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Successful Treatment of Cerebral Tuberculoma in Acquired Immune Deficiency Syndrome Patient a Case Report

Rachmad Aji Saksana[1], Ika Trisnawati[2], Eko Budiono[3]

[1]Pulmonology and Critical Care Medicine fellowship FK-KMK UGM / Dr. Sardjito Central General Hospital

[2,3]Division Pulmonologi Departement Internal Medicine FK-KMK UGM / Dr. Sardjito Central General Hospital

ABSTRACT

Introduction: Tuberculosis (TB) remains a leading problem in developing and endemic countries. Cerebral tuberculosis is a rare but dangerous complication of tuberculosis infection in the central nervous system. The immunosuppressive condition in human immunodeficiency virus infection is a risk factor for severe tuberculosis.

Case Report: An Indonesian man, 32 years old, married, came with complaints of headaches, dizziness, delirium, nausea and vomiting since 1 month before the examination. He had a history of TB treatment 1 year before the examination. The results of the neurological examination were within normal limits, the HIV test was reactive and there was a decrease in CD4. Head MRI examination with contrast showed multiple solid nodules in the thalamus with the largest size 2.3×2.7 cm, indicating cerebral tuberculoma. Chest x-ray was normal, GeneXpert MTB sputum was not detected. Next, primary treatment is given with anti-tuberculosis drugs, Highly Active Antiretroviral Therapy (HAART), co-trimoxazole, and dexamethasone. There was clinical, laboratory and radiological improvement after 12 months of treatment. Viral load is undetectable, CD4 is elevated. A head CT scan did not show tuberculoma. He became healthy and was able to return to work

Discussion: Cerebral tuberculoma is a condition characterized by the presence of intracranial tuberculoma. The clinical manifestations are non-specific, such as headaches or seizures. This is caused by space occupying lesions and increase intracranial pressure. In this case, the diagnosis of cerebral tuberculoma was made through head MRI with contrast. TB therapy and co-trimoxazole are given as soon as the diagnosis is made, while antiretrovirals are given 2 weeks after he has tolerated the TB medication. The minimum duration of therapy for cerebral tuberculosis is 12 months. He require lifelong antiretroviral medication.

Conclusion: Tuberculoma should be considered as differential diagnosis of space-occupying lesions in patients HIV/AIDS. Early diagnosis, adequate therapy, patient adherence and family support can cure severe tuberculosis.

KEYWORDS: Tuberculoma, tuberculosis, HIV / AIDS

ARTICLE DETAILS

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INTRODUCTION:

Tuberculosis (TB) remains a problem in developing and endemic countries (Kartasasmita, 2016). Tuberculosis is a major health problem, even though economic status is improving and the effectiveness of anti-tuberculosis drugs is increasing. M. tuberculosis bacteria mostly infect the lungs, but as many as 21.5% infect extra-lungs. Tuberculosis (TB) is the most common opportunistic infection in HIV/AIDS. HIV-TB coinfection increases the incidence of extrapulmonary TB. The clinical manifestation of extra-pulmonary TB depends on the organ affected (Hendytama & Hadi, 2022).

Central nervous system (CNS) TB accounts 1.3% of all tuberculosis and 6.3% of extrapulmonary tuberculosis. Cerebral tuberculoma is the rarest and most dangerous form of CNS TB besides meningitis or TB brain abscess (Yogi et al., 2021). Tuberculoma is the main cause of intracranial space-occupying lesions (SOLs) in areas where TB is

endemic and in patients with HIV infection. Lesions usually occur in the brain parenchyma, but can affect the meninges and extend to the ventricular system (Marais et al., 2020). Tuberculoma is associated with TB meningitis, but can develop without meningeal signs or central nervous signs (Bovijn, 2019).

The clinical manifestations of tuberculoma in HIV patients are similar to non-HIV patients. Neurological symptoms depend on the location of the lesion, increased intra-cranial pressure (headache, vomiting, papilledema, decreased consciousness), visual impairment or progressive focal neurological deficit (Bovijn, 2019).

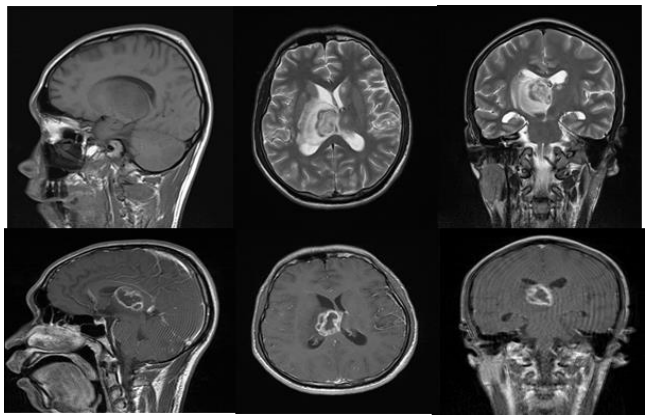
Definitive diagnosis is made through brain biopsy, but because it is an invasive intervention, it is difficult to carry out in areas with a high prevalence of TB/HIV. Lumbar puncture should be performed because it can support the diagnosis and rule out other etiologies, unless there are contraindications. This also supports the findings of TB meningitis. Chest x-ray examination is also needed in cases of extra-pulmonary TB (Bovijn, 2019).

CASE REPORT

An Indonesian man, 32 years old, married, came with his family and complained of headaches since 1 month before the examination. Patients also complain of dizziness, nausea and vomiting. Based on family information, the patient looked confused, spoke unclearly, and looked sleepy. There are no seizures, weakness in the limbs, a feeling of fullness, or problems with urination and defecation. Past medical history, the patient suffered from pulmonary tuberculosis 1 year ago, had received anti-tuberculosis medication for 6 months and was declared cured. Previous history of brain infection, tumor, hypertension, diabetes mellitus, stroke, and head trauma was denied.

The results of the physical examination showed a general impression of looking drowsy, Glasgow Coma Scale E3V4M4, blood pressure 107/75 mmHg, pulse rate 65 beats/minute, respiratory rate 20 breaths/minute, body temperature 36.2˚C, and body mass index 19.75. Generalist status, head, ears, nose, mouth, neck, lungs, heart, stomach and extremities were all within normal limits. Neurological status, normal physiological reflexes, negative pathological reflexes. Cranial nerve examination, meningeal excitatory signs, and cerebellar examination were within normal limits.

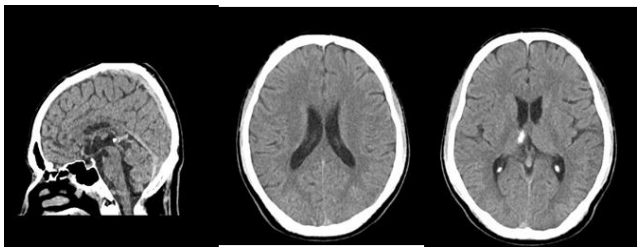
Laboratory examination showed an increase in CRP (29 mg/dL) and ESR (78 mm/hour). HIV test showed reactive results with decreased CD4 levels (23 c/UL). Serological examination showed reactive IgG Anti-Toxoplasma and IgG Anti-CMV results. Gene Xpert MTB sputum was undetectable, chest x-ray was normal. Head MRI with contrast results were consistent with cerebral tuberculoma.



Picture1. Head MRI with contrast

Multiple solid nodules in the right thalamus, bilateral frontal lobes, right temporal lobes,
left occipital lobes, and bilateral cerebellum, the largest size 2.3 x 2.7 cm in the right thalamus
consistent with cerebral tuberculoma

The diagnoses in this patients were tuberculosis, HIV/AIDS, cerebral opportunistic infections, toxoplasmosis, and CMV. TB therapy, dexamethasone, co-trimoxazole were given immediately after the diagnosis was made. Anti-tuberculosis drugs using rifampicin, INH, ethambutol and pyrazinamide. Streptomycin was given for 2 months, followed by rifampicin and INH for 10 months. Antiretrovirals was given 2 weeks after TB drugs can be tolerated, using tenovofir, lamivudine and dolutegravir. There was clinical, laboratory and radiological improvement after 12 months of treatment. He returned to health, had no complaints of headaches, nausea and vomiting, and was able to work again. The results of head CT scan did not show any tuberculoma. Laboratory results showed that the viral load was undetectable and CD4 increased to 92 c/Ul.



Picture 2. Head CT scan results with contrast after 12 months of treatment.

Lacunar infarcts were found in the left lentiform nucleus and left caudate nucleus.
There are no tuberculomas.

DISCUSSION

People with HIV who experience altered mental status or an abnormal neurologic examination are often found to have intracranial parenchymal lesions. HIV/AIDS predisposes to several CNS opportunistic infections such as tuberculosis, toxoplasmosis, cryptococcus, and progressive

multifocal leukoencephalopathy. Tuberculoma is the most common cause of intracranial lesions in HIV in TB endemic areas (Madi et al., 2012). Central nervous system (CNS) tuberculosis is found in 5-10% of pulmonary tuberculosis patients. CNS TB can be a reactivation of latent TB infection or spread from a focus of TB infection in other parts of the body. Tuberculoma is the rarest but most dangerous form of CNS TB (Vidal et al., 2004; Marais et al., 2020; Priyadarshi et al., 2021).

Cerebral tuberculoma is defined as a lesion of brain tissue in the form of a granulomatous mass consisting of tubercles (incipient tuberculoma) and other inflammatory cells. Tuberculomas are well-defined, solitary or multiple (ratio 4:1), hard, nodular, avascular, and can reach several mm to 3-4 cm so they can cause significant mass effects around them such as perifocal edema and gliosis (Kumar, 2016); Vidal et al., 2004). Cerebral tuberculoma is a mass of granulomatous tissue that develops due to the hematogenous spread of distant tuberculosis infection. This occurs due to conglomeration and conjugation of tuberculous microgranulomas which tend to occur at the gray-white matter junction due to the cessation of hematogenous spread of microbes caused by a decrease in the caliber of blood vessels in this region. Outside the capsule, the brain parenchyma is edematous and shows astrocytic proliferation. Sometimes the melting of the necrotic core accompanied by the formation of pus causes a tuberculous abscess which is difficult to differentiate from a pyogenic brain abscess (Ibrahim, 2022).

The pathogenesis of tuberculoma is not completely understood, but it is generally explained that the spread of TB bacteria to the brain cortex or meninges occurs hematogenously and at various times after primary lung infection with the formation of small granulomas called 'Rich foci'. These foci can join to form a tuberculoma which then develops into a central point of caseous necrosis surrounded by a wall formed by inflammatory cells containing a network of collagen, epithelioid cells, Langhans giant cells, and lymphocytes; acid-fast bacteria can be demonstrated in the necrotic core surrounded by a capsule (Marais et al., 2020). The necrotic core has a fatty content with macrophage infiltration, regional fibrosis, and perilesional cellular infiltrate with some acid-fast bacteria in the center. Liquefaction of the dense caseous core starts from the necrotic core. The capsule consists of granulation tissue and compressed glial tissue. There is perilesion edema associated with some astrocyte proliferation in the surrounding brain parenchyma (Ibrahim, 2022).

In person with HIV, a decrease in CD-4 T lymphocytes causes a decrease in the immunological response to M. tuberculosis which can lead to reactivation from the latent period of TB to active infection. On the other hand, activation of pro-inflammatory cytokines in TB cases increases the regulation of HIV infection which further causes a decrease in CD4 counts (Kumar, 2016; Cahyati, 2019). In this case, patient was known to have a history of HIV/AIDS and a previous history of pulmonary TB as the main comorbidities.

This patient was first admitted at the Internal Medicine clinic with complaints of abdominal pain, nausea, headache, chills and fever for 2 weeks. This is in accordance with the literature which states that patients with tuberculoma present with signs and symptoms of increased intracranial pressure caused by compression of the intracranial space. The clinical symptoms of cerebral tuberculoma sufferers are varied and non-specific, such as headache, vomiting, drowsiness, papilledema, hemiparesis, or seizures may be the symptoms that appear in these patients. According to Ibrahim (2022), slowly progressive constitutional symptoms are dominant in the early stages of the disease, including general weakness, malaise, night sweats, fever, and weight loss. Clinical symptoms depend on the size and anatomical location of the lesion. The patient's clinical course is usually asymptomatic with minimal parenchymal lesions, whereas if the lesions are multiple or large, the patient may experience symptoms such as headache, focal neurological deficits, seizures, vomiting, hydrocephalus, signs of meningeal irritation, and intracranial hypertension with papilledema (Kumar et al. , 2022). In this case, the patient also complained of headaches and changes in mental status in the form of confusion. The diagnosis was made based on anamnesis, physical examination, laboratory and radiology to confirm cerebral tuberculoma. Non-invasive diagnostics are recommended over invasive methods such as brain biopsy. The microbiological examination that can be carried out is GeneXpert MTB which is obtained from analysis of sputum and cerebrospinal fluid. (Wijaya et al., 2020; Kushnurrokhman & Kusmiati, 2020). In this case, there were no samples from either biopsy or cerebrospinal fluid.

Magnetic Resonance Imaging (MRI) with contrast is the recommended and ideal imaging for diagnosing cerebral tuberculoma with a sensitivity of 86% and a specificity of 90%. Tuberculomas may appear as round or lobulated masses of varying size that may be accompanied by perifocal edema. Most images show central hypointense with rim hypointense. (Ikbal & Sugianto, 2021). According to Turgut (2017), on contrast-enhanced CT scans and head MRI, tuberculomas appear as ring-enhancing lesions followed by a conglomerate appearance. In this case, several solid nodules with the largest size of 2.3 X 2.7 cm were found in the thalamus area followed by rim enhancement during contrast administration.

In cases of tuberculoma, head CT scan with contrast is more feasible because the cost is more affordable, and is more widely available at secondary referral hospitals. CT scan of the head with contrast has a sensitivity of 41% and a specificity of 100%. Tuberculomas may appear as isodense or hyperdense masses with peripheral or complete mass enhancement. Pyogenic abscesses can be found with a hypodense center, while enlargement can be found on the

periphery with an isodense center. Calcifications can be identified in around 10% of cerebral tuberculomas using CT scans (Ikbal & Sugianto, 2021; Kushnurrokhman & Kusmiati, 2020).

The main priority in the management of TB patients co-infected with HIV is starting TB therapy followed by ARVs. ARV therapy is given as soon as 2 weeks and no later than 8 weeks after TB therapy can be tolerated (Ajmala & Wulandari, 2015). Anti-tuberculosis drugs are recommended to be given for 10-12 months in HIV/AIDS patients with CNS extrapulmonary TB (Wijaya et al., 2020).

Regarding HIV problems, the patient was treated with the TLD regimen (Tenofovir + Lamivudine + Dolutegravir) two weeks after administration of antituberculosis drugs. The use of a combination of antiretroviral drugs is important because it can reduce resistance, suppress HIV replication effectively, reduce transmission, opportunistic infections and other complications (Permatasari, 2021). Highly active antiretroviral therapy (HAART) improves survival and quality of life of AIDS patients (Tancredi, 2022). Tenofovir was chosen because it is sufficient to take it once a day, making it easier for HIV patients and increasing drug acceptance, considering that antiretroviral therapy is taken for life (Permatasari, 2021). Dolutegravir is available in fixed-dose combination with tenofovir and lamivudine (TLD). Dolutegravir has better efficacy and tolerability than the lopinavir-ritonavir regimen (Keene, 2021). Coadministration of rifampicin and dolutegravir will contribute to a reduction in delutographic exposure dose, raising concerns about efficacy and potential development of HIV resistance. This causes the dose of dolutegravir to be increased twofold.

In cases of CNS TB, corticosteroids are given as additional therapy. Steroids control the systemic effects of TNF, INF and other immune mediators. Steroids can reduce the initial intracerebral inflammatory response, prevent infarction, tuberculoma formation, and reduce the incidence of immune reconstitution syndrome (IRIS). Immune Recovery Syndrome or IRIS is a spectrum of worsening clinical symptoms in PLWHA due to an excessive inflammatory response during the recovery period of the immune response after starting ARV therapy. Dexamethasone 6-12 mg/day or prednisone 60-80 mg/day can be given to patients and then tapered off (Winarno, 2018).

Opportunistic infections in HIV can be prevented by administering prophylactic therapy. In this case, the patient was given cotrimoxazole 480 mg/12 hours. Cotrimoxazole is a broad-spectrum antibiotic that targets a variety of gram-positive and gram-negative aerobic bacteria, fungi and protozoa. WHO reports that prophylactic cotrimoxazole is considered capable of reducing the number of opportunistic infections in HIV cases (WHO, 2014; Gebresillassie et al., 2016).

CONCLUSION

Tuberculoma should be considered as differential diagnosis of space-occupying lesions in patients HIV/AIDS. Early diagnosis, adequate therapy, patient adherence and family support can cure severe tuberculosis.

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