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Case Reports

Cyclosporin induced fatal rhabdomyolysis in a Young Patient with Acquired Aplastic Anemia: a Case Report

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Introduction

Cyclosporin is used as an immunosuppressive agent in the management of a variety of autoimmune disorders[1] and in patients of organ transplant to suppress host immunity and prevent rejection.[2] It is now well established that acquired aplastic anemia is secondary to immune mediated destruction of stem cells in the bone marrow[3] and hence Cyclosporin is used as a first line immunosuppressive drug alone or in combination with anti lymphocyte globulin in the management of aplastic anemia.[1] Rhabdomyolysis is a rare side effect of Cyclosporin.[4] Here we describe a case of fatal rhabdomyolysis in a young patient who received cyclosporin for treatment of aplastic anemia.

Case Report

A sixteen years old male presented to the hematology outpatient with history of fever and increasing pallor since two weeks. There was no significant past medical, drug or family history. On examination, he was grossly pale. Petechial hemorrhages were evident on both legs and feet. Other general and systemic examination was unremarkable. Subsequently, a complete blood count, reticulocyte count, bone marrow and trephine were carried out which was consistent with the diagnosis of severe aplastic anemia according to the Camitta classification.[5] Hepatitis B surface antigen was non-reactive. Chromosomal studies were normal while Ham's test was negative.

Various treatment options were discussed and the patient opted for immunosuppressive therapy. He was given injection anti lymphocyte globulin 10mg/kg daily intravenously for five days and injection methyl prednisolone 2mg/kg intravenously for four days. On fifth day of the treatment, he was started on oral Cyclosporin 5mg/kg daily. After just three doses of cyclosporin, he developed severe pain in both calf muscles.

Examination revealed a heart rate of 120 per minute, temperature 38^{o}C and blood pressure 105/65 mm Hg. There was bilateral calf muscles swelling and marked tenderness with a complete functional disability of both lower limbs. Skin color was normal. Pedal pulse was palpable in both lower limbs. Laboratory investigations done at that time revealed hemoglobin 7.3gm/dl, white cell count 700/cumm, platelet count 15,000/cumm, prothrombin time 18 seconds (control 13 seconds), activated partial thrombin time 42 seconds (control 30 seconds), blood urea nitrogen 27mg/dl (6-16), serum creatinine 3.1mg/dl (0.8-1.3), uric acid 7.9mg/dl (4.1-8.0), total bilirubin 3.8mg/dl (0.2-1.2), SGPT 167i.u. /L (0-55), creatine phosphokinase 7451i.u. (17-176), serum myoglobin 6150ug/L (upto 70). Ultrasound Doppler of both lower limbs revealed no evidence of deep venous thrombosis. Ultrasound of the abdomen was within normal limits.

He was admitted to the hospital. Cyclosporin was stopped. He was started on intravenous fluids along with empiric antibiotics. But his condition deteriorated and he developed anuria. Subsequent laboratory investigations revealed a further rise in serum creatinine to 4.2mg/dl and serum creatine phosphokinase was 3407i.u. (17-76). He developed tachycardia, tachypnea and hypotension after 24 hours of admission. Oxygen saturation dropped and he was resuscitated and intubated, but could not be revived and expired.

Discussion

Cyclosporin is used as an immunosuppressive that inhibits interleukin-2 production by T lymphocytes and prevents the expansion of cytotoxic T cells. It is commonly used in patients of acquired aplastic anemia, post allogenic bone marrow transplant graft versus host disease, other organ transplant patients and in many autoimmune disorders.[6] Apartfrom immunosuppression, Cyclosporin may affect skeletal muscles. Most of the cases suggest that Cyclosporin associated muscular disorders have two patterns. First is the myopathy without myolysis. In this case muscle enzymes are usually

normal with non-specific myopathy on muscle biopsy, if performed. This type of myopathy appears to be dose dependent and symptoms usually improve as soon as the drug is stopped.[7] The second pattern is that of rhabdomyolysis and most of the time it occurs from interaction with other drugs notably the statins[8] and cholchicine.[9] The pathophysiology of drug interaction has not been established.

However, Cyclosporin alone can induce rhabdomyolysis as we have seen in this case and to our knowledge has not been reported in a patient of aplastic anemia. Previously, Cyclosporin induced fatal rhabdomyolysis was seen in individuals receiving statins and in a patient of post bone marrow transplant .[4]

Conclusion

Our report concludes that myopathy and habdomyolysis are well-established rare side effects of cyclosporin. As the indications for the use of cyclosporine is increasing, we recommend a close clinical surveillance along with laboratory parameters in patients on cyclosporin.

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