Deferasirox/hydroxychloroquine

S

Various toxicities and off-label use in coronavirus disease 2019: case report

A 19-year-old woman developed hepatic injury in the form of liver failure and acute hepatic encephalopathy during iron chelation treatment with deferasirox and off-label treatment with hydroxychloroquine for coronavirus disease 2019 (COVID-19) [*routes and times to reactions onsets not stated*].

The woman, who had sickle cell disease (SCD) S/β^0 thalassaemia and history of hepatic crisis, had been receiving chronic transfusions for 3 years. She had iron overload, for which she had been receiving chelation with deferasirox 1800 mg/day. Concomitantly, she had been receiving unspecified home medications. She was diagnosed with COVID-19 and admitted due to vaso-occlusive crisis (VOC). She started receiving off-label treatment with hydroxychloroquine for COVID-19. She was discharged with improvement in the pain. However, she presented with emesis and transient AST/ALT elevation (hepatic injury), which was considered to have been caused due to off-label hydroxychloroquine.

Therefore, the woman's therapy with hydroxychloroquine was discontinued. Four days after the diagnosis of COVID-19, she developed acute chest syndrome with decreased haemoglobin and fever. She was treated unspecified antibacterials [antibiotics] and received blood transfusion. After four weeks, she was again hospitalised due to fatigue, anorexia and worsening abdominal pain. She was treated with ketorolac and morphine, and home medications including deferasirox were continued. She developed fever on hospital day 3. She was treated with ceftriaxone. She became acutely encephalopathic after 5 hours. Laboratory evaluations were significant for hyperammonaemia. She started receiving neomycin and lactulose for hyperammonaemia. Deferasirox was stopped due to suspicion of possible toxicity. Clinical examination and EEG showed severe hepatic encephalopathy, which was considered to be secondary to the acute liver failure with hyperammonaemia and neurologic insult. She was therefore intubated and haemodialysis was also initiated. A subsequent improvement was noted in the ammonia level. Subsequently, she developed elevated transaminases, thrombocytopenia, worsened synthetic liver function, increased creatinine, coagulopathy and shock. Vasopressors were therefore initiated. Her condition was consistent with multiorgan failure syndrome (MOFS), and therefore, she underwent red blood cell exchange. However, she had increased CRP along with fever, persistent thrombocytopenia, mildly decreased a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member-13 and von Willebrand factor antigen level >196%, and these findings were consistent with thrombocytopenia-associated MOFS. Hence, she underwent therapeutic plasma exchange (TPE), until platelet count was noted to be >100 000. After undergoing TPE, ammonia, AST/ALT and INR levels normalised and CRP decreased. Also, the fever resolved, and neurologic examination improved. Repeat brain MRI showed interval bilateral thalamic T2 hyperintensity, which indicated cytotoxic oedema from hepatic encephalopathy, for which she was treated with hydrocortisone. She was noted to have a non-occlusive catheter-related femoral vein thrombus, for which she started receiving enoxaparin sodium [enoxaparin]. Five days after TPE, she returned to baseline neurological status. On hospital day 15, she was discharged with improved pain, and she had improved levels of D-dimer and CRP and normal liver function tests. It was determined that hydroxychloroquine and deferasirox in addition to iron overload and history of hepatic crisis might have contributed to the hepatic injury. Additionally, she experienced COVID-19-related hyperinflammation that might also have triggered the SCD-MOFS and deferasirox-induced hepatic injury with hyperammonaemia.

Martone GM, et al. Acute hepatic encephalopathy and multiorgan failure in sickle cell disease and COVID-19. Pediatric Blood and Cancer 68: No. 5, May 2021. Available from: URL: http://doi.org/10.1002/pbc.28874

803554605