IS - 40

Thrombotic microangiopathy following snake envenomation

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Thrombotic microangiopathy (TMA) is a haematological disorder characterized by micro vascular thrombosis, thrombocytopenia and microangiopathic haemolytic anaemia (MAHA), leading to end organ ischaemia affecting particularly the kidney and brain. The two most common forms are thrombotic thrombocytopaenic purpura (TTP) and haemolytic uraemic syndrome (HUS). TTP results from reduced activity of ADAMTS13, which is the cleaving protease for von Willebrand factor (vWF), leading to accumulation of multimers of vWF within the blood vessels causing consumption of platelets and fragmentation of red blood cells. HUS is classically seen in children following a diarrhoeal infection with Shiga toxin producing strains of Escherichia coli or Shigella. Non-shiga toxin mediated 'atypical' forms of HUS (aHUS) can occur due acquired or inherited deficiency or dysfunction of regulatory proteins (complement factor H (CFH), complement factor I (CFI), membrane co-factor protein (MCP) etc.) of alternative complement pathway. Apart from the classic types of HUS described above there are many agents/ diseases associated with TMA- which include infections, pregnancy, autoimmine diseases, drugs, cancer and transplantation.

Snakebite has not been recognized as a cause for TMA up until recently. The snakes, which are now known to cause TMA, include Australian elapidae such as Australian brown snake (*Pseudechis* spp.), coastal Taipan (*Oxyuranus scutellatus*), rough scale snake (*Tropidechis carinatus*), common tiger snake (*Notechis scutatus*) and a number viperidae including the Saharan horned viper (*Cerastes cerastes*). In Sri Lanka TMA is a recognized complication following Russell's viper (*Daboia ruselli*) and hump-nosed pit viper (*Hypnale* spp.) bites.

Acute kidney injury is a known complication of snake venom associated TMA. However the exact pathogenic role of TMA in causing nephrotoxicity is not clear. It is considered to be secondary to renal ishaemia resulting from microthrombi occluding the renal arterioles and capillaries. The non-renal ischemic effects of venom induced TMA include strokes and myocardial infarctions.The diagnosis is made with the demonstration of MAHA on the blood film and thrombocytopenia in the presence clinical evidence of organ ischaemia. Presence of intravascular haemolysis is supported by the increased reticulocyte count, increased serum lactate dehydrogenase level and the reduction of serum haptoglobin.

The treatment of venom induced TMA is generally supportive. The use of fresh frozen plasma and therapeutic plasma exchange, which is shown to be effective in TTP and some forms of atypical HUS, could be harmful in the treatment of TMA associated with snake bites, since the procedure may result in removal of the anti-venom.