Cryptococcal Meningitis in a Patient with Idiopathic CD4+ T-lymphocytopenia.A case report

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Citation

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Abstract

A case is presented of a 66 year old lady with long standing lymphocytopenia who developed the sudden onset of inability to walk. She was subsequently diagnosed with both cryptococcal meningitis and idiopathic CD4+ T-lymphocytopenia. This report highlights important points regarding these diagnoses and their association.

CASE

Ms PC, a 66 year old Sri Lankan lady, presented to an emergency department in February 2008 due to the sudden onset of inability to walk. She had sustained a fall the day prior but denied any injury, loss of consciousness or prodromal symptoms. Her family did not witness any seizure activity or evidence of incontinence. Furthermore, there was no history of headache or fever.

Ms PC's presentation was in the setting of a mild deterioration in memory over the last two years. Her medical history was significant for recurrent transient ischaemic attacks (TIA's) in 2001, at which time blood investigations had revealed a lymphocytopenia of 0.50 x10^9/L. Carotid Doppler and CT brain were normal, and the lymphocytopenia was not investigated further. In 2007 she was investigated for a fall. Her lymphocytopenia was persistent and a CT and MRI brain were suggestive of normal pressure hydrocephalus (NPH). She was seen in the Neurology Clinic at the same hospital, however there was no convincing evidence that Ms PC had any of the 3 cardinal features of NPH, and a follow up appointment was made for 12 months' time. Ms PC also had a diagnosis of hypertension and her medications were asasantin and metoprolol.

Ms PC had moved to Australia from Sri Lanka 10 years previously. She had no risk factors for human immunodeficiency virus (HIV). She was usually completely independent and required no gait aids.

On initial examination Ms PC was afebrile with normal vitals apart from a blood pressure of 150/80 mmHg. She was fully oriented and able to follow commands. She had postural instability and a magnetic gait with the feet appearing to be stuck to the ground. She also had brisk but symmetrical reflexes and power of 4/5 throughout. The remainder of her neurological and general examination were normal.

Ms PC was again found to have a lymphocytopenia (0.41 x10^9/L), and slightly elevated values for CRP and ESR. Otherwise, initial blood investigations were unremarkable. A CT brain was unchanged compared to the imaging from 2007. It showed hydrocephalus involving the lateral and third ventricles, and a fourth ventricle of normal size. An MRI brain showed no definite evidence of flow void through the cerebral aqueduct, but possible adhesions in the aqueduct.

Ms PC deteriorated acutely on the ward, in that she was unable to stand or follow even simple commands. A lumbar tap test was performed. The opening pressure was 19 cm H20 and Ms PC's gait did not improve afterwards. Examination of the cerebral spinal fluid (CSF) revealed no polymorphs, 2 x10^6/L lymphocytes and 4 x10^6 red blood cells. However the protein was elevated at 4.37 g/L, with a glucose of 1.5 mmol/L and lactate of 4.9 mmol/L. This result prompted further evaluation of her CSF which revealed a cryptococcal antigen titre of 1:128, and subsequent growth of Cryptococcus neoformans. Additional blood work up was negative for T pallidum, HIV and tuberculosis, however the CD4+ count was significantly reduced at 2 x10^6/L (normal value 389-1569 x10^6/L). The immunoglobulin profile was within the normal range.

Ms PC was therefore diagnosed with both idiopathic CD4+ T-lymphocytopenia (ICL) and cryptococcal meningitis, and was commenced on amphotericin B and 5-flucytosine. She also went on to have a ventriculoperitoneal shunt inserted and showed marked improvement after this in terms of her cognitive state and gait.

DISCUSSION

The diagnosis of cryptococcal meningitis can be a difficult one as the disease often presents with a subacute onset and non specific symptoms and signs. A major risk factor for its development is infection with HIV, indeed the disease is one of the AIDS-defining illnesses. The fall in CD4+ lymphocytes translates to impaired cell-mediated immunity and renders the patient susceptible to infections such as fungal infections. Cryptococcal meningitis also occurs in non-HIV patients who are immunocompromised due to other causes such as diabetes, cancer, long term steroid therapy, immunosuppressive treatment, and chemotherapeutic drug use, and has also been described in healthy patients with no identified predisposing factors [1].

In Mrs PC's case, an underlying immunocompromised state was identified, that being ICL. ICL is a rare condition. It is defined as persistent CD4+ T-lymphocyte depletion, in the absence of HIV-1 or HIV-2 infection or other known causes of immunodeficiency, with CD4+ counts below 300 cells/mm3 or less than 20 percent of total lymphocytes [2]. The condition can be asymptomatic, but more typically is manifested by mycobacterial and other opportunistic infections.

ICL has been described in the literature in a number of cases associated with cryptococcal meningitis [23], and Ms PC's case highlights important points regarding this association. A clue to the diagnosis of ICL existed since Ms PC's presentation with TIA's in 2001 when the lymphocytopenia was first revealed. ICL can be asymptomatic and transient, and it may well have been the case that the ICL was not complicated by cryptococcal meningitis at this early stage. However, interestingly, cases of cryptococcal meningitis presenting as ischaemic stroke, via a vasculitic mechanism, have been described in the literature [4]. Had ICL been diagnosed in 2001, or even in 2007, the additional diagnosis of cryptococcal meningitis may have been sought, given that Cryptococcus is the commonest central nervous system fungal pathogen in immunocompromised patients [1]. Thus, despite the often subtle presentation, a high index of suspicion for cryptococcal meningitis is required in all patients with neurological symptoms and lymphocytopenia. In addition, ICL should be included in the differential diagnosis of patients who have unexplained opportunistic infections, especially those who have a non-HIV associated lymphocytopenia.

References

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