

Cerebral Venous Thrombosis as a Complication of Plasmodium Vivax Malaria: A Report of 2 Cases

Sir,

Cerebral malaria is the most severe complication associated with *Plasmodium falciparum* infection.^[1] This clinical syndrome is defined by coma (at least 1 h after seizure termination or hypoglycemia correction) along with the presence of asexual parasite forms on peripheral blood smear, with no plausible alternative cause for to account for coma.^[2] Patients develop fever, body ache, and/or headache with progressive deterioration in sensorium.^[1] This results from sequestration of the parasitized red blood

cells in the cerebral microcirculation, and potentiated by concomitant metabolic abnormalities and proinflammatory milieu.^[3] Similar sequestration elsewhere in the body leads to anemia, thrombocytopenia, hepatic and renal impairment, and pulmonary edema.^[1] Neuroimaging in cerebral malaria reveals cerebral edema with or without small hemorrhagic cortical infarcts and white matter changes.^[4,5] Rarely, cerebral venous thrombosis (CVT) can result.^[6,7] It has been described with *Plasmodium falciparum* infection alone or with mixed *falciparum* and *vivax* infections, and is rarely reported with

Plasmodium vivax infection. We report 2 cases of CVT from isolated infection with the same.

Case 1: A 21-year-old gentleman presented with moderate grade, intermittent fever with holocranial headache of 3 days duration followed by 2 episodes of seizures (unknown onset to bilateral tonic-clonic; regained awareness after the first episode) and altered sensorium. He was started on intravenous anti-seizure drugs and electroencephalogram showed diffuse slowing, without features suggestive of nonconvulsive status epilepticus. His routine blood investigations were normal but the peripheral smear revealed the presence of trophozoites of *Plasmodium vivax*. Non-contrast computed tomography (NCCT) head revealed a hemorrhagic infarct in the right temporo-occipital region with perilesional edema and midline shift [Figure 1a]. Magnetic resonance imaging (MRI) brain revealed similar findings with magnetic resonance venography (MRV) suggestive of thrombosis of right transverse and sigmoid sinus [Figure 1b-f]. He was thereafter started on parenteral artesunate with oral doxycycline and subcutaneous low molecular weight heparin. He started improving from day 2 and was fully conscious and oriented by day 6 of therapy. Artesunate was given for 7 days followed by 2-week treatment with oral primaquine. Work up for all other causes (vasculitic profile, chronic infections like HIV, hepatitis B and C, leptospira, and pro-coagulant status) was negative and the patient denied any addictions. Oral anticoagulation was continued for 3 months and then stopped, and the patient continues to be asymptomatic.

Case 2: A 20-year-old gentleman presented with high grade, intermittent fever and left hemi-cranial throbbing headache of moderate intensity for 7 days followed by acute onset horizontal binocular diplopia with reduced alertness and responsiveness. On examination, his Glasgow Coma Scale score was 13/15

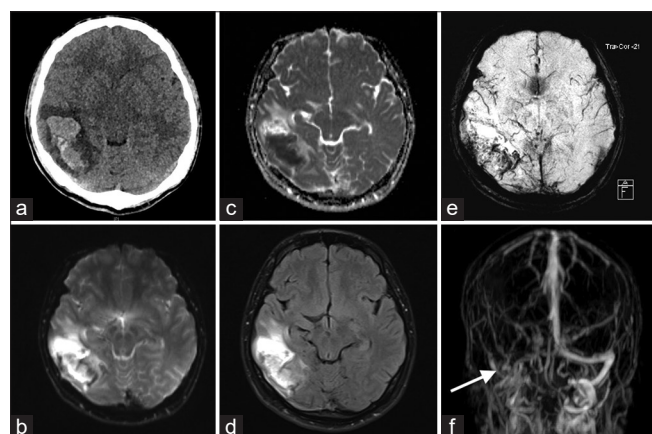


Figure 1: (a) NCCT head revealing right temporo-occipital intraparenchymal hemorrhage with perilesional edema and midline shift. (b-e) MRI brain revealing a hemorrhagic infarct on FLAIR (d) with Diffusion weighted imaging (DWI) imaging (b) and Apparent diffusion coefficient (ADC) maps (c) showing diffusion restriction. Susceptibility weighted imaging (SWI) images (e) show evidence of hemorrhages. (f) MRV shows right transverse and sigmoid sinus thrombosis (arrow)

with bilateral papilloedema and left lateral rectus palsy and mild splenomegaly. His routine investigations were normal apart from thrombocytopenia (platelet count 59,000/mm³) and peripheral smear revealed *Plasmodium vivax* trophozoites. NCCT head revealed a hemorrhagic infarct in the left frontal region with perilesional edema [Figure 2a]. MRI brain with MRV revealed similar parenchymal changes with cortical vein thrombosis in the left frontal lobe [Figure 2b-f]. He was managed with parenteral artesunate and doxycycline for 7 days along with subcutaneous low molecular weight heparin with complete recovery. Work up for other potential causes (listed in case 1) were all normal. He was also treated with oral anticoagulants for 3 months and was asymptomatic at last follow-up visit.

Atypical manifestations of malaria are rising in endemic regions probably due to the large patient number, development of immunity, anti-malarial drug resistance, and its indiscriminate use.^[7] CVT is one such manifestation and may result from hypercoagulability secondary to alteration in phospholipids in infected cells which leads to increased levels of von Willebrand factor^[8] and release of tissue factor from damaged endothelial cells.^[9] Treatment with artesunate may lead to good response unlike the past where parenteral quinine was the drug of choice in severe malarial infections. Both our patients improved when compared with mortality in 2 out of the 3 cases reported by Krishnan *et al.*^[6] (treated with quinine). It is imperative to investigate and treat concomitant malarial infection in CVT, since early diagnosis improves outcome and prevents sequelae.

We seek to emphasize a low threshold for malarial testing in patients presenting with fever and neurological deficits, especially in endemic regions, where atypical presentations may commonly occur. Early diagnosis and treatment lead to good patient outcomes.

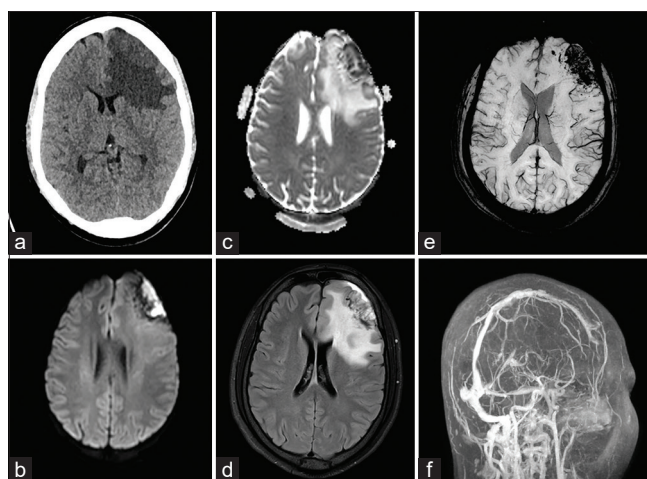


Figure 2: (a) NCCT head revealing left frontal intraparenchymal hemorrhage with perilesional edema and midline shift. (b-e) MRI brain revealing a hemorrhagic infarct on FLAIR (d) with DWI imaging (b) and ADC maps (c) showing diffusion restriction. SWI images (e) show evidence of hemorrhages. (f) MRV shows thrombosis left frontal cortical veins

Key points

1. Rule out malarial infection in all patients presenting with fever and CVT, especially in endemic regions.
2. Plasmodium vivax infections can also lead to vascular and microvascular complications like Plasmodium falciparum.
3. Early treatment with parenteral artesunate usually leads to good functional outcomes.

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.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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