CASE REPORT

Fatal Non-Bacterial Thrombotic Endocarditis Following Viperine Bite

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Non-bacterial thrombotic endocarditis (NBTE) commonly occurs in patients with wasting disease (e.g. malignancy) or with valves damaged following trauma due to intra-cardiac foreign body, scarring or marked turbulence. Although disseminated intravascular coagulation (DIC) is well documented following viperine bite and the underlying mechanism of NBTE is thought to be DIC, there is no report of NBTE in humans following snake bite. We report a young male who following viperine bite developed local swelling, superficial gangrene of tissues at the site of bite, and oliguria and died following multiple cerebral infarcts and acute renal failure. The post-mortem examination showed NBTE of the aortic valve, multiple embolic infarcts of brain, spleen and kidneys, acute tubular necrosis and features of DIC in the brain in the form of fibrin thrombi in the capillaries, perivascular hemorrhages and necrosis.

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Key words: viper bite, disseminated intravascular coagulation (DIC), non-bacterial thrombotic endocarditis

Introduction

Snake bite is an important occupational hazard in rural tropics with approximately 40,000 deaths in a year globally, of which 25% occur in India (1). The venomous snakes commonly found in India are cobras, kraits, Russell’s viper and saw scaled viper (2). In this report, we describe a patient who died due to acute renal failure and other complications following viperine bite and the post-mortem examination revealed sterile vegetations over aortic valves with multiple infarcts in brain, spleen and kidneys.

Case Report

The patient, a 23-year-old male was admitted to Nehru hospital attached to the Postgraduate Institute of Medical Education and Research, Chandigarh with a history of snake bite on the medial aspect of the left ankle 3 days prior to admission. Following the bite, he developed diarrhea and vomiting, which lasted for one day and swelling of the foot and leg. On the third day of the bite he developed oliguria followed by anuria for which he was taken to a local hospital where he was managed conservatively for about 8 hours before being transferred to this hospital. No anti-snake venin was administered at the local hospital. At admission his physical examination was unremarkable except that he was drowsy and confused. The left foot was red and swollen up to 15 cm above the ankle and there was superficial gangrene over the medial aspect of left ankle. Investigations revealed hemoglobin (Hb) 10.8 mg/dl; TLC 8,500 cumm with normal differential count but platelets were reduced. Blood biochemistry showed markedly elevated blood urea (385 mg/dl); serum creatinine 12.9 mg/dl and inorganic phosphate 7.0 mg/dl with normal serum calcium. The PTTK was prolonged at 42 seconds (control: 39 seconds) and the prothrombin index (PTI) was 75%. The EKG and chest X-ray were normal. The X-ray of left foot revealed soft tissue swelling. He was given 20 cycles of peritoneal dialysis on the day of admission following which his sensorium improved. However his sensorium deteriorated again on the next day and computerized tomography of head revealed multiple hypodense areas in right frontal, parietal and occipital areas with hyperdense areas in between suggestive of multiple infarcts as well as hemorrhages in brain. He was given polyvalent anti-snake venin, and antibiotics, and debridement of gangrenous tissues was undertaken. His sensorium however further deteriorated and he died the day after admission.

A complete autopsy was performed which revealed exposed muscle at the site of bite following debridement. The right
Non-Bacterial Thrombotic Endocarditis

Figure 1. Vegetations over the aortic valve cusps.

Figure 2. Vegetations composed of fibrin and platelets and the adjacent valvular endocardium showing mild inflammatory reaction.

Figure 3. Embolic infarcts in brain.

kidney was hydronephrotic with an impacted calculus at the pelvis of ureter. The left kidney was grossly normal but histology revealed dilated tubules with degenerated tubular epithelial cells, extensive pigment granular casts and deposition of hemosiderin pigment in the proximal and distal convoluted tubules. Electron microscopy revealed degenerated organelles within degenerated tubules. These histopathological features were those of acute tubular necrosis with evidence of hemolysis. Examination of the heart showed multiple friable vegetations ranging from 0.5–0.8 cm over the non-coronary and left coronary cusps of aortic valve (Fig. 1). Histopathological examination showed that these vegetations were composed of fibrin and platelets with mild inflammatory infiltrate in the adjacent valvular endocardium (Fig. 2). No organisms were detected on special staining of these vegetations and none could be grown on culture. These features suggested non-bacterial thrombotic endocarditis. Multiple recent embolic infarcts were identified in the kidneys, spleen and brain (Fig. 3). In addition, fibrin thrombi in capillaries, perivascular hemorrhages and necrosis were present throughout the brain particularly in the cerebral white matter.

Discussion

The non-bacterial thrombotic endocarditis (NBTE) develops over the traumatized endothelium of valves either due to intracardiac foreign body or marked turbulence (deformed valve) or in patients with wasting disease particularly in malignancies (marantic endocarditis) (3). The underlying mechanism at least in some situations is thought to be disseminated intravascular coagulation (DIC). To the best of our knowledge, the development of NBTE following snake bite has not been described in humans although coagulation disturbances and development of DIC are common after viperine bite.

In coagulation, the three basic steps are the formation of autothrombin (factor Xa), thrombin and fibrin. The viperine snake venom contains enzymes which can disturb blood coagulation at all three steps. It can convert prothrombin to thrombin, can cause fibrinolysis as well as inhibit it (4) and the Russell’s viper venom in addition can directly convert factor Xa to X (5). In rodents who form the natural prey of snakes, massive coagulation occurs in heart and great vessels soon after Russell’s viper bite (6). In a clinical study, the cardiac findings observed in patients dying of viper bite were shock and EKG findings suggestive of myocardial infarction and heart blocks (7) and at autopsy following Russell’s viper bite, focal cardiac hemorrhages have been observed in the heart but no clotting has been found (8). The lack of development of clotting in the heart is probably due to the insufficient dose of venom relative to the body weight (6). The present patient did not develop bleeding but had evidence of DIC on histopathology in the form of fibrin thrombi in brain. The vegetations over the aortic valve could either be a manifestation of DIC or NBTE. The large size of vegetations and the inflammatory reaction in the adjacent valvular endocardium however, supports the possibility of NBTE. Our patient also had evidence of intra-vascular hemolysis which is caused
by enzyme phospholipase A2 present in abundance in viper venom (1).

We suggest a prospective echocardiographic study to find the incidence of this complication in patients with viperine bite and to determine whether NBTE can be reversed with anti-snake venin and if there is any role of heparin in its management. The present patient received polyvalent anti-venin and not specific viper anti-venin as that is not available in India and whether specific anti-venin could alter the outcome, needs to be determined.

References
