Unusual Cause of Severe Dyspnea Following Kidney Transplantation: Dapsone Induced Simultaneous Methemoglobinemia and Hemolysis

Dear Editor,

Methemoglobinemia, a condition involving heme iron oxidation [ferrous (Fe^{2+}) to ferric (Fe^{3+})], with subsequent reduced tissue oxygen delivery, can be congenital or have varied etiology.[1] We present a patient in whom dapsone caused hemolysis and methemoglobinemia soon after kidney transplantation.

A 55-year-old woman underwent deceased donor kidney transplantation using thymoglobulin induction, followed by tacrolimus/mycophenolic acid/steroid maintenance. Donor and recipient were CMV IgG negative and EBV IgG positive. The patient had documented sulfa allergy. Dapsone (100 mg daily) was started for pneumocystis jirovecii prophylaxis after documenting normal glucose 6 phosphate dehydrogenase (G6PD) enzyme activity. Acyclovir was used for viral prophylaxis. There was immediate allograft function. On post-operative day 5, the patient started experiencing fatigue, malaise, and dyspnea requiring 4 L/min supplemental oxygen via a nasal canula. She had central cyanosis. The chest X-ray was clear, the venous thrombo-embolic study was negative. Hemoglobin decreased to 6.3 g/dL (12.3-15.3) without evidence of blood loss, with a haptoglobin level <10 mg/dL (16-200) and MCV of 96.6 fL (80-96) indicating hemolysis. Arterial blood gas was remarkable for a pO_2 of 64.4 mmHg (75.0-100.0) and methemoglobin of 13.9% (0.4-1.5). Dapsone-induced methemoglobinemia and hemolysis were diagnosed. Medication was changed to atovaquone, and blood transfusion was given. The symptoms resolved. On the 6-week follow-up, her hemoglobin and serum creatinine were 12.5 g/dL and 0.65 mg/dL, respectively.

The hemolysis was likely due to dapsone, despite normal G6PD activity, which is rare.[2] Oxidative stress from hydroxylamine metabolites of dapsone induces methemoglobinemia; its severity can range from self-limiting to life-threatening. A high index of suspicion is needed for early diagnosis, which can be confirmed with blood gas. Milder cases require only stopping dapsone and supportive care, while severe cases may need additional treatment with methylene blue and/or ascorbic acid.[3,4]

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