IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 8 Ver. 10 (August. 2018), PP 22-24
www.iosrjournals.org

Cerebral Venous Sinus Thrombosis: A Rare Complication of Cryptococcal Meningitis in HIV/AIDS Patient

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Conflicts of Interest: *None*
Funding Statement: *This research did not receive any specific grant from funding agencies in the public, commercial, ornot-for-profit sectors.*
Ethical statement: *An informed consent form has been obtained from the patient for academic publication*
Keywords *Human immunodeficiency virus (HIV)Cryptococcal meningitisCerebral venous sinus thrombosis (CVT)Highlighting points-Cerebral venous sinus thrombosis in HIV/AIDS patients is multifactorial. Diagnosis of cerebral venous sinus thrombosis is often missed as an infective thrombotic complication of cryptococcal meningitis in HIV/AIDS patients. High index of clinical suspicion and treatment with anticoagulation gives better outcome in these group of patients.*

Date of Submission: 07-08-2018 Date of acceptance: 24-08-2018

I. Introduction

Cryptococcal Meningitis (CM)is a serious opportunistic central nervous system infection in patients infected with human immunodeficiency virus(1). Cerebral venous sinus thrombosis is not a well-recognized complication after cryptococcal meningitis and most of the time it is under reported due to less clinical suspicion and lack of ordering MRI imagingused for studying cerebral vessels. Cerebral venous sinus thrombosis in HIV infected cryptococcal meningitis is rarely reported in the literatures(2).Physicians treating HIV/AIDS positive patients should able to recognize and treat not only the well-known opportunistic infections but also be aware of the less common complications such as cerebral venous sinus thrombosis which are potentially treatable.

II. Case Presentation

A 37-year-old male known case of retroviral disease presented with history of holocranial headache since 15 days and altered sensorium since one day. Headache was bilateral, progressive in nature with nocturnal worsening.Headacheused toaggravate on straining ,coughing but relieved on taking painkillers. There was no history of seizures, focal neurological deficit, visual defects.On examination patient was drowsy,irritablewith positive meningeal signs.In view of clinical worsening patient was intubated and kept on mechanical ventilator.Clinical diagnosis of meningoencephalitis was made.MRI brain plain plus contrast study showedleptomeningeal enhancement with acute lacunar infarcts in right temporal lobe. Patients baseline CD-4 count was 24 cells/cl.Cerebrospinal fluid (CSF)report showed 20 cells with 100%lymphocytes,protein of 75mg/dl and glucose of 76 mg/dl(blood glucose level- 156 mg/dl) .CSF for gram stain showed gram positive budding yeast cells and Indian ink stain for cryptococcal infection was positive.CSF GeneXpert for tuberculosis report was negative. The treatment of cryptococcalmeninigitis is divided into induction, consolidation and maintenance phases. Patient was started on liposomal amphotericin B (3-4mg/kg)with oral flucytosine as an induction course for cryptococcal meningitis.Patient developed adverse side effect of injectable amphotericin in form of acute kidney injury and oliguria which did not respond to dose adjustment hence liposomal amphotericin was discontinued and patient continued on tab.fluconazole and other supportive medication.Patient showed clinical improvement after receiving antifungal treatment and completely weaned off from the ventilator.

After initial improvement, patient started complaining of worsening holocranial headache with transient visual obscuration after two months of treatment. Neurological examination showed presence of papilledema without focal MRI neurological deficits. Repeat MRI brain contrast study revealed acute thrombosis in right transverse sinus,superior sagittal sinus and proximal internal jugular vein. Repeat CSF examination revealed 2 cells with 100% lymphocytes with 47 mg/dl protein and glucose of 67 mg/dl (110 mg/dl).CSF opening pressure was 350 mm of CSF.CSF for gram, acid fast stain, Indian ink and CSF cultures were negative. Cortical venous sinus thrombosis was treated with adequate dosage of anticoagulation,

antioedema measures along with continuation of antifungal treatment(Tab.fluconazole) for cryptococcal infection. Patient showed clinical improvement and discharged in stable condition on oral anticoagulation.

III. Discussion

In HIV/AIDS infected patientcerebral venous sinus thrombosis occurs due to multiple factors and include the presence of antiphospholipid antibodies and deficiency of protein C, protein S, heparin cofactor II, and antithrombin anticoagulants. Other Causes include concomitant cytomegalovirus infection, toxoplasmosis, Cryptococcosis, primary cerebral lymphoma, dehydration, AIDS-associated nephrotic syndrome or cachexia(3,4). There issignificant correlation between thrombotic disease and CD4 counts (<200/mm3) as well as the presence of opportunistic infections, AIDS-related neoplasms, or autoimmune disorders associated with HIV such as Autoimmune haemolytic anaemia(AIHA)(4).The prothrombotic effect of highly active antiretroviral therapy (HAART) mainly Protease inhibitors based therapy promotes thrombosis by inducing platelets and endothelial dysfunction.Our patient had risk factors for cerebral venous sinus thrombosis like cryptococcal meningitis with low CD-4 count, however patient was not on HAART before.

The clinical presentation of cerebral venous thrombosis in the setting of neuro-infection is vastly variable and often there is a significant delay in diagnosis of CVT due to less clinical suspicion andlack of orderingneuroimaging to cerebral vessels in HIV/AIDS patients. In present case there was delay in diagnosis of associated CVT with cryptococcal meningitis because of attribution of clinical manifestations like persistent headache,transient visual obscuration, papilledema of raised ICT to cryptococcalmeningitis but later appropriate diagnosis was clenched after doing MRI brain contrast study showing filling defect in cerebral venous sinuses.

Despite the infectious aetiology, treatment of CVT associated with cryptococcal infection consists of anticoagulation therapy. The evidence shows that anticoagulant treatment is associated with reduction in the risk of death and complications.Duration for use ofanticoagulation is not specified literature(5).The prognosis depends significantly on the treatment,underlying opportunistic infectionsand the baseline clinical status of the patient. Our patient tolerated anticoagulation treatment well with consolidation and maintenance treatment with antifungal drug(Tab.fluconazole).

IV. Conclusion

Cerebral venous sinus thrombosis is a rare complication of cryptococcal meningitis, with very few cases described in the literature. High index of clinical suspicion is required in setting of HIV / AIDS positive status with opportunistic infections. Treatment includes anticoagulation ,adequate hydration and treatment of an opportunistic infections.

Figure legends

Figure 1:MRI Brain contrast sagittal and axial images showing acute thrombosis in superior sagittal sinus, right transverse sinus respectively.

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Aarati Kulkarni1" Cerebral Venous Sinus Thrombosis: A Rare Complication of Cryptococcal Meningitis in HIV/AIDS Patient."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 8, 2018, pp 22-24.