Peripheral gangrene in a case of severe dengue

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Abstract
We report the case of a 10-year-old male who developed gangrene of his fingers and toes following severe dengue fever complicated by disseminated intravascular coagulation (DIC). Child developed bilateral dry gangrene of fingers and toes. All the peripheral pulses of the affected limbs were palpable. The child had no history of taking B-blockers, ergot alkaloids or other related medications. Color Doppler of peripheral arterial and venous systems of all limbs indicated normal flow. Blood was positive for D-dimers and fibrin degradation products. The patient was managed with broad spectrum antibiotics, fluid resuscitation, low molecular weight heparin, blood transfusions, fresh frozen plasma and other supportive measures. Peripheral gangrene seen in DIC associated with dengue is very rare and carries a higher mortality.

Key words: Disseminated intravascular coagulation, peripheral gangrene, severe dengue

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Introduction
The spectrum of disease manifestations in dengue fever is wide. It ranges from asymptomatic or mild infection to serious manifestations such as dengue hemorrhagic fever, dengue shock syndrome and multiorgan failure. Dengue fever can cause liver damage, rhabdomyolysis, myocardial depression, and various neurologic and ophthalmologic manifestations. It is usually associated with conditions of decreased blood flow such as cardiogenic and hypovolemic shock or various infectious processes involving either bacterial or viral pathogens.

Gangrene is the term used to describe the decay or death of an organ or tissue caused by a lack of blood supply. Peripheral gangrene of the fingers and toes is seen in a wide variety of medical conditions but rarely in dengue fever. It presents as gangrene of two or more extremities without large vessel obstruction or vasculitis. This is a rare case report of a child who developed peripheral gangrene of the fingers and toes of both hands and feet during an episode of severe acute dengue viral infection. Though there have been a short series of about twelve cases of peripheral gangrene due to multiple causes, we could find only two cases reported in world literature specifically due to dengue fever.

Case Report
A 10-year-old male child with Down's syndrome was admitted to our hospital with a history of fever of 6 days duration, body aches and rash of 1-day. On admission, the child looked toxic, pale and had a hemorrhagic maculopapular confluent rash all over the body with evidence of gum bleeding. He was febrile with a temperature of 102°F. There was evidence of impending shock with low volume pulse rate of 136 beats/min, capillary refill time of 5 s and systolic blood pressure of 60 mmHg and diastolic of 40 mmHg.

He was drowsy, had pedal edema and few petechiae over both lower parts of his legs both anteriorly and posteriorly. Abdominal examination revealed hepatomegaly of 8 cm under right costal margin and splenomegaly of 5 cm under
left costal margin. There was also evidence of fluid leakage in the form of pleural effusion and ascites. He developed generalized tonic-clonic seizures and respiratory distress 15 min after admission. In view of the critical condition of the child, he was transferred to the intensive care unit and was electively ventilated immediately. He received rapid fluid resuscitation, inotropic support (noradrenaline), blood transfusions and other supportive measures.

On admission, his hemoglobin was 6 g/dl, Total leucocyte count - 6300/mm$^3$; platelet count of 40,000/mm$^3$ which later dropped to 15,000/mm$^3$. His initial serum electrolytes, liver function tests and renal function tests were normal. However, his condition deteriorated progressively. On the 2nd day of admission, he developed conjunctival hemorrhages [Figure 1], and the hemorrhagic rash increased further. Multiple ecchymotic patches were also seen all over the body, and there was bleeding from puncture sites.

It was also noticed that there was bluish discoloration of fingers and toes which progressively got worse over the next few hours to become gangrenous [Figure 2]. There was no history of jaundice, hematuria, Raynaud’s phenomenon, joint pains or consumption of B-blockers or ergot alkaloids. Radial and dorsalis pedis pulsations were well felt in both upper and lower limbs respectively. The child deteriorated further and developed multi-organ failure. He had acute kidney injury, pneumonia and upper gastrointestinal bleed on the 3rd day of admission.

The investigations showed D-dimers >10 mg/L (N = −0.5 mg/L), FDP was positive, prothrombin time 28 s, activated partial thromboplastin time 34 s and INR 2.5. Dengue serology for IgM and IgG was both positive. Blood and urine cultures were negative. In view of a dengue epidemic in the area, there was a high index of suspicion of dengue fever in our child. The history and clinical findings were corroborated with lab investigations and a diagnosis of severe dengue fever with disseminated intravascular coagulation (DIC) was made.

He was started on broad spectrum antibiotics (meropenem and linezolid) along with the therapeutic dose of enoxaparin and fresh frozen plasma infusions. Child showed progressive improvement with adequate urine output. After a period of 6 days, his pneumonia resolved, and he was finally weaned off the ventilator.

The skin lesions and the platelet count improved significantly over 7 days. All his routine investigations and coagulation profile returned to normal by 1 week. The discoloration of the fingers and the toes receded. The sensation of the fingers and toes also returned to normal. There was sloughing of the soft tissue of the fingers and toes but no auto-amputation of the digits.

Echocardiogram and computed tomography scan of the aorta were normal. A color Doppler study of peripheral arterial and venous system showed no evidence of large vessel obstruction. Full autoimmune serology (including antiphospholipid antibodies and acquired or congenital C and S protein deficiency) was negative. Complement levels sent on 3rd day of treatment were found to be normal.

After an intensive rehabilitation program comprising of nutritional support and physiotherapy, the child was back again on his feet 2 weeks after being taken off the ventilator.

**Discussion**

Dengue fever is one of the most important arboviral infection in the tropical region. World Health Organisation currently estimates that 50–100 million dengue infections occur worldwide annually. Dengue fever is quite common
Peripheral gangrene is an extremely rare complication of severe dengue fever and to our knowledge, perhaps this has not been reported so far in any pediatric case with dengue fever. Peripheral gangrene is a well-documented, but rare clinical syndrome characterized by symmetrical distal ischemic damage leading to gangrene of two or more sites in the absence of large vessel obstruction or vasculitis. It was initially described in 1981 by Hutchison.\(^{[3]}\)

Multiple factors like DIC, dehydration due to third space losses due to pleural effusion and ascites, inotropic support (noradrenaline infusion) and hypotension may be implicated in our case. Although Gram-positive and less commonly, Gram-negative bacteria are associated with peripheral gangrene,\(^{[8,9]}\) in our case, blood and urine cultures were all negative.

The pathogenesis of peripheral gangrene may include the Schwartzman reaction, bacterial endotoxin release, and platelet plugging in peripheral arterioles due to vascular collapse and DIC.\(^{[10,11]}\) Larger vessels are spared, and peripheral pulses are generally palpable. In spite of the ever-widening etiological spectrum, DIC is considered the final common pathway of pathogenesis of peripheral gangrene. It is proposed to be a cutaneous marker of the same.\(^{[12,13]}\)

Treatment success has been reported for patients who received anticoagulation with heparin and aspirin, eprostenol and tissue plasminogen activator infusion, sympathetic blockade, combination of plasmapheresis, leukapheresis and antibiotics.\(^{[14]}\) Though we managed our case with broad spectrum antibiotics (meropenem and linezolid), enoxaparin and fresh frozen plasma infusions. Amputation of the affected area may have to be undertaken occasionally, once demarcation develops, and the patient is stable. At times, spontaneous dropping off is seen. By exclusion of other possible causes, it is tempting to consider dengue infection as the cause of peripheral gangrene in our case. Peripheral gangrene carries a high incidence of morbidity and mortality.

Peripheral gangrene is a rare complication of dengue fever. A high index of suspicion and prompt management with usual measures may limit the progression and damage of gangrene. In our case, as exclusion of differentials such as embolic phenomena, atherosclerosis and immunological disorders were done. Hence, this unusual association of peripheral gangrene of the fingers and toes was attributed to severe dengue infection because of the clinical features and positive serology for dengue.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**References**

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