

PLASMA LEVELS OF BETA 2-MICROGLOBULIN IN PATIENTS WITH IDIOPATHIC DILATED CARDIOMYOPATHY

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SUMMARY: It is recently reported that Beta 2-microglobulin (β 2M) is a serologic marker for cellular immune activation in inflammatory heart diseases. This study was designed to assess the plasma levels of β 2M in 21 patients with dilated cardiomyopathy. 10 men and 11 women, aged 54.8 ± 13.9 years were subjected to these studies. The control group consisted of 25 healthy donors (11 men and 14 women, aged 46.4 ± 12.7 years. The patients with idiopathic dilated cardiomyopathy were in New York Heart functional class II to IV and had an ejection fraction of $< 40\%$ assessed by echocardiography at the time of evaluation. They had no evidence of active infection, inflammatory disease, cancer, hypertension or renal failure. They received a standardized therapeutic regimen consisting of angiotensin-converting enzyme inhibitor, long-acting nitrates, digitalis and furosemide (40 to 160 mg/day). Endomyocardial biopsy and cardiac catheterization were not performed. Native serum and ethylene diaminetetraacetate plasma were stored at -20°C until use. The plasma values of β 2M were determined by radioimmunoassay kits. The plasma levels of β 2M were significantly elevated in patients group compared with control subjects (2153.73 ± 22.79 vs 880.99 ± 228.97 microgram/liter, respectively, $p < 0.001$).

In conclusion, plasma β 2M was associated with the T cellular hyperresponsiveness and may serve as useful marker of disease activity reflecting different aspects in the multifactorial pathogenesis of dilated cardiomyopathy. Future studies are necessary to detect prognostic or predictive roles of β 2M in heart failure.

Key Words: Beta 2-Microglobulin, idiopathic cardiomyopathy.

INTRODUCTION

Idiopathic dilated cardiomyopathy (IDC) is a disease of unknown etiology and principally affects the myocardium (1,2). The diagnosis of IDC is established by the presence of left ventricular dilatation and sys-

tolic dysfunction in the absence of congenital, coronary, valvular, hypertensive, or pericardial heart disease. In some patients the development of IDC is associated with clinical factors such as alcoholism, pregnancy, or a family history of cardiomyopathy (1,2). However, IDC is distinct from secondary myocardial disease that occur with a specific systemic disorder that may be metabolic, collagen-vascular, infiltrative,

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neuromuscular, inflammatory, toxic, genetic, or neoplastic in origin. The smaller unit of the class-1 antigen is β2M and this protein is not encoded within the major histocompatibility complex (MHC) (3). The precise role of β2M is not known. There has been speculation that it has a role in transport of the class-1 molecule to the cell surface, and this is supported by studies on class-1 negative cell lines that become positive for surface expression when β2M is supplied. A number of immune regulatory abnormalities have been identified in IDC, including humoral and cellular autoimmune reactivity against myocytes, decreased natural killer cell activity, and abnormal suppressor cell activity (4-6). These abnormalities suggest that immune defects may be important etiologic factors in the development of IDC. It is recently described that beta 2 microglobulin (β2M) as a serologic marker for cellular immune activation of inflammatory heart diseases. Therefore, in our study serum levels β2M in the patients of IDC were investigated.

MATERIALS AND METHODS

This study was designed to assess the plasma levels of β2-M in 25 patients with dilated cardiomyopathy. (11 men and 14 women, aged 53.08 ± 15.55). The control group consisted of 25 healthy donors (11 men and 14 women, aged 46.36 ± 12.64 years). The patients with either idiopathic or ischemic cardiomyopathy were in New York Heart Functional Class-II to IV and had an ejection fraction of < 40% (assessed by echocardiography) at the time of evaluation. They had no evidence of active infection, inflammatory disease, cancer, hypertension, or renal failure. They received a standardized therapeutic regimen consisting of angiotensin converting enzyme inhibitor, long action nitrate, digitalis, and furosemine the daily dose of which was titrated clinically and ranged from 40-160 mg/day. Endomyocardial biopsy, and cardiac catheterization were not performed. Native serum and ethylenediaminetetra acetate plasma were stored at -20°C until use. The plasma values of β2-M were determined by radio immune assay kits.

RESULTS

This study was designed to assess the plasma levels of β2M in 25 patients with dilated cardiomyopathy. The control group consisted of 25 healthy donors of comparable age. The mean ages in the two groups were not significantly different ($p > 0.05$).

The plasma values of β2M were determined by radio immune assay kits. The plasma levels of β2M were significantly elevated in the patient group [2162.26 ± 1016.2 (923.1-4811) microgram/liter, compared to that of the control subjects 881.4 ± 229.1 (458.6-1512.6) microgram/liter respectively ($p < 0.001$)].

DISCUSSION

Human β2-M was isolated from the urine of patients with damaged renal tubules and was assigned a MW of 11,600 daltons. Aminoacid sequence data indicated that this molecule is 99 residues long and contains two cysteine residues involved in a disulfide bond.

The increased levels of serum β2M are seen in both non malignant diseases such as rheumatoid arthritis (7), systemic lupus erythematosus (8), and Crohn disease (9), and malignant diseases such as small cell lung cancer (10), bladder cancer (11), ovarium cancer, choleorectal cancer (12), Hodgkin lymphoma (13), acute leukemia (14), chronic lymphocytic leukemia (15), and multiple myeloma (16). In these disease entities, the levels of serum β2M have been considered as a prognostic factor. But in fact the reason of the rise of serum β2M compared to that of patients with control subjects is elevated is not known.

The etiologies of IDC are different, most of them are unknown. Probably some of them are secondary to infectious, or/and inflammatory diseases. The abnormalities in immune regulation and the variety of antimyocardial antibodies present in IDC are consistent with this hypothesis. HLA associations have also been identified in IDC; the frequency of HLA B-27, HLA A2, HLA DR4 and HLA DQ4 is increased compared to controls and the frequency of HLADRW6 is decreased compared to controls (17). But it is not possible to perform the endomyocardial biopsy in all patients. β2M may be

a noninvasive marker of immunologic reactions.

In our study, the levels of serum β2M were significantly elevated in IDC patients compared with control subjects. We think that this is the first study in IDC patients. We were unable to find any reports of previous studies in literature where in β2M was measured in IDC patients.

In conclusion, plasma β2M was associated with the T cellular hyper responsiveness and may serve as a useful marker of disease activity reflecting different aspects in the multifactorial pathogenesis of dilated cardiomyopathy. Future studies are necessary to detect prognostic or predictive roles of β2M in IDC.

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