

Case Report

Acute pancreatitis and acute respiratory distress syndrome complicating *Plasmodium vivax* malaria

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Key words Acute respiratory distress syndrome; malaria; pancreatitis; *Plasmodium vivax*

A 42-yr female presented to our emergency with fever since seven days which was moderate to high grade, intermittent, associated with chills and rigors along with diffuse abdominal pain with nausea and vomiting. She subsequently developed breathlessness and coughing not associated with sputum production. The patient was non-alcoholic and had no similar episodes in the past. There was no history of any chronic medical illness, jaundice or colicky abdominal pain suggesting gall-bladder disease or surgical intervention.

On examination she was febrile 102°F, pulse rate was 110 per min and blood pressure 102/60 mm of mercury. She was breathless and her arterial oxygen saturation was 80% in arterial blood gas analysis without oxygen. The patient was conscious oriented to time, place and person. Her abdominal examination revealed tenderness in upper abdomen with no guarding, rigidity and no organomegaly but bowel sounds were absent. On auscultation of chest there were bilateral crepitations all over the lung fields.

Investigations revealed total leucocyte count 9800/mm³ with a differential of 75% polymorphs, and 20% lymphocytes. Serum calcium of patient was 8.1 mg/dl and random blood sugar was 81mg/dl. The liver function test revealed a total bilirubin of 2.5 mg/dl of which unconjugated fraction was 1.2 mg/dl, serum aspartate transaminase 114 U/l, serum alanine transaminase 39 U/l and serum alkaline transferase 221 U/l. On examination of peripheral blood smear of patient it was positive for *Plasmodium vivax* which remained positive after four days in a repeat test. On antigen testing for lactate dehydrogenase antigen, it was positive for *P. vivax* and negative for *P. falciparum*. Further confirmation of negativity of *P. falciparum* with polymerase chain reaction could not be done due to lack of facilities for PCR in our institute. Dengue serology was found to be negative. The X-ray

chest of the patient showed diffuse infiltrates throughout the lungs indicating ARDS (Fig.1). Arterial blood gas analysis showed hypoxemia with the arterial oxygen partial pressure PaO₂ (in mmHg)/FIO₂ (inspiratory O₂ fraction) ratio was 160. Serum amylase and lipase levels of the patient were done considering abdominal pain, which resulted 1230 and 800 U/l respectively following which an urgent abdominal ultrasound was done which showed bulky heterogeneous pancreas (Fig. 2). To confirm the diagnosis, a computerized tomography scan of abdomen was done which showed heterogenous, post-contrast enhancement with fuzzy margins and liquefied necrosis in head of pancreas with peripancreatic, pericholecystic, mesenteric and omental fat plane stranding suggesting acute pancreatitis (Fig. 3).

Patient was kept on continuous oxygen inhalation and was immediately started on intravenous injectible Artesunate therapy at dose of 120 mg 12 hourly (2.4 mg/kg stat

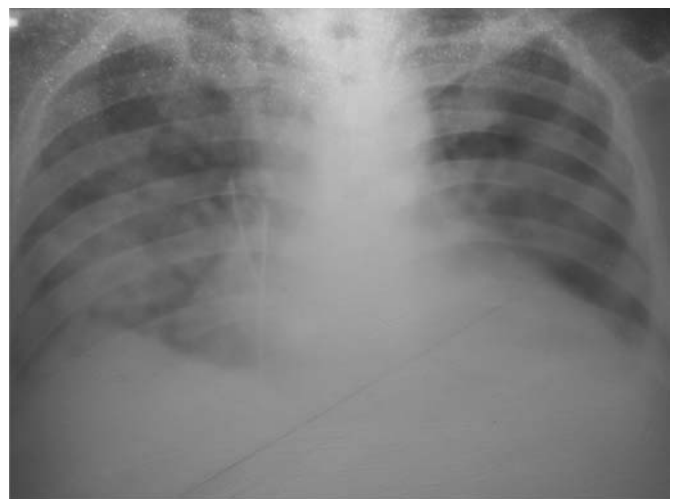


Fig. 1: Chest X-ray showing diffuse infiltrates throughout the lungs indicating ARDS.

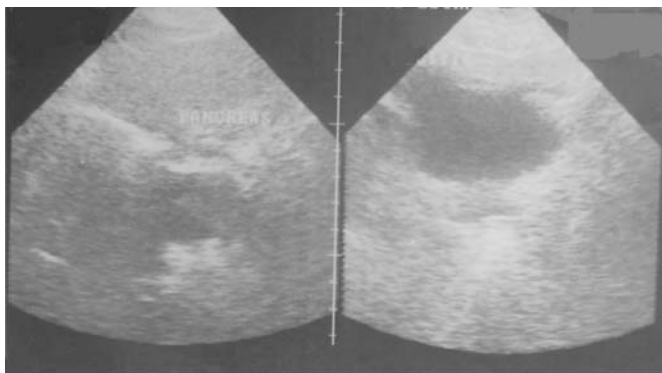


Fig. 2: Abdominal ultrasound showing bulky heterogenous pancreas and ascetic fluid.

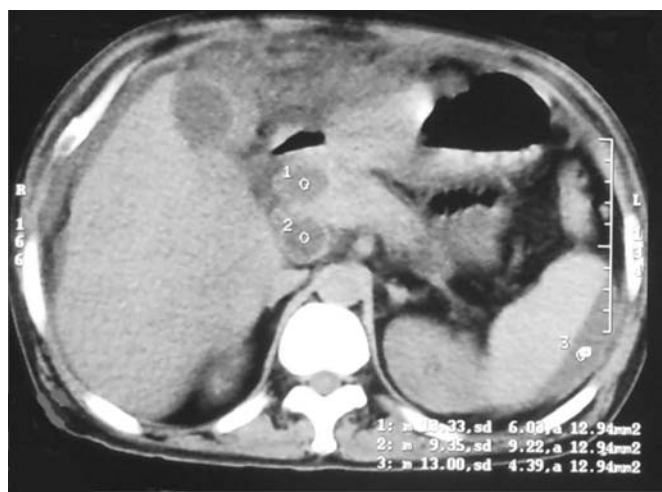


Fig. 3: Computed tomography scan of abdomen showing heterogeneous post-contrast enhancement with fuzzy margins and liquefied necrosis in head of pancreas with peripancreatic, pericholecystitis, mesenteric and omental fat plane stranding suggesting acute pancreatitis.

followed by 2.4 mg/kg at 12 and 24 h and then daily) along with intravenous injectible Imipenem and Cilastatin combination (500 mg plus 500 mg) every six hourly through peripheral intravenous line which were given for five continuous days. Along with these agents injectible antipyretics and adequate intravenous crystalloids were given. But patient did not responded and kept deteriorating with further decline of oxygen saturation even with high flow oxygen inhalation. Following this, the patient was shifted to intensive care unit and put on mechanical ventilation but her blood pressure kept on falling despite intravenous vasopressors infusion. Patient ultimately expired after 5 days of hospitalization despite our intense management. Clinical postmortem was important in this patient to establish proper diagnosis and causes of the events but could not be done due to unwillingness of the relatives.

DISCUSSION

It is well-known fact that *P. falciparum* malaria is associated with grave complications such as hypoglycemia, acidosis, cerebral malaria, acute respiratory distress syndrome (ARDS), and acute pancreatitis. The severe malaria is caused by erythrocyte sequestration leading to organ failure. *Plasmodium vivax* malaria most of the time presents only as acute febrile syndrome. It is also called as benign tertian malaria, but now it seems to be no longer benign¹. There are few case reports of *P. vivax* malaria presenting as ARDS²⁻⁴, pulmonary edema⁵, and bronchiolitis obliterans⁶. The sequestration and cytoadherence was a characteristic feature of *P. falciparum* malaria but now there is evidence that the same phenomenon also occur in *P. vivax* infection^{7,8}. Small airway obstruction, gas exchange alteration, increased phagocytic activity and accumulation of pulmonary monocytes are the suggested mechanisms³.

Clinical data from patients strongly indicate that *P. vivax* can cause sequestration related and non-sequestration related complications as result of accumulation of pulmonary monocytes and intravascular inflammatory responses⁹. These factors are, thus, also responsible for ARDS in the cases of *P. vivax* malaria. In our institute we have noticed an increasing trend of complicated infection by *vivax* malaria against the conventional view that complicated malaria is mostly caused by *P. falciparum* malaria. The total number of *P. vivax* malaria cases diagnosed by microscopy and antigen testing were 906 during the year 2011–12 and according to our hospital register, out of these cases complicated by thrombocytopenia were only 198, ARDS was seen in 12 cases, acute renal failure was diagnosed in 9 cases, and disseminated intravascular coagulation was found in 7 cases.

Similar studies have shown this changing pattern of complicated infection by *P. vivax* malaria in other parts of the country also¹. We have not noticed any case of cerebral malaria in our set up as noticed by Thapa *et al* who reported two cases in Kolkata¹⁰. Acute pancreatitis is associated with various causal factors but a protozoon like *Plasmodium* has never been mentioned in past. Other causal factors for development of acute pancreatitis like gallstones, alcohol (acute and chronic alcoholism), hypertriglyceridemia or hypercalcemia were absent in this patient. Pancreatitis is a disease that evolves in three phases. The initial phase is characterized by intra-pancreatic digestive enzyme activation and acinar cell injury. The second phase of pancreatitis involves the activation, chemoattraction, and sequestration

of leukocytes and macrophages in the pancreas, resulting in an enhanced intrapancreatic inflammatory reaction. The third phase of pancreatitis is due to the effects of activated proteolytic enzymes and cytokines, released by the inflamed pancreas, on distant organs.

The systemic inflammatory response syndrome and ARDS as well as multiorgan failure may occur as a result of this cascade of local as well as distant effects which may be one cause in this patient. Though the pathogenesis of acute pancreatitis in *P. vivax* malaria is not clear but it can be hypothesized that it may be developed due to ongoing pancreatic injury due to systemic infestation or direct invasion of pancreatic tissue by *P. vivax* through mechanisms of sequestration and cytoadherence. It has also been proposed that acute pancreatitis may occur due to multiorgan failure or capillary thrombosis caused by parasitized red blood corpuscles^{11, 12}. In this case acute pancreatitis was suspected because of patient's significant complains of vomiting and abdominal pain and later on got confirmed by the elevated enzymes, findings of ultrasonography and CT scan of abdomen.

The diagnosis of acute pancreatitis is usually established by the detection of an increased level of serum amylase and lipase. Values threefold or more above normal virtually clinch the diagnosis. Other differential diagnosis like perforated viscus, especially peptic ulcer, acute cholecystitis and biliary colic, acute intestinal obstruction, mesenteric vascular occlusion, renal colic and dissecting aortic aneurysm were ruled out as the abdominal pain of patient was non-colicky, and imaging modalities like USG and CT scan ruled out these possibilities providing no evidence of gall-bladder wall inflammation, multiple air fluid levels in abdomen, renal stone or any aneurysmal growth over aorta.

Elevation of serum amylase/lipase or inflammatory changes seen on CT scans prompt for vigorous fluid resuscitation along with conventional measures like analgesics for pain, colloids to maintain normal intravascular volume, no oral alimentation and prophylactic antibiotics. Treatment options for severe *vivax* malaria available were intravenous artemisinin compounds or quinine dihydrochloride though continuous cardiac monitoring is required due to risk of arrhythmias. The patient with unremitting severe necrotizing pancreatitis requires vigorous fluid resuscitation and close attention to complications such as cardiovascular collapse, respiratory insufficiency, and pancreatic infection. The most important clinical parameter is persistent organ failure (i.e. lasting longer than 48 h), which is the usual

cause of death. Elevated liver enzymes were suggestive of organ failure in this case and thus despite treatment with proper antimalarial patient expired. To our knowledge *P. vivax* malaria presenting as acute pancreatitis and ARDS has not been mentioned in literature and this is the first illustration of such type.

CONCLUSION

Plasmodium vivax malaria has diverse clinical presentation which can manifest as acute pancreatitis and ARDS. This case description highlights the fatal and unusual complication of *P. vivax* malaria. The spectrum of *P. vivax* malaria and its complications needs further evaluation. Physicians in this part of world should therefore expand their outlook regarding current knowledge about physiopathological concepts of this serious, widespread disease and also act promptly to salvage such patients. As a clinician our aim in such case is just not to restrict ourselves to antimalarial treatment but to also focus on subsidiary hazardous manifestations of ARDS and acute pancreatitis.

The authors have no potential conflict of interest.

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