Which mass is this? Diagnostic dilemma of an HIV patient presenting with intracranial mass

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Abstract— Patients living with HIV (PLWHA) suffer from many medical condition, neurological complaints being one of the commonest. Intracranial masses are frequently found upon radiological examination on these patients. Differential diagnoses of intracranial mass in these patients vary, with several features overlapping each other, making diagnosis, and thus management, challenging. A patient diagnosed previously with HIV, a woman in her thirties, presented to the ER complaining headache for 2 weeks. Upon examination, she also exhibited left-sided hemiparesis and cranial nerve symptoms. A computed tomography (CT) scan showed multiple contrast-enhancing lesions with meningeal enhancement, which can be attributed to toxoplasmic encephalitis (TE), primary central nervous system lymphoma (PCNSL), progressive multiple leukoencephalopathy (PML), or tuberculous (TB) meningitis. Her toxoplasma serology came up positive, therefore the empirical treatment was focused on eliminating the parasite *Toxoplasma gondii*, as well as supportive therapy, after which she showed significant improvement in her clinical symptoms as well as brain imaging. Determining the etiology of intracranial mass in HIV patients are not always straightforward; consideration of several factors and administering therapy according to algorithms can deliver good outcome.

Keywords— HIV, AIDS, PLWHA, intracranial mass lesion

1. Introduction

Patients living with HIV (PLWHA) suffer from many medical condition, neurological complaints being one of the commonest. Intracranial masses are frequently found upon radiological examination on these patients. Differential diagnoses of intracranial mass in these patients vary, with several features overlapping each other, making diagnosis, and thus management, challenging. Microbiologic agents such as *Toxoplasma gondii*, *Mycobacterium tuberculosis*, *Cryptococcus neoformans*, *Treponema pallidum* and others, and primary central nervous system (CNS) lymphoma can appear as a lesion difficult to distinguish radiologically. It is of paramount importance to determine the etiology these intracranial lesions to provide a specific and precise therapy.

Determining the etiology of intracranial mass in HIV patients are not always straightforward. The most undistinguishable etiologies reported in the case reports are toxoplasmic encephalitis (TE) and primary CNS lymphoma (PCNSL) [1–4].

In this case report, we present an HIV-positive patient on antiretroviral therapy (ART) presenting with CNS symptoms. Her brain CT revealed multiple ring-enhancing lesion with meningeal enhancement, features commonly found in either TE, PCNSL, progressive multiple leukoencephalopathy (PML), and tuberculoma caused by tuberculosis (TB). Anti-toxoplasmosis regimen was given empirically and her symptoms improved. A head CT evaluation after 5 weeks of treatment showed a complete resolution of her brain lesion.

A diagnostic approach of PLWHA presenting with CNS symptoms have been published by the

American Academy of Neurology in 1998. Since then, various algorithms have been proposed, especially for developing regions where certain infectious etiologies are endemic. We encourage

clinicians treating PLWHAs with CNS symptoms to follow these algorithms to effectively diagnose and treat these patients [5–9].

2. Case Description

A 33-year-old female presented at the Emergency Department with chief complaint of headache, which she had been suffering from for the last 14 days. She identified the headache as around her right, frontal aspect of head, throbbing, and subsided only briefly with administration of analgesics. She also complained of nausea, vomiting and low-grade fever for 14 days before presentation. She and her family denied any convulsions, altered mental status, weakness of extremities, tingling sensations nor pain on extremities, nor decrease of sensation at extremities. She also denied any blurred vision, double vision, facial pain, or weakness or decrease of sensation at facial area, or difficulty swallowing. She denied any diarrhea, oral thrush, chronic cough, nor shortness of breath. She denied having ear discharge nor toothache. She had never experienced headache of this intensity before.

She was diagnosed with HIV for 8 years ago, and she had been taking anti-retroviral therapy (ART) with low adherence. Her record also showed a history of tuberculous pleurisy at 2011, at which she took anti-tuberculous drug (ATD) for 6 months.

At presentation, she was alert and appeared in pain. Her vital signs were as follows: BP 120/60, HR 89 bpm, respiratory 20 cycles/minutes, temperature 36,5ºC. There was slight left hemifacial palsy, central type. Motoric strength examination revealed a slight left hemiparesis of the upper and lower limbs. The rest of her physical examination was unremarkable.

Her laboratory examination was as follows: Hb 12,6 g/dL; WBC 6790/µl; Platelets 297000/ µl; HbsAg non-reactive; Random Blood Sugar 103 mg/dL; Creatinine 0,55 mg/dL; BUN 8 mg/dL; AST 30 U/L; ALT 46 U/L; Albumin 3,9 g/dL; Sodium 135 mmol/L; Potassium 3,2 mmol/L; Chloride 97 mmol/L.

A head CT with contrast was done, and the result was: multiple hypodense (28 HU) lesions at right basal ganglia with greatest dimension of 1,3x1,7x1,8 cm, with rim contrast enhancement (64 HU) upon contrast injection with perifocal edema, which compresses and the right ventricle and causing midline shift to left side for 0,5 cm, and dilatation of left lateral ventricle. There is also gyral and meningeal enhancement at the right and left parieto-temporo-occipital (Figure 1). A supine Chest X-Ray was also done, which turned out to be normal.

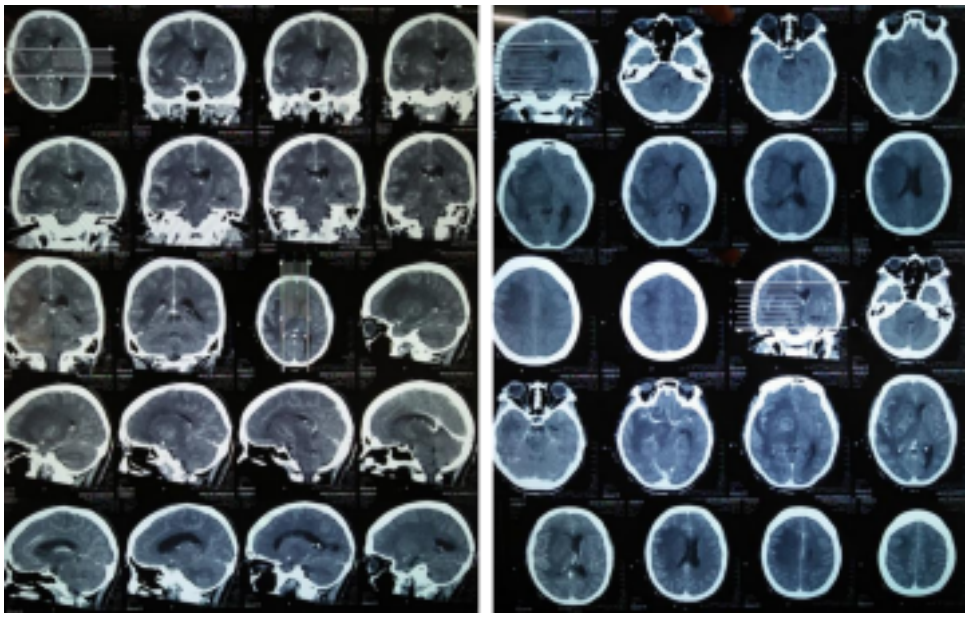

Figure 1 Head CT on presentation

Toxoplasmic encephalitis was suspected, along with cerebral tuberculoma and primary central nervous system lymphoma (PCNSL). She was given intravenous dexamethasone injection, and was empirically

treated with pyrimethamine, folic acid, and clindamycin orally. Her ART was also continued with the same regimen as previously taken. ELISA test showed positive anti toxoplasma IgG with a titer exceeding 700 IU/ml. After 6 days, the patient showed marked improvement in her symptoms, and was discharged home. At this point, her head MRI showed multiple irregular enhancing lesion at the right internal capsule and midbrain, which showed no increase of intralesional Ch/Cr ratio and Ch/NAA ratio on spectroscopy, an increase intralesional lipid lactate without increase of intralesional rCBV; conforms with infection process (Figure 2). This finding also further excludes PCNSL as the etiology. The patient continued the medication and repeat head CT after two months showed complete resolution of the lesions (Figure 3).

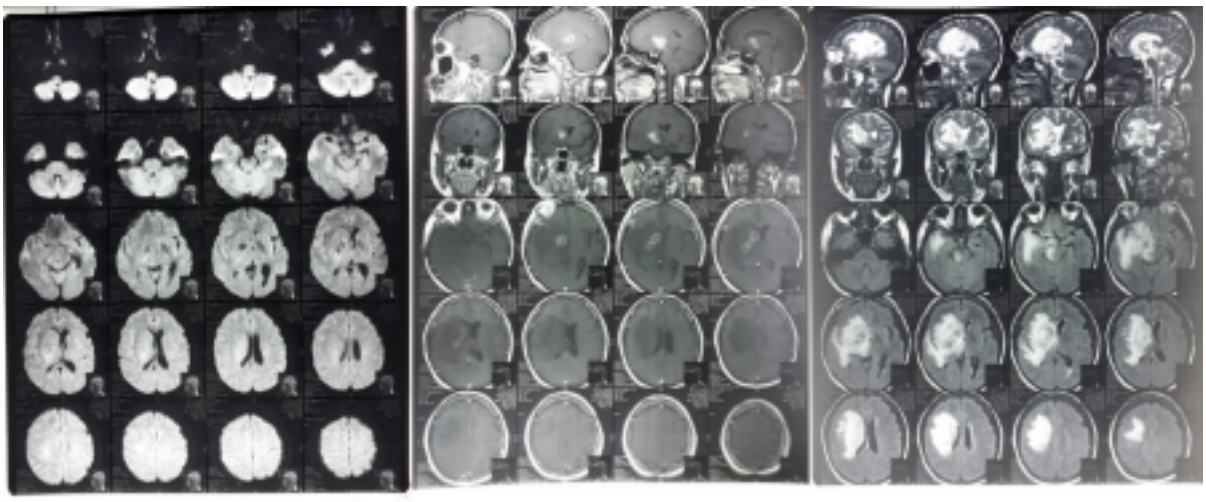

Figure 2 Head MRI on presentation

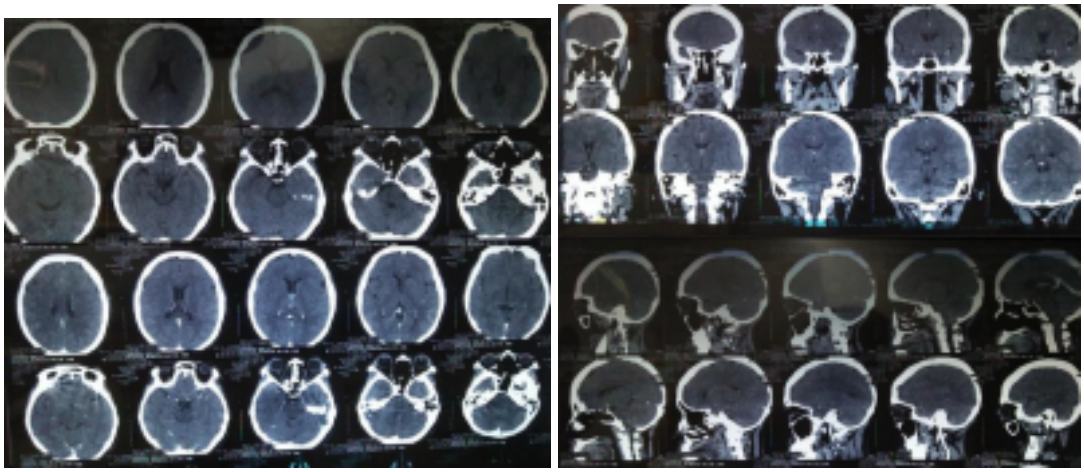

Figure 3 Head CT after 2 months of therapy

3. Discussion

Diagnosis approach of a PLWHA presenting with neurological symptoms can be based on the etiological agent (primary by HIV itself or secondary by opportunistic infections or neoplasms) and by the neuroanatomical localization (CNS or peripheral nervous system). Neurological abnormalities affecting brain can be classified according to the predominant neurological syndrome in meningitis or encephalitis. The encephalic syndrome comprises of focal or diffuse brain lesion. Non-focal or diffuse brain lesion usually presents with a diffuse alteration in cognition and symmetrical motor dysfunction,

with absence of aphasia, apraxia, agnosia, dysmetria, and hemiparesis. Non-focal brain diseases can be further divided into those presenting with cognitive decline and normal consciousness, which is almost always caused by AIDS dementia complex (ADC), and those presenting with decrease of both consciousness and cognitive function, which can be caused by cryptococcal meningitis, toxic/metabolic encephalopathies, and CMV/HSV encephalitis. Focal brain disease usually presents with focal neurological deficit, hemiparesis, dysmetria, and asymmetrical motor dysfunction. There are numerous etiologies of focal brain disease in PLWHA; the most common etiologies are toxoplasmic encephalitis, primary CNS lymphoma, progressive multifocal encephalopathies (PML), and tuberculous meningitis/encephalitis. In addition to the syndromic diagnosis, 3 aspects are relevant to establish the most probable etiologies of expansive focal brain lesions in PLWHA. The first thing to consider is local neuroepidemiology, for example tuberculomas is usually more common than primary central nervous system lymphoma (PCNSL) in low- and middle-income countries. The second thing is degree of immunosuppression, in which a patient presenting with lymphocyte CD4 count <200 cells/mm3 suggests opportunistic diseases, while PCNSL usually occurs with lymphocyte CD4 count <50 cells/mm3). The last thing to consider is the individual clinical, laboratorial, and neuroradiological features, as PCNSL usually presents with increased intralesional rCBV and Ch/Cr ratio on brain MRI[10–13].

American Academy of Neurology on 1998 has suggested an algorithmic approach in treating PLWHAs presenting with CNS symptoms. In this guideline, toxoplasmosis is the first differential to consider; brain biopsy should be performed after ruling out this diagnosis or in uncertain cases. Neurosurgical intervention is warranted if herniation develops. In principle, multiple brain lesion on head CT with positive toxoplasma serology suggests toxoplasmic etiology. In this regard, antitoxoplasmosis therapy can be given empirically and continued when the patient responds. Brain biopsy should be performed to determine the etiology if the patient fails to response to this 'trial' therapy[8,9,11].

Toxoplasmic encephalitis is the most common cause of focal brain disease in PLWHA. Additionally,

toxoplasmic encephalitis is also the most common etiology of central nervous system opportunistic infection in patients with immunosuppression. The causative agent is *Toxoplasma gondii*, an obligate intracellular protozoon that reactivates from latent infection in immunocompromised host. Upon reactivation and infection of brain tissue, symptoms such as headache, focal neurological deficit, fever, mental confusion, seizure, psychomotor or behavioral change, cranial nerve palsy, ataxia, and visual abnormalities can occur, typically in subacute onset. Symptoms associated with meningeal involvement are rare. On head CT or MRI with contrast, the lesion(s) typically appear as single/multiple contrast ring-enhancement lesions, diameter 1-2 cm, mainly at basal ganglia, frontal lobe, and parietal lobe, with surrounding perifocal edema. Although the lesion is typically multiple, single lesion is reported in 30- 40% case of biopsy-proven toxoplasmic encephalitis. Radiologically, toxoplasmic lesion cannot be clearly distinguished from primary CNS lymphoma. Important imaging signs are eccentric target sign and/or concentric target sign, as opposed to central target sign which is usually found in tuberculomas. Positive toxoplasma serology in blood can help in establishing diagnosis, since negative serology in toxoplasmic encephalitis is rare (only 3% of case). Positive *Toxoplasma gondii* DNA found in CSF confirms the diagnosis (Specificity almost 100%), although negative result does not exclude the diagnosis. The golden standard diagnostic tool is by obtaining *Toxoplasma gondii* from tissue biopsy. Toxoplasmic encephalitis rarely occurs in CD4 count more than 200 cell/μL[8,11–13].

Generally, patients with toxoplasmic encephalitis show a good clinical response after 14 days of acute phase treatment. The regimen of chronic phase maintenance therapy is similar to the acute phase treatment, with half the dose. Maintenance treatment is given continuously until CD4 count > 200 cell/μL for subsequent 6 months after ART initiation. In a clinical trial of patients given empiric treatment of toxoplasmic encephalitis, the median time until response is 5 days; 74% patients show improvement on 7th day of treatment, and 91% show response within 14 days of therapy. Diagnosis should be evaluated if patient's condition remain unresponsive to therapy within 10-14 since treatment initiation, and brain biopsy or SPECT (single-photon emission computed tomography) thallium-201 should be considered[8,14].

4. Conclusion

PLWHA presenting with CNS symptom may pose a diagnostic, and thus, therapeutic challenge to clinicians, due to similarities in symptoms and signs. Neuroepidemiology, degree of immunosuppression, and individual clinical, laboratorial, and neuroradiological features can help narrow the differentials. Clinicians can also use algorithmic approach in managing these patients, which can potentially avoid unnecessary invasive procedure such as brain biopsy.

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