**Plasmodium vivax Malaria Presenting with Acute Systemic Capillary Leak Syndrome**

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**Abstract**

Systemic capillary leak syndrome (SCLS) is a very rare disorder characterized by hypotension with hemoconcentration, hypoalbuminemia without albuminuria and generalized edema, the etiology of which are snake bites, viral hemorrhagic fever, drugs, sepsis, upper respiratory tract infection, Hanta virus and West Nile virus infection and serum paraproteinemia. Typically, the syndrome manifests in two phases: initial capillary leak phase characterized by edema, serous effusion, hypotension which is followed by phase of volume overload or recruitment phase. Treatment is in the form of fluid replacement, inotropic support and vasopressor therapy during leak phase and diuretics during volume overload phase. Prognosis of this disease is very poor. Here we are presenting a rare case of plasmodium vivax with SCLS.

**Introduction**

Systemic capillary leak syndrome was first described by Clarkson in 1960. Thus, it is also known as Clarkson’s syndrome.¹ It is characterized by hypoalbuminemia, generalized edema. This syndrome is due to capillary hyperpermeability with massive extravasation of plasma containing macromolecules smaller than 200kD and sometimes up to 900kD. It has two phases: capillary leak phase and volume overload phase. Capillary leak may occur as a part of SCLS or secondary to systemic inflammatory response syndrome. This syndrome is observed in patients who demonstrate a state of generalized leaky capillaries following toxemia, shock syndromes, poisoning and ischemia-reperfusion injuries. It can lead to generalized edema and multiple organ failure. Volume overload state is characterized by flash pulmonary edema as sudden relocation of the extravasated plasma. There are two causes of SCLS: primary or idiopathic SCLS caused by serum paraproteinemias in 90% of cases and secondary SCLS caused by drugs (interleukin-2, gemcitabane), snake bite, viral hemorrhagic fever, toxins (abrin, ricin, sanguinarine), hypothyroidism, diabetes mellitus, sepsis related, viral infections like Dengue, Hanta, West Nile. We report a rare case of acute systemic capillary leak syndrome (SCLS) due to plasmodium vivax malaria infection.

**Case Report**

A 38 years male developed bilateral pedal edema (Figure 1) after second day of intermittent high temperature with chills and rigor. In next 4-5 days he noticed gradual distension of abdomen along with heaviness of chest and shortness of breath. He consulted a local doctor and was referred to us in a state of shock on 10th day of fever. There was no history of nausea, vomiting, headache, diarrhea or abdominal pain. Urine output and bowel motions were normal during this period. There was no past history of oliguria, facial puffiness, pedal edema or respiratory distress. He had normal built and he was restless. His BP was < 90/60 mm of Hg and pulse was 116/min, low in volume. Respiratory rate was 28/min and there was bilateral pedal edema. JVP was not elevated. Abdomen was soft, distended with mild ascites and splenomegaly and no other organomegaly or tenderness. Breath sounds were diminished in both lower lung fields with features of pleural effusion. Cardiovascular examination was normal. His blood sugar at admission was 109 mg/dl. He was treated with antibiotic ceftriaxone, inotropic agent i.e. dopamine and fluid replacement keeping in mind that he might be suffering from septicemia. Blood parameters revealed Hemoglobin-10.5 g/dl, hematocrit- 39, Total leukocyte count-8,700/cu mm, Platelets count-110,000/cu mm, ESR-32 mm. Blood slide as well as malarial antigen was positive for Plasmodium vivax malaria. Serum urea-27 mg/dl, creatinine-0.8 mg/dl, Ca+-8.3, Na+-128, K+-3.8. Liver function test showed normal bilirubin level (1.0 mg%), total serum protein-5.4 g/dl, albumin-2.5 gm%, SGPT-20 IU/L, SGOT-38 IU/L, alkaline phosphatase-322 IU/L. Urine examination showed no obvious abnormality and Albumin: creatinine ratio was 2:1 mg/mmol. Blood cultures for both aerobic and non-aerobic bacteria were negative. X-ray chest showed normal cardiothoracic ratio with blunted costophrenic angles (Figure 2). USG revealed mild ascites, splenomegaly and bilateral pleural effusion. Aspiration revealed exudative pleural effusion and AFB stain was negative. Echocardiography with color Doppler shows good left ventricular function with ejection fraction of 60%. Patient was started with chloroquine 300 mg base, 2 tabs stat and then 1 tab after 12 hr, 24 hr and 36 hr of initial dose along with other supportive treatments. Patient showed signs of recovery from shock and edema and on 6th day of treatment his respiratory distress aggravated with diffuse bilateral crackles for which he was treated with diuretics and injectable theophylline. Patient responded and recovered completely on 7th day after treatment was initiated. Repeat blood reports showed restoration of hematocrit (29) and serum albumin level (3.8 g/dl) level. He was then discharged but lost to follow up.

**Discussion**

The systemic capillary leak syndrome (SCLS) is an extremely
Discussion

The systemic capillary leak syndrome (SCLS) is an extremely rare disease of reversible plasma extravasation and vascular collapse accompanied by hemoconcentration and hypoalbuminemia and is believed to be caused by transient endothelial dysfunction that was first described in 1960 by Clarkson et al.1 Acute attacks of SCLS develop within hours and are at increased risk for ischemia-induced organ failure, rhabdomyolysis, muscle compartment syndromes and venous thromboembolism due to profound shock and edema and it resolves within 1 to 4 days at which time patients are at increased risk for death from flash pulmonary edema due to rapid fluid remobilization. In addition to the acute form, a few cases of chronic SCLS have also been reported with history of progressive generalized edema with pericardial and pleural effusions, associated with a serum paraproteinemia.2,3 Diagnosis is made clinically and by exclusion of other diseases that cause similar signs and symptoms, most notably sepsis, anaphylaxis, angioedema and common causes of generalized edema like congestive heart failure, kidney failure, liver failure and nephrotic syndrome. The diagnosis should be suspected in patients with unexplained edema, increased hematocrit, hypoalbuminemia and hypotension.4 In absence of definite sepsis, cardiovascular, renal and hepatic dysfunction a diagnosis of acute systemic capillary leak syndrome was made in our case.

The pathophysiology of SCLS is still unclear but influenced by hemodynamic forces, cytokines and inflammatory mediators. Components from the serum of patients with acute SCLS in contrast to healthy subject mediate early and extensive endothelial apoptosis in vitro is associated with oxidation injury. So oxidation injury mediated endothelial apoptosis might be a mechanism of development of SCLS. Though SCLS is associated with monoclonal gammopathy in 90% of cases, absence does not rule out its diagnosis and an infection and inflammatory response could be a triggering factor.5,6

Conclusion

SCLS is a very rare clinically diagnosed disorder with poor prognosis as it can cause death both in capillary leak phase and volume overload phase. In absence of definite diagnostic test it can be easily missed as it shares many of its signs and symptoms with more common causes of edema and respiratory distress. High degree of suspicion and early diagnosis can save the patient and malarial fever to be kept in mind as a treatable cause of SCLS specially in tropical countries like us.

References