Cerebral toxoplasmosis in a human immunodeficiency virus (HIV) seronegative patient with liver cirrhosis

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Abstract:

Cerebral toxoplasmosis can affect a patient who is immunocompromised with chronic liver disease. Liver cirrhotic patients with central nervous system (CNS) infection could easily be misdiagnosed for hepatic encephalopathy. A case of cerebral toxoplasmosis in an HIV-seronegative patient with liver cirrhosis in a low-resource setting is reported. Although the cerebral toxoplasmosis improved with medical treatment, the patient died from progressive hepatic failure. Despite the usually poor prognosis, early diagnosis and prompt treatment of CNS infection complicating immunosuppression would prevent early death.

Keywords : Liver, cirrhosis, brain, toxoplasmosis, sepsis, encephalopathy

Key Clinical message

Liver cirrhotic patients with central nervous system (CNS) infection could easily be misdiagnosed for hepatic encephalopathy. A clinical suspicion of a cranial infection would necessitate a brain CT or an MRI to exclude the presence of CNS lesions.

INTRODUCTION

CNS infection often develops as an opportunistic infection in patients with impaired host defence mechanisms due to malignancy, diabetes mellitus, alcoholism, liver cirrhosis and, the prognosis is usually poor[1, 2]. It develops either by spread from a contiguous focus or by haematogenous spread from a distant focus, such as intra-abdominal infection, endocarditis, urinary tract infection, or pulmonary infection. It is rare and life-threatening in decompensated liver cirrhosis. Liver cirrhosis is an immune-compromised state because of reticuloendothelial dysfunction and porto-systemic shunting[3]. Bacterial infections in cirrhosis are common, particularly in decompensated patients and account for significant mortality [4, 5]. A case of a cerebral parasitic toxoplasmosis in an HIV-seronegative patient with liver cirrhosis is reported.

CASE HISTORY/ EXAMINATION

A 40-year-old African man was admitted as an emergency with a sudden left arm and leg weakness. He had no history of hypertension, diabetes mellitus, cardiovascular disease, atrial fibrillation or human immunodeficiency virus (HIV) infection. He was single and a severe alcohol consumer. On admission, he was conscious with a Glasgow Coma Scale score of 15. His blood pressure was 120/80 mmHg, pulse rate 80/minute and regular, respiratory rate 20/min, and normal body temperature, 37°C. The conjunctivae were pink and oral mucosa moist. Chest and cardiovascular examinations were unremarkable. Abdominal examination revealed dilated supraumbilical veins consistent with *caput medusa* a sign of chronic liver disease and portal hypertension. Apart from a nodular liver, there was no other stigmata of chronic liver disease. He had a left hemiparesis, but there was no neck stiffness nor flapping tremor indicating meningism or encephalopathy respectively. The laboratory test results revealed anaemia (Haemoglobin 7.6 g/dl) , a normal white cell count (WBC 9.5 x 10^9/mm3, thrombocytopenia (119 x 109/ mm3), negative HIV serology and malaria parasite, normal urea, creatinine, clotting screen and serum albumin. Urinary urobilinogen, glucose, bilirubin and ketone were negative. Liver function tests and a toxoplasma IgG serology were not done due to financial constraints. Abdominal ultrasound showed a nodular liver with irregular borders. A cerebral computed tomography (CT) scan revealed multiple cerebral contrast ring-enhancing lesions with massive perifocal oedema and mass effect with effacement of the right frontal horn (figure 1).The findings were suggestive of cerebral toxoplasmosis and CNS tuberculosis was a possible differential. The patient was treated empirically for cerebral toxoplasmosis with a combination of double strength pyrimethanine (*dihydrofolate reductase inhibitor*) and sulphadiazine (*sulphonamide antibiotic*) (960mg) thrice daily for 6 weeks, vitamin B1, proton pump inhibitor (omeprazole) and physiotherapy. There were both clinical (regaining of motor strength in both left upper and lower limbs) and radiological (CT scan) response (figure 2) after a week of treatment. The patient was discharged a week later with continuation of medical treatment. He returned after 12 months with decompensated liver disease and died from hepatic encephalopathy a few months later.

DISCUSSION

The case demonstrated the presentation of cerebral toxoplasmosis in an HIV-negative patient immunocompromised from probable alcoholic liver cirrhosis. The presumptive diagnosis was made from the clinical findings, ultrasound of the liver, and a brain CT scan. The neurological symptoms were relieved following the empirical treatment of cerebral toxoplasmosis. The patient, however, died of hepatic encephalopathy from the progressive liver disease about a year later. Cirrhotic patients are susceptible to several infectious diseases, such as septicaemia, meningitis, pneumonia, urinary tract infection, and spontaneous bacterial peritonitis (SBP) [5]. Six (11%) of 53 cases of brain abscess had liver cirrhosis, presenting with non-specific symptoms and all died soon after [6] The high mortality in cirrhotic patients is firstly due to the difficulty in differentiating brain abscess from hepatic encephalopathy. Only 34% of the patients have the complete triad of headache, fever, and focal neurological deficits [1] In the advanced stage of liver cirrhosis, hepatic encephalopathy is common and usually presents with disorientation, confusion, drowsiness and coma. Furthermore, cirrhotic patients can often have episodes of fever caused by endotoxaemia or SBP. Neck stiffness occurs in only 8% of patients with brain abscess and it is not always easy in clinical settings to detect mild neurological findings in patients with impaired consciousness. Secondly, bacteria infections worsen hepatic failure. The systemic inflammatory response syndrome (SIRS) from increased endotoxins, bile acids, nitric oxide, and cytokines such as *τυμουρ νεϛροσις φαϛτορ- α* and *interleukin 6* , may occur resulting in sepsis, renal failure, encephalopathy and death. It is important to start treatment as quickly as possible to prevent SIRS as the cytokine cascade is usually irreversible. Thirdly, most cirrhotic patients are not surgical candidates because of their bleeding tendency and low hepatic reserve. Only 33% of cirrhotic patients received surgical treatment, compared with 66% of non-cirrhotic patients [1]. Liver dysfunction leads to several abnormalities of defence mechanisms because of the depressed humoral and cell-mediated immunity. Bacterial translocation from the intestine induces bacteraemia, and impaired hepatic bacterial clearance results in failure to control bacteraemia[3] Severe bacteraemia may cause infections of several organs, but pathogenic bacteria may not be identified in 30% of brain abscesses [1, 4]. In the present case, the causative pathogen was the parasite, *Toxoplasma gondii. T. gondii* infection of humans occurs either congenitally or by ingestion of foodstuffs contaminated by infected cat faeces or lamb or pork contaminated with *T. gondii* cysts [7]. Primary infec-

tion in immune competent host is asymptomatic or may produce a mild flu-like illness, malaise, headache, cervical lymphadenopathy. Infection acquired during pregnancy may lead to serious fetal malformations[8]. After primary infection cysts are formed in the tissue and remained inactive until reactivation. Cellular immunity mediated by T cells, macrophages and cytokines plays a crucial role in controlling the tissue cysts [9]. The infection is self-limiting in immunocompetent individuals because an efficient immune control limits the dissemination of the rapidly multiplying tachyzoite stage [7]. However, the parasite still remains viable in the tissue cysts. Chronically infected individuals who possess defects in cell-mediated immunity as in chronic liver disease (CLD), HIV/AIDS etc, are at risk for reactivation of the infection and its dissemination, causing serious complications and death[10- 12]. *T. gondii* is the most frequent obligate intracellular protozoan causing opportunistic infections in immunocompromised patients mostly in the developing world[10]. An association between *T. gondii* infection and chronic liver disease (CLD) has been observed. Co-infection in both *T. gondii* / hepatitis B virus (HBV) and *T. gondii* / hepatitis C virus (HCV) was 33.3% and 31.4% , respectively with a highly significant association between *T. gondii* parasitaemia and HCV viral load. There was also a significant increase of liver enzymes in the serum of patients positive for *T. gondii* compared with negative patients [11].Toxoplasma seropositivity was higher in patients with Child-Pugh class C CLD than Child- Pugh class A and, may signify disease evolution [12]. Several studies have reported the parasite found in 20%- 90% of patients with cirrhosis through IgG and polymerase chain reactions PCR tests[13]. The three forms of cerebral toxoplasmosis are focal toxoplasma meningoencephalitis, multifocal encephalitis and diffuse toxoplasma meningoencephalitis. The common presentations include decreased consciousness, headache, hemiparesis, cranial nerve palsy, seizure, meningeal signs, dementia and psychosis [13, 14]. Diagnosis is considered from clinical findings, CT scan, or magnetic resonance imaging (MRI) of the brain with serological findings[1.]

CONCLUSIONS

Cerebral toxoplasmosis can affect an HIV-negative patient who is immunocompromised with liver cirrhosis. Cirrhotic patients with CNS infection could easily be misdiagnosed for hepatic encephalopathy. A clinical suspicion of a cranial infection is important when encountering cirrhotic patients with disturbance of consciousness and fever. Brain CT or MRI must be considered to exclude the presence of CNS lesions. Early treatment is important for this complication of immunosuppression which has a poor prognosis.

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None

CONFLICT OF INTEREST

The authors declares no competing interests

AUTHOR CONTRIBUTIONS

EPW was the main author, FZ was the main physician and contributed to literature search and writing of the paper

CONSENT

Written informed consent from the next of kin to the patient was granted to write and publish the paper.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restriction.

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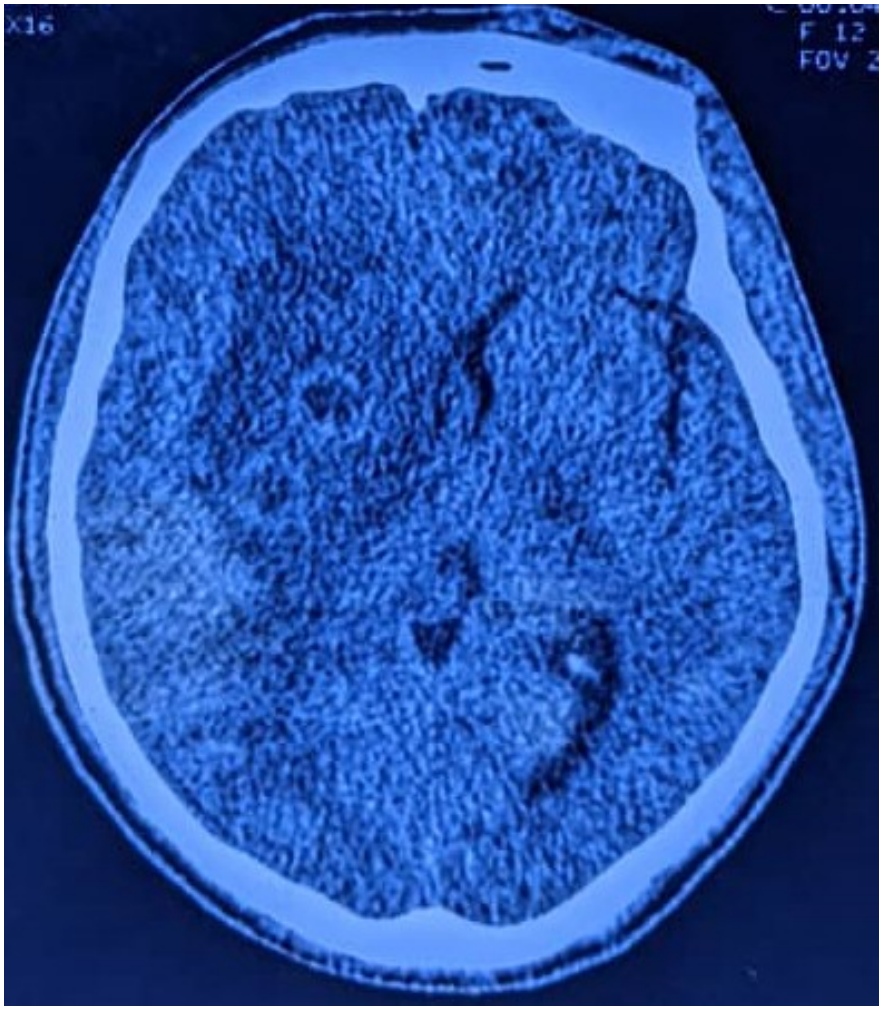
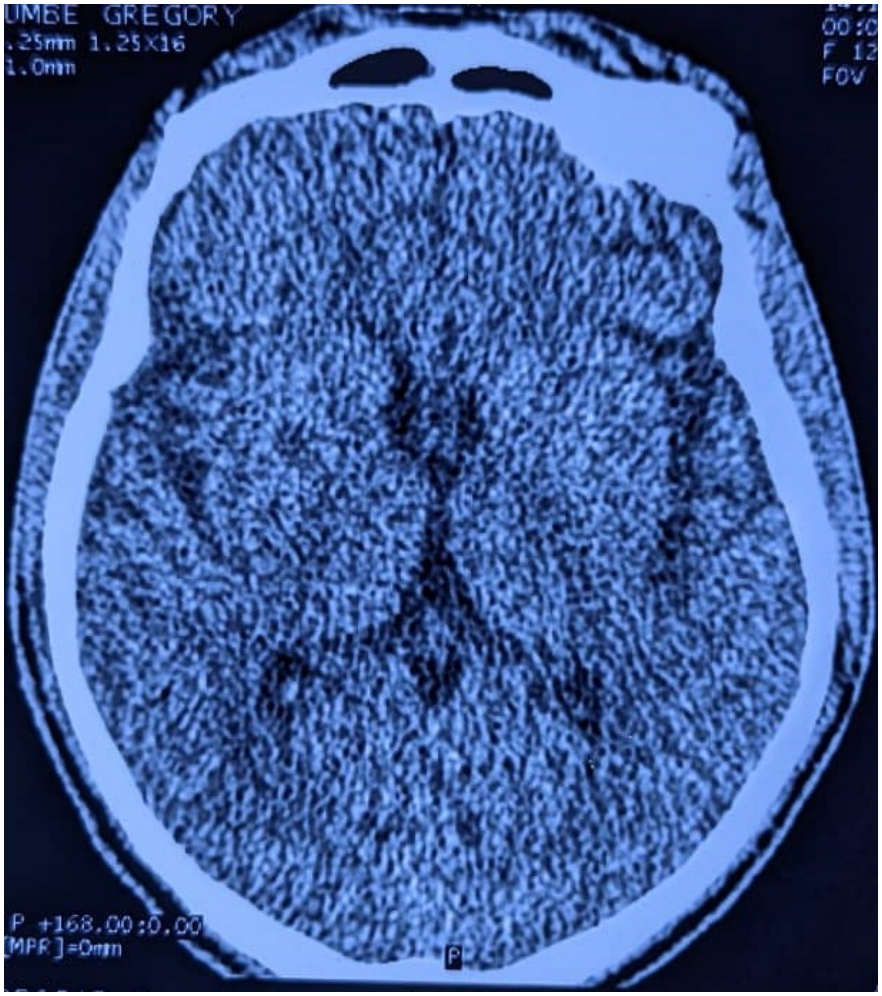


Figure 1: Brain CT scan showing contrast enhanced rings of *T. gondii* with surrounding oedema and effacement of right lateral ventricular horn.



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