

Adenosine Deaminase Activity in Sera of Patients with Psoriasis, Mycosis fungoides and Adult T Cell Leukemia

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Adenosine deaminase activities in sera were measured in 18 psoriatic patients, 8 mycosis fungoides patients, and 9 patients with adult T cell leukemia. Adenosine deaminase activity in the sera of the psoriatic patients showed no significant increase. An elevated adenosine deaminase activity was observed in 7 of the 8 patients with mycosis fungoides and 8 of the 9 patients with adult T cell leukemia. After chemotherapy, adenosine deaminase activity in serum of acute adult T cell leukemia was reduced. Adenosine deaminase activity in the sera of 2 patients with smoldering adult T cell leukemia was more elevated, with exacerbation of the disease. It is difficult to grade the extension of the tumors in plaque stage mycosis fungoides and smoldering adult T cell leukemia. To know the progression of the disease is critical in determining its management. These results indicate that adenosine deaminase activity in serum is one of the reliable indicators for the grading of mycosis fungoides and adult T cell leukemia. *Key word: T lymphocyte.*

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Adenosine deaminase (ADA) (E.C. 3.5.4.4.) catalyzes the hydrolytic deamination of either adenosine or deoxyadenosine to produce inosine and deoxyinosine respectively (1). This is an essential step in adenosine and deoxyadenosine metabolism, which as a part of the purine salvage pathway enables the efficient reutilization of these nucleosides and detoxification of an excess deoxyadenosine triphosphate (2, 3).

The enzyme dose exists in most of the human tissues. Reduced or absent ADA activity is associated with a severe combined immunodeficiency syndrome, which is characterized by a profound deficiency in both B and T lymphocytes (4). These findings suggest an important role for this enzyme in lymphocyte function. High ADA activity is reported in lymphatic tissues (5) and leukemic cells, especially the tumors of T cell origin (6-9). An increase of ADA activity in peripheral lymphocytes of Sezary's syndrome and acute adult T cell leukemia (ATL) has been reported (10-13). Deoxycytosine, a newly synthesized ADA inhibitor, has been developed as an antitumor agent against T cell leukemia.

The presence of ADA in epidermis has already been reported (14, 15). ADA activity in epidermis is relatively low; however, in involved epidermis of psoriasis and squamous cell carcinoma, the enzyme activity is elevated (16, 17). High ADA activity is compatible with hyperproliferative states of the epidermal keratinocytes with pronounced DNA synthesis.

ADA activity in sera can be measured with only a minor risk to the patients and with an easier extraction technique as

compared with measuring it in peripheral lymphocytes or epidermis. Since the plaque stage of mycosis fungoides (MF) and smoldering adult T cell leukemia (ATL) contain few atypical lymphocytes in peripheral blood, alteration of ADA activity in peripheral lymphocytes could not be detected. However, infiltration of atypical lymphocytes to the skin is observed at this stage. ADA from these atypical T lymphocytes and from proliferating epidermal keratinocytes might relate to serum ADA level. Therefore we investigated ADA activities in the sera of patients with psoriasis, MF, and ATL.

MATERIALS AND METHODS

1. *Patient population. Psoriasis:* Eighteen psoriatic patients (13 males and 5 females) aged 17-69 years were investigated. The extent of their lesions varied from 9 % to 80 % of the whole body surface. The severest one was erythrodermic type. Except for antihistamines, topical steroids, and topical PUVA therapy, no systemic treatment was administered to the patients. The patients had no liver dysfunction.

Mycosis fungoides: Eight MF patients without visceral involvement (4 males and 4 females) aged 19-65 years were investigated. They had poikilodermatous plaques. Two patients had localized tumors on the abdominal and leg skins. Six patients were at plaque stage of MF. Two were considered at early tumor stage of MF. Neither systemic chemotherapy nor radiation had been administered to the patients. The patients had no liver dysfunction and no high LDH.

Adult T cell leukemia: Two cases of acute ATL and 7 cases of smoldering ATL were investigated. A female patient, 59 years of age, who had erythematous plaques on the four extremities, was diagnosed as ATL with 94600 of white blood cell count (75 % flower cells) and bone marrow invasion of leukemia cells. LDH was high with 1325. Atypical cells were depleted by chemotherapy to become 9800 white blood cell count and LDH 372. ADA activity in serum was measured before and after chemotherapy. Another acute ATL male patient, of 77 years of age, showed 4100 white blood cell count after chemotherapy with depleted atypical lymphocytes and 503 of LDH. ADA activities in the sera of 7 patients with smoldering ATL (6 males and 1 female) aged 28-65 years were investigated. No systemic chemotherapy had been administered to the patients. The patients with smoldering ATL had skin lesions but no liver dysfunction.

2. *Adenosine deaminase assay:* Peripheral blood was drawn from the patients. The serum was separated by centrifugation. ADA activity in serum was measured by Fujii's method with spectrophotometry at SRL laboratory. In brief, the serum was incubated with adenosine for 30 min at 37° C. Then phenol and perchloric acid were added in the presence of sodium nitroprusside (Na₂Fe (CN)₅NO). Produced one molecule of NH₃ by ADA reacted to these chemicals to make one molecule of indophenolblue. The synthesized indophenolblue was quantitated with spectrophotometer in absorbance at 630 nm.

RESULTS

The results of measuring ADA activities in the sera of 18 psoriatic patients, 8 patients with MF, and 9 patients with ATL are shown in Fig. 1.

The normal range of ADA in serum is 5.3-17.8 IU/l. For the psoriatic patients, the mean ADA activity was 14.9 IU/l (range

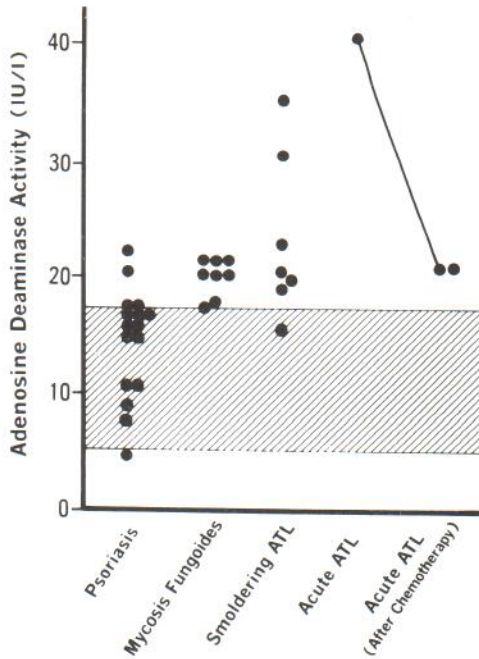


Fig. 1. Adenosine deaminase (ADA) activity (IU/l) in the sera of 18 patients with psoriasis, 8 with mycosis fungoides, and 9 with adult T cell leukemia. ADA activity was spectrophotometrically measured as described in Materials and Methods. Shaded area shows normal range of ADA activity. A line indicates same patient.

4.8–22.0). The average was within the normal range. Four patients showed slightly higher and one patient showed lower activities than normal range. The extent of their lesions was not related to ADA activity. The erythrodermic psoriatic patient showed 9.1 IU/l of ADA activity.

On the other hand, increased ADA activities in the sera were observed in patients with MF. The mean ADA activity was 19.7 IU/l (range 16.9–21.5). Seven patients showed higher activities than the normal. Two patients with tumor on the skin without visceral involvement did not show higher activity (21.5, 19.7 IU/l) as compared to other plaque stage patients. However, one of them developed tumor invasion to muscles and nerve 18 months later. At that time he showed high ADA activity of 60.9 IU/l.

One patient with acute ATL showed high enzyme activity of 40.4 IU/l before chemotherapy and 21.1 IU/l after successful chemotherapy. ADA activity of another acute ATL patient after chemotherapy was 21.1 IU/l. Abnormally high ADA activity was observed in patients with smoldering ATL as well. The mean ADA activity in smoldering ATL was 23.6 IU/l (range 15.4–36.0). Six out of 7 patients recorded above normal range.

In 2 cases of smoldering ATL, ADA activities were measured several times. The course of a 41-year-old male is shown in Fig. 2. In December 1989, nodular lesions and papules were scattering on his body. Superficial lymphnodes were palpable. Neither lymphnodes swelling on the thorax or abdomen, nor visceral involvement could be detected with CT scan. In peripheral white blood cells, no atypical lymphocytes were found. ADA activity in serum was 20.5 IU/l. One month later, the nodules had increased in number and the lymphnodes had

become larger. Although no leukemia cells were detected in periphery, ADA activity was much elevated. In the following month, ADA activity was elevated to 50.0 IU/l. At that time no leukemic change was detected. However, lymphnodes and nodules on the skin were more enlarged. In another patient, ADA activity became higher as the number and the size of nodules on the skin increased (data not shown).

DISCUSSION

Increased ADA activities in the sera were observed in patients of MF and ATL. ADA activity in the sera of psoriatic patients was not increased.

Since ADA is present in the cytosol fraction of the cell and the enzyme could easily be eluted to the blood from the cells, serum ADA is detectable in normal humans. The activity is reported to be elevated in liver diseases (18). Therefore the enzyme is assumed to be leaked from hepatocytes into the serum. In some types of leukemia ADA activity in serum is observed to be increased as well, and the level is correlated with the severity of the disease (19). In these cases leukemia cells in the peripheral blood are assumed to be the ADA source in serum (20).

In our results, ADA activities in sera from psoriatic patients did not increase despite of the increased ADA activity in the psoriatic epidermal cells (14). Since ADA activity in the epidermis is low, elevated epidermal ADA activity does not cause ADA increase in the sera in such a skin disease.

On the other hand, in MF at plaque stage, in which neither atypical cells in peripheral lymphocytes nor visceral infiltration could be detected, ADA activity in serum showed a relatively high level. In smoldering ATL, a considerable amount of

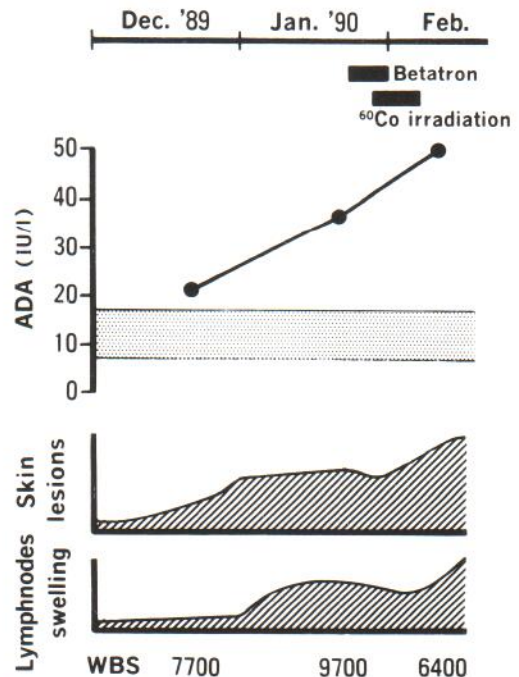


Fig. 2. The course of disease and ADA activity in the serum of a patient with smoldering adult T cell leukemia. Shaded area shows normal range of ADA activity.

tumor cells may be circulating, even though leukemic changes are not observed at that stage. The tumor cells circulating and invading to the skin will cause an increase in ADA activities in the sera.

The extension of the tumor cells is difficult to grade in plaque stage mycosis fungoides and smoldering adult T cell leukemia. To know the progression of the disease is critical in determining its management. These results indicate that adenosine deaminase activity in serum is one of the reliable indicators for the grading of mycosis fungoides and adult T cell leukemia. We would like to further investigate the significance of ADA in serum of MF and ATL.

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