Digital gangrene in a child with atypical hemolytic uremic syndrome associated with anti-factor H antibodies

Sir,

A 10-year-old boy presented with generalized edema, pallor, dark colored urine, jaundice, vomiting, and abdominal pain for 5 days without preceding fever or bleeding manifestations. Hemoglobin was 6.3 g/dl, platelet count 0.72 × 10^3/μL, total leukocyte count 8000/μL, with abundant schistocytes on peripheral smear. He had retic count 3%, depressed serum haptoglobin, normal G6PD, and negative direct Coomb's test. Prothrombin time, activated partial thromboplastin time and fibrinogen levels were normal. D-Dimer was mildly elevated. Urinalysis revealed albumin 3+ and, 18–20 pus cells/hpf. Urine was strongly positive for hemoglobin. Biochemistry suggested blood urea nitrogen 150 mg/dl, serum creatinine 3.9 mg/dl, serum aspartate aminotransferase 210 U/L, serum alanine transaminase 110 U/L, serum bilirubin 3.3 mg/dl, direct bilirubin 1.1 mg/dl, serum lactate dehydrogenase 13,610 U/L, serum uric acid 12 mg/dl, and serum complement (C3) 53 mg/dl. Malarial parasites on peripheral smear, leptospira IgM, human immunodeficiency virus, hepatitis B surface antigen, and anti-hepatitis C virus was negative. Tests for anti-nuclear antibody, anti-double stranded DNA, antiphospholipid antibody, and anti-neutrophil cytoplasmic antibody were negative. Ultrasound revealed normal sized kidneys. Anti-factor H antibody level was elevated at 2,900 AU/mL (normal <150 AU). The diagnosis was consistent with atypical hemolytic uremic syndrome (HUS). He progressively developed oliguria, malignant hypertension with painful duskiness of all digits of all 4 limbs. There was no evidence of infective endocarditis and radial Doppler ultrasound ruled out vascular thrombosis. He was managed with daily single volume plasma exchange, hemodialysis and immunosuppression (6 doses of IV pulse dexamethasone at 5 mg/kg/dose and 3 doses of IVIG at 400 mg/kg/dose). The acral cyanosis progressed to frank gangrene [Figure 1] despite antiplatelet and anticoagulation therapy. He developed cardiac failure requiring inotropes and mechanical ventilation and later succumbed to the illness. Postmortem renal biopsy confirmed thrombotic microangiopathy (TMA).

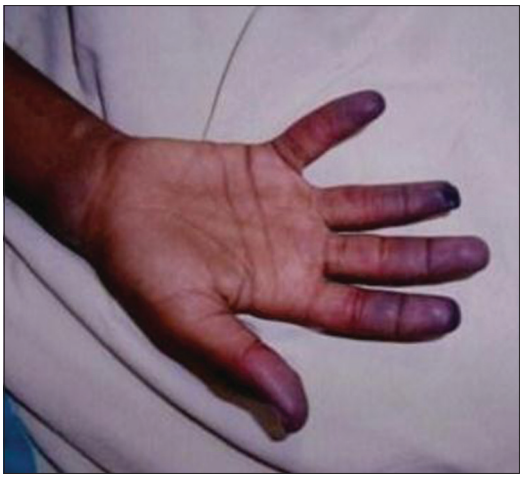

Figure 1: Photograph of right hand showing duskiness of all digits progressing to frank gangrene

Our patient presented with HUS-TMA with anti-factor H antibodies. Anti-Factor H antibodies result in uncontrolled complement activation and have emerged as a major cause of HUS in the Indian subcontinent.[1] Although HUS can have extrarenal involvement in one-third of the cases, peripheral gangrene is extremely rare as the size of the vessels supplying the digits is relatively much larger than the microvasculature commonly affected in HUS.[2,3] Comorbid infections, vasculitis or prothrombotic disorders that can lead to digital gangrene were ruled out. The digital gangrene was thus attributed to persistent HUS activity. Eculizumab, a C5 blocking antibody that has been found effective in salvaging such cases,[2] could not be offered due to unaffordability.

There are only seven reported cases of peripheral gangrene in association with HUS including only one case in association with anti-factor H antibody. The presentation of digital gangrene in HUS has been found to be associated with poor outcome with about 50% cases developing dialysis dependence and mortality despite aggressive management.[1-5]

Digital gangrene can thus result from malignant HUS activity and may portend a poor outcome.

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Conflicts of interest

There are no conflicts of interest.

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