A CASE OF SEVERE CEFTRIAXONE-INDUCED IMMUNE HEMOLYTIC ANEMIA

Young-Lan Song[1,3], Matthias Felber [2], Antigoni Zorbas[1], Markus Schmugge Liner [2], Beat M. Frey[1], Charlotte Engström[1]

[1] Blood Transfusion Service Zurich, Swiss Red Cross, Switzerland
[2] University Children's Hospital Zurich, Eleonore Foundation, Switzerland
[3] Departement of Medical Oncology and Hematology, Triemli Hospital, Switzerland

Introduction:

Drug-induced immune hemolytic anemia(DIHA) is a rare but potentially fatal complication caused by frequently administered medications like antibiotics. As clinical signs are variable and serological investigations are challenging, DIHA may be underdiagnosed. We report a 13-year old boy with Tetralogy of Fallot who received intravenous (IV) Ceftriaxone to treat endocarditis. On day(d) 23 and 24 of treatment he developed hypotensive shock and acute hemolysis during drug administration.

Methods:

Standard serological methods such as direct(DAT) and indirect antiglobulin test(IAT) (ID-system, BioRad/Grifols, CH) were applied on samples obtained after the second hemolytic crisis. An advanced search for drug-dependent antibodies(ab) was performed by incubating the patient's sera with group O red blood cells(RBCs) in the presence and absence of Ceftriaxone as well as its metabolites(patient's urine sample) as described previously (Mayer et al., 2015). As negative controls, a random AB serum instead of the patient's serum and saline instead of the drug were used. Tests were repeated 16 and 39 days after discontinuation of the drug. Hb and hemolytic laboratory markers(e.g. bilirubin, LDH and haptoglobin) were monitored.

Results:

Hb dropped from 82 to 27 (d23) and from 96 to 39 g/l (d24) following IV Ceftriaxone. Three packed RBCs were administered. LDH and bilirubin were slightly elevated; contrary to expectations, the results of haptoglobin and free hemoglobin were normal. Serological investigations revealed a strong C3d-positive DAT. The serum ab screening test was negative in IAT and the eluate was non-reactive. Serum drawn at the time of the hemolytic reaction was strongly reactive when incubating with RBCs in the presence of the drug (3+) and its metabolite (2+), while controls remained negative, clearly demonstrating presence of Ceftriaxone ab. Repeated testing d16 after drug cessation showed a similar result. On d39 no Ceftriaxone ab were detected.

Conclusions:

Here we present a pediatric case with acute, life-threatening Ceftriaxone-dependent hemolysis and hemodynamic instability. After discontinuation of Ceftriaxone and administration of Methylprednisolone, Clemastine plus transfusion, hematologic remission was rapid. Notably, hemolytic markers remained proportionally unaffected.

DIHA needs to be considered in individuals with acute C3d-positive hemolysis coinciding with new drug treatment and the relevant medication has to be stopped at once.