (r= 0.38, $p < 0.05$).

($p<0.001$, $p<0.001$, $p<0.001$ and $p<0.05$, respectively).

In the patient group there was a statistically significant correlation between B2M and CRP (r=-0.366, $p<0.05$), but not ESR (r= 0.343, $p>0.05$). A positive correlation between ESR, CRP and urine DPD was observed (r=-0.396, $p<0.05$, r= 0.466, $p<0.01$ respectively).

There was a statistically significant positive correlation between serum B2M and urinary DPD (r= 0.381, $p< 0.05$) (Figure 1).

Discussion

Possession of the human leucocyte antigen HLA-B27 is important in the pathogenesis, severity and chronicity of a group of diseases called spondyloarthritis (10). B2M is the beta-chain of major histocompatibility complex (MHC) class I molecules. The principle natural function of HLA B27 is to complex with B2M, forming a structure that can bind short antigenic peptides, derived for example from infectious agents within cells. These complexes then travel to the cell surface where they can be specifically recognized by cytotoxic T lymphocytes, which kill the infected cell (11). B2M must be associated with class I for processing and cell surface expression of class I molecules (12). Without the B2M, the class I antigen will not be expressed on the cell surface and hence have a deficiency of cytotoxic T cells. Elevated serum concentrations in the presence of a normal glomerular filtration rate suggest increased B2M production or release in inflammatory diseases. Increased serum B2M levels have been reported in AS (13,14). Our findings confirm previous reports which showed elevated serum levels of B2M in patients with AS. B2M is synthesized concentrations are detectable due to elevated cell biosyntehesis. Higher levels of B2M in patients with AS could be attributed to activation of monocyte macrophages system in subpopulation of cytotoxic T-lymphocytes, which might be the evidence of the involvement of cytotoxic-T cell mechanism in the pathogenesis of this disease (13). Since B2M is produced by lymphocytes which increased in inflammatory diseases, it is obvious that its levels are elevated in AS. In our study, urinary DPD concentrations of the patients were higher than in the healthy control group. DPD have also an impact on urinary excretion of these collagen compounds. This data has been proven by the previous studies (15, 16). Inflammatory joint diseases such as rheumatoid arthritis, seronegative spondyloarthropathies and juvenile arthritis comprise a heterogeneous group of disorders that share a propensity to destroy the extracellular matrices of joint cartilage and bone (17).

Inflammation is a part of AS pathogenesis could lead to bone loss in the so-called inflammation-mediated osteopenia (18). DPD, a biochemical marker of bone resorption, is mainly used for follow up of treatment and the degree of inflammation. B2Ms are regulatory factors in bone metabolism mainly stimulating the osteoclastic activity. They are also bone-derived growth factors (19). In the light of the fact increased DPD levels is a result of osteoclastic activity; a positive correlation may exist between these two parameters. Our data which urine DPD correlated significantly with serum B2M suggests that the mechanism responsible for increased B2M production in AS may also play a cause in the increased collagen degradation seen in this disease.

In conclusion, urinary DPD and serum B2M levels may be a useful indicator for disease activity and inflammation-mediated bone loss in patients with AS.

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