Ceftriaxone induced immune hemolytic anemia with disseminated intravascular coagulation

Sir,

A 52-year-old male with diabetes mellitus, hypertension and autosomal dominant polycystic kidney disease with the chronic kidney disease was admitted for renal transplantation (RTx). His pre-transplant complete blood count (CBC), liver functions (serum bilirubin, 0.6 mg/dl) and coagulation profile were in normal range and he was negative for hepatitis B,C and human immunodeficiency virus. G6PD enzyme was not deficient. Immunological markers were negative. There was no history of hematuria or drug allergy in the past. Patient had respiratory tract infection before 10 days of RTx and treated with cefoperazone-sulbactam. He became asymptomatic and was prepared for RTx and was given injection cefriaxone (1 g) as pre-operative prophylaxis. Within 1 h, he had uneasiness; swelling of face followed by macroscopic hematuria, nasal bleeding and hematoma at fistula site and had altered coagulation profile (prothrombin time with international normalized ratio, 6.58; activated partial thromboplastin time, 75 s with test 30 s). CBC showing hemoglobin, 9.1 g/dl; total count, 24.40 × 10^3/μL; platelet count, 152 × 10^3/μL. Ultrasound showed no evidence of cyst hemorrhages. He was treated with hemodialysis and four units of fresh frozen plasma (FFP), but had further drop of hemoglobin and platelet count to 6.4 g/dl and 76 × 10^3/μl respectively within 24 h and had persistent altered coagulation profile. Further evaluation revealed hemolysis on peripheral smear and a high lactate dehydrogenase at 4020U/L; low C3, C4 and fibrinogen level and a high D-dimer level at >4000 ng/ml. He developed icterus and altered liver function (serum bilirubin, 20.4 mg/dl; serum glutamic pyruvic transaminase, 51U/L; serum glutamic oxaloacetic transaminase, 374U/L). Direct antiglobulin test was positive. Indirect antiglobulin test was negative. Markers for hepatitis A, B, C and E were negative. Anti-cardiolipin antibody and lupus anticoagulant were carried out and repeated after 1 month, which were negative ruling out catastrophic lupus. Hence, the diagnosis of ceftriaxone induced immune hemolytic anemia (IHA) with disseminated intravascular coagulation (DIC) was arrived at.

Patient was treated with four units of packed cell volume, eight units of FFP; intravenous methyl-prednisolone 500 mg/day with intravenous immunoglobulin (IVIG) 10 g/day for 5 days. Patient responded to the above treatment and coagulation parameters became normal within 3 days; and liver function, complement level and direct antiglobulin tests returned to within 15 days.

Drug induced immune hemolytic anemia (DIIHA) is much less frequent as compared to drug induced thrombocytopenia. More than 125 drugs are implicated.[1] Common drugs implicated for this are changing in each decade, and now it is commonly seen with the cephalosporin group and ceftriaxone was considered to be the second most common drug to cause DIIHA.[2]

DIC after IHA is very rare but it can be due to the following: (1) platelets contain lipid which is active in activating the coagulation cascade. (2) immune complexes triggering coagulation can be taken up by the reticuloendothelial system (RES) thereby decreasing the capacity of RES to clear procoagulant present in the blood.[3]

For treatment, removing the drug that causes hemolysis would be the mainstay.[4] It is imperative to avoid future exposure to any antibiotic of the cephalosporin group as a second bout is expected to be worse. We used steroids and IVIG in our case as we had considered the probability of catastrophic lupus but the data supporting its use in DIIHA are limited.[5]

Jigar D. Shrimali, Himanshu V. Patel, Manoj R. Gumber, Vivek B. Kute, Pankaj R. Shah, Aruna V. Vanikar[1], Hargovind L. Trivedi

Departments of Nephrology and Clinical Transplantation and [1]Pathology, Laboratory Medicine, Transfusion Services and Immunohematology, Institute of Kidney Diseases Research Center, Dr. HL Trivedi Institute of Transplantation Sciences, Ahmedabad, Gujarat, India

Correspondence:
Dr. Jigar D. Shrimali,
Department of Nephrology and Clinical Transplantation,
Institute of Kidney Diseases and Research Centre,
Dr. HL Trivedi Institute of Transplantation Sciences,
Civil Hospital Campus, Asarwa,
Ahmedabad - 380 016, Gujarat, India.
E-mail: dr.jdshrimali@gmail.com

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