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Serum adenosine deaminase activity as a predictor of disease severity in ulcerative colitis

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Abstract

Background and aim: Ulcerative colitis (UC) is a chronic inflammatory disease characterized by recurrent inflammation and ulcerations of colonic mucosa and an inappropriate and delayed healing. Adenosine deaminase (ADA) is a cytoplasmic enzyme involved in the catabolism of purine bases, capable of catalyzing the deamination of adenosine, forming inosine in the result process. Although ADA has been shown to increase in several inflammatory conditions, there are no literature data indicating an alteration in UC.
Methods: This study evaluated the activity of total ADA in serum of 43 patients with UC and 18 healthy controls. Patients' age, disease duration, drug intake, and other medical history were all noted for each subject. Complete blood count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were determined for both patients and controls. Correlation analysis was also performed between ADA and other inflammation markers of UC.
Results: Serum mean ADA levels were 11.12±2.03 and 7.99±2.04 U/l for patients with UC in active state and in remission and 8.55±2.26 U/l in the healthy control group. Mean serum ADA levels were significantly elevated in active UC patients compared with patients with UC in remission and control groups. Overall accuracy of ADA in determination of active UC was 83.7 with sensitivity 83.3%, specificity 84.2%.
Conclusions: Serum ADA levels were found to be elevated in UC patients in active state suggesting a partial role of activated T-cell response in the disease pathophysiology. Further randomized controlled studies are warranted to demonstrate the role of ADA in UC patients, with

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a special interest in specifically targeted therapies against ADA for achieving disease remission.

1. Introduction

Ulcerative colitis (UC) is a chronic immunologically mediated disorder that is characterized by colonic mucosal inflammation and a chronic relapsing course resulting from the complex interplay between several genetic and environmental risk factors.[1] The diagnosis of UC is best made with endoscopy and mucosal biopsy for histopathology. Laboratory studies and imaging tests are also helpful to establish the precise diagnosis.[1–3] Although medical therapy has advanced during the past decades and colectomy rates may be decreasing, surgery continues to play an important role in the therapeutic armamentarium in severe UC.[4] It is therefore not surprising that the early detection of disease activity will significantly reduce the surgery rate, and therefore will reduce mortality in patients with serious UC.[5] Noninvasive tests, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood cells (WBC), fecal calprotectin and PMN-elastase are being widely recognized as important, both for initial diagnosis and for accurately monitoring disease activity in UC. Nevertheless, an ideal test has not yet been developed.[6,7] For this reason the adjunctive use of additional serum markers may add significant benefit for predicting disease severity and achieving diagnostic accuracy.

Adenosine deaminase (ADA) is a purine catabolic enzyme, capable of catalyzing the deamination of adenosine, forming inosine in the result process.[8] It is widely distributed in tissues and body fluids. The most important biological activity of ADA is related to lymphoid tissue and is necessary for proliferation and differentiation of T lymphocytes as well as for the maturation and function of blood monocytes and macrophages.[9–11] The activity of ADA is ten times greater in lymphocytic cells than in erythrocytes and, in relation, ADA level is greater in T lymphocytes than in B lymphocytes and varies during T-cell differentiation, with significant increases of its level in immature or undifferentiated states.[12–14] The assay of ADA activity in the serum and other biologic fluids is very important for a precise diagnosis of many pathological situations. In this respect ADA has been shown to increase in several inflammatory conditions such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), pancreatic disorders, acute appendicitis, celiac disease (CD) and tuberculosis.[14–18] Although ADA has been considered as an indicator of a nonspecific marker of T-cell activation, the precise mechanisms by which serum ADA activity is altered have not been clearly identified yet.

With this respect the present study was undertaken in order to investigate whether the levels of ADA alter in UC patients and its correlation with serum inflammation markers. The clarification of the complex network of immune-inflammatory mediators operating in the gut of patients with ulcerative colitis could led to the identification of new therapeutic targets that could, in turn, drive the development of effective therapeutic managements. To the best of our knowledge, this study is the first to investigate the level of ADA in UC patients; therefore, we consider that present study is important because it facilitates additional research into the immunopathogenesis of UC.

2. Materials and methods

2.1. Patients

Forty-three patients with UC (22 men and 21 women) and 18 healthy controls attending at the Gastroenterology Clinic of Ankara Education and Research Hospital between September 2009 and February 2011 were enrolled in the study. The diagnosis of UC was based on standard clinical, radiological, endoscopic and histological criteria. Patients' age, disease duration, drug intake, and other medical history were all noted for each subject. Complete blood count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were determined for both patients and controls. All UC patients underwent colonoscopy at study entry.

Disease activities of UC patients were calculated according to endoscopic activity index (EAI) suggested by Rachmilewitz et al.[19] EAI score encompasses granularity (none = 0, yes = 2), mucosal friability (none = 0, with touch = 2, spontaneous bleeding = 4), vascular pattern alterations (normal = 0, decreased = 1, disappeared = 2), and mucosal damage in the affected colonic segment (none = 0, mild = 2, severe = 4). Based on initial colonoscopic examination, patients were divided into two subgroups according to EAI scores. Patients with EAI scores 4 or higher were classified as active UC (55.8%) and patients with a lower score than 4 were considered in remission (44.2%).

2.2. Serum samples

Blood samples were collected from a peripheral vein after an overnight fast without using any anticoagulant and were subjected to centrifugation with the speed of 3000 rounds per minute for 10 min (Nuvefuge CN180), at 4 °C to obtain serum. All serum samples were stored at −80 °C immediately after separation from peripheral blood prior to analysis.

2.3. ADA assay

Total serum ADA was measured with an automatic spectrophotometric analyzer (Cobas Mira, Roche, Basel, Switzerland). Serum ADA activities were estimated by the method of Giusti and Galanti.[20] Briefly, samples were incubated with adenosine and the released ammonium ions were determined. To control for ammonium present before the addition of exogenous adenosine, untreated samples were run in parallel. ADA activity was defined as the concentration of ammonium ions (_ mol/l) formed in 1 min and expressed as units per liter.