LETTER TO THE EDITOR
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Cutaneous Finding in Anti Thymocyte Globulin Induced Serum Sickness

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ABSTRACT

Polyclonal anti-thymocyte globulin (ATG) is used as an immunosuppressive agent in the treatment of aplastic anemia (AA). Serum sickness is a recognized side effect of ATG. We observed abnormal skin manifestation in patient with aplastic anemia who had been treated with ATG. We conclude that abnormal immune function caused by aplastic anemia and ATG and corticosteroids may aggravate the signs of serum sickness.

Key words: Anti thymocyte globulin; Cutaneous; Serum sickness

LETTER

Anti-Thymocyte globulin (ATG) is a purified, concentrated sterile IgG fraction from pooled hyper immune sera obtained from several horses immunized with homogenates of human thymuses.[1]

ATG is the treatment of choice for patients with severe aplastic anemia (AA) who are ineligible for Bone Marrow Transplant (BMT) from an HLA-identical sibling and for patients with non-severe AA who are transfusion dependent.[2] Response rates of 50-80% were achieved when ATG was used alone, or in combination with cyclosporine, androgenic steroid or granulocyte colony-stimulating factor (G-CSF).[3] Recognized side-effects of ATG include immediate allergic reactions such as fever, rigors, hypertension or hypotension. However it has rarely been associated with anaphylaxis, hemolysis, neutropenia, and serum sickness, which was reported to occur 7-14 days after the onset of ATG therapy.[4] Clinical findings of ATG mediated serum sickness have been reported to include fever, malaise, cutaneous eruptions, arthralgias gastrointestinal complaints, cephalgia, blurring of vision, arthritis, and lymphadenopathy.[5]

Here, we report a case with unusual skin manifestation during the course of serum sickness induced by ATG therapy.

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The case was a 13 year old boy with AA admitted to immunology ward of Namazi Hospital in Shiraz.

The illness of patient started 3 years earlier during which he had a history of recurrent bone pain, epistaxis and pancytopenia. He had been on prednisolone, folic acid, cyclosporine and ATG for the last 5 months without significant improvement.

On admission the patient had hairy and cushingoid facies (Figure 1) and laboratory data showed: platelet count of 27000, white cell count of 5700, Haemoglobulin of 11.8, RBC of 2.1×10^6 and ESR of 34 mm/h. The patient was then treated with ATG 1200 mg intravenously and gradually with hydrocortisone, clemastine, ranitidine daily.

After 4 doses of ATG he developed malaise, high grade fever, decreased blood pressure, swelling of joints and prearticular areas of both hands, petechia on extremities and high ESR=97mm/ħ. He also developed large triangular ecchymoesis on lower abdomen after 3 days. The size of lesion was 10×8×8 cm with dark red color (Figure 1). Such symptoms were indicative of serum sickness, therefore ATG administration was discontinued, and the patient was treated with steroid, antihistamine and antipyretic. The signs and symptoms of serum sickness disappeared gradually.

Von Priquet and Schick[6] clearly documented the syndrome of serum sickness, consisting of fever, cutaneous eruptions, arthralgias, and lymphadenopathy occurring 8 to 12 days after the injection of horse antidiphtheria serum. Urticaria and morbilliform rashes are the predominant types of skin eruptions.[7] In a patient who had received equine ATG, initial rashes were a thin serpiginous bands of erythema along the sides of the hand fingers, feet and toes at the junction of the palmar or plantar.[8] Moreover in many cases, the erythematous lesions are replaced by petechia or purpura in exactly the same distribution, presumably because of low platelet counts.[9]

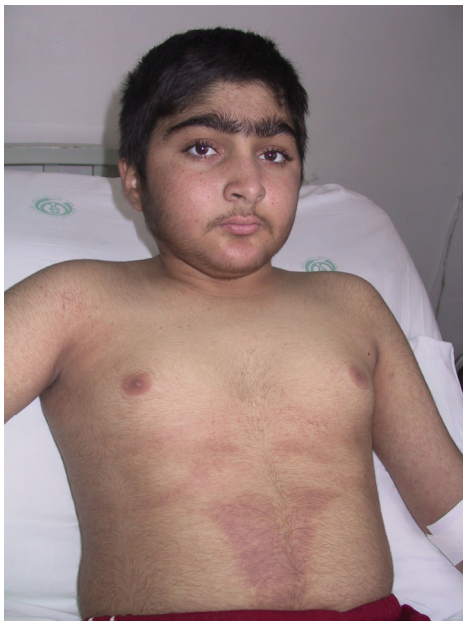

Figure 1. Large triangular ecchymoesis lesion on lower abdomen of patients with aplastic anemia due to Anti Thymocyte Globulin

The patient in the present report had skin lesions, fever, edema, myalgia, arthralgia in hands and laboratory findings including high sedimentation rate and thrombocytopenia. These clinical and laboratory findings were indicative of serum sickness. The onset of manifestations of disease was short which was due to pervious ATG usage. The cutaneous findings, namely large well circumscribed ecchymotic lesion on abdomen, in our patient differed from those described by von Priquet and Schick.[6] Such symptoms have not been reported before, and clearly are another expression of the sickness .Such symptoms might be due to aplastic anemia associated abnormalities of immune system, including abnormal helper/suppressor lymphocyte ratio, decreased natural killer cell activity, abnormal production of interleukin and gamma-interferon ,and abnormal hematopoiesis.[9] T lymphocyte with the activated suppressor phenotype are consistently decreased following ATG therapy and probably represent the patho-physiologically appropriate target of treatment.[9] The serum sickness in the present patient was responsive to corticosteroid and resolved after 7 days of treatment. In conclusion the cutaneous findings in the present patient were more severe and different from that described by von Priquet and Schick[6] and others.[7-9] Immunologic disturbance caused by an underlying disease and ATG and corticosteroid maybe the cause of this event.

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