MANAGEMENT OF GIANT TUBERCULOMA IN A YOUNG PAPUAN MAN: CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

Tuberculoma infection in Papua is still quite high. Tuberculoma is a focus of caseous tubercles found in the brain parenchyma caused by the bacteria Mycobacterium tuberculosis. This study aims to report the outcomes of tuberculosis patients who underwent craniotomy resection of large tuberculoma lesions and continued with therapy using anti-tuberculosis drugs (OAT). There are challenges in the radiological and clinical diagnostic approaches to tuberculoma lesions in these patients who have no history of previous pulmonary tuberculosis infection. A definite diagnosis of tuberculoma is obtained from the establishment of anatomical pathology diagnostics so that the patient is then given FDC category I of anti-tuberculosis drugs for up to 9 months. The patient showed clinical improvement and brain tissue repair after surgery as evidenced by neuroimaging evaluation 7 months after surgery. Management of tuberculosis in Papua requires an educational focus on increasing the synergy of promotive and preventive aspects and finding new cases of tuberculoma to be treated as early as possible.

Keywords : tuberculosis, tuberculoma, Papua, neuroimaging

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ABSTRAK

Infeksi tuberkulosis (TBC) di Papua masih cukup tinggi. Tuberkuloma adalah suatu fokus tuberkel kaseosa yang terdapat dalam parenkim otak yang disebabkan oleh bakteri *Mycobacterium tuberculosis*. Penelitian ini bertujuan untuk melaporkan luaran pasien tuberkuloma yang dilakukan kraniotomi reseksi lesi tuberculoma berukuran besar dan dilanjutkan dengan terapi menggunakan Obat Anti Tuberculosis (OAT). Terdapat tantangan pendekatan diagnostik radiologis dan klinis lesi tuberculoma pada pasien ini yang tidak memiliki riwayat infeksi TBC paru sebelumnya. Diagnosis pasti tuberculoma diperoleh dari penegakan diagnostic patologi anatomi sehingga pasien selanjutnya diberikan obat anti tuberculosis *Fixed Drugs Combination* (FDC) kategori I sampai 9 bulan. Pasien menujukkan perbaikan klinis dan perbaikan jaringan otak paska pembedahan yang dibuktikan dengan evaluasi neuroimaji 7 bulan paska operasi. Tatalaksana tuberkuloma di Papua memerlukan fokus edukasi pada peningkatan sinergitas aspek promotive dan preventif serta penemuan kasus tuberculoma baru untuk diterapi sedini mungkin.

Kata kunci: tuberkulosis, tuberkuloma, Papua, *neuroimaging*

Introduction

Tuberculosis (TB) is one of the global health problems caused by the bacteria *Mycobacterium tuberculosis* (MTB). Data from the 2023 Indonesian Health Survey (SKI) showed that the prevalence of TB in Papua reached 0.58% (95% CI: 0.4-0.85) which is above the national prevalence rate of 0.3%. (1) The incidence of tuberculoma in brain tissue varies from 2-33%, while brain tuberculoma occurs in 15-50% of all intracranial lesions in developing countries with a high incidence of TB infection. (2) Tuberculoma contributes to 4% of deaths in areas endemic for pulmonary TB and includes 1% of cases of central nervous system tuberculosis. (2,3) Until now, there has never been any specific data related to brain tuberculoma in Papua, even in Indonesia. Research reports base the method of establishing the diagnosis of tuberculosis on anatomical pathology (19%), clinical symptoms (and/or neuroimaging) after responding to anti-tuberculosis therapy (57%), and 24% depending on evidence of systemic tuberculosis. (4) Patients with a diagnosis of brain tuberculosis can have a good quality of life if a targeted diagnosis is performed, surgery according to clinical indications, and appropriate and optimal treatment management. In this paper, we report a case of a 22-year-old man who had a large tuberculoma lesion in the parietal lobe.

Case Report

A 22-year-old man was brought by his family to the hospital emergency room due to decreased consciousness after previously experiencing two generalized seizures at home. There was no history of previous head injury or previous illness. The results of family heteroanamnesis, show the patient only often complained of headaches for the past 5 months and in the past 3 months complained of weakness of the right side of the limbs. There was no history of specific symptoms related to pulmonary tuberculosis or history of contact with other tuberculosis patients before. Every time he complained of headaches, the patient only consumed 500 mg of mefenamic acid. Physical examination showed GCS E3M6V4 with other neurological examinations within normal limits, except for mild hemiparesis of the right extremity (motor strength 4+). After administration of anticonvulsant injections (phenytoin 100 mg) and dexamethasone 10 mg, the patient's GCS increased to full consciousness. The results of a non-contrast CT scan of the head showed a solid mass lesion measuring 7x5x5 cm3, round, well-defined, isodense, and a hypodense edema picture around the

mass (Figure 1A). There were no significant changes in routine blood laboratory tests. Screening for TB co-infection showed negative results. Expert MTB-RIF examination did not detect MTB germs. Chest X-ray results showed normal lungs, without signs of infection or a history of specific tuberculosis infection. The patient was diagnosed with a space-occupying lesion (SOL) suspected of being tuberculoma and was advised to undergo a tumor resection craniotomy. The patient and family agreed to the procedure. The patient underwent a tumor resection craniotomy under general anesthesia. Intraoperatively, a solid, yellowish-white lesion was found, an avascular lesion, easily separated from the surrounding brain parenchyma tissue. The lesion was removed gradually until it was completely removed and separated for histopathological examination (PA results in Figure 1B-C-D). Postoperatively, the patient was treated for 24 hours in the ICU and then moved to a regular care room (Figure 1E). The patient was treated for 4 days and received intravenous therapy of Ceftriaxone 1g twice a day, Ketorolac 30 mg twice a day, Phenytoin 100 mg three times a day, Dexamethasone 5 mg twice a day, and Ranitidine 50 mg twice a day. The patient was then discharged without seizures, GCS 15, no hemiparesis, and was given continued therapy of phenytoin 100 mg three times a day orally. Seven days after leaving the hospital, the patient was checked without any complaints of seizures or hemiparesis. The results of the histopathological examination showed a microscopic picture of extensive necrotic tissue accompanied by epithelioid cells, lymphocytes, and Langhans giant cells accompanied by connective tissue (Figure 1F-G). The pathologist concluded that it was a specific tuberculosis granulomatous inflammation. The patient was then given anti-tuberculosis drug therapy (OAT) FDC Category I for 9 months. In the 7th month, the patient requested a control head CT scan and the results showed complete improvement in the previous lesion area (Figure 1H). The patient continued to be given OAT for 9 months. The last control after 12 months post-surgery, the patient showed complete improvement (without seizures and other neurological deficits) and the patient was able to return to his activities as a bachelor's student. The patient has obtained information and given consent for his case to be published in the media and scientific activities.

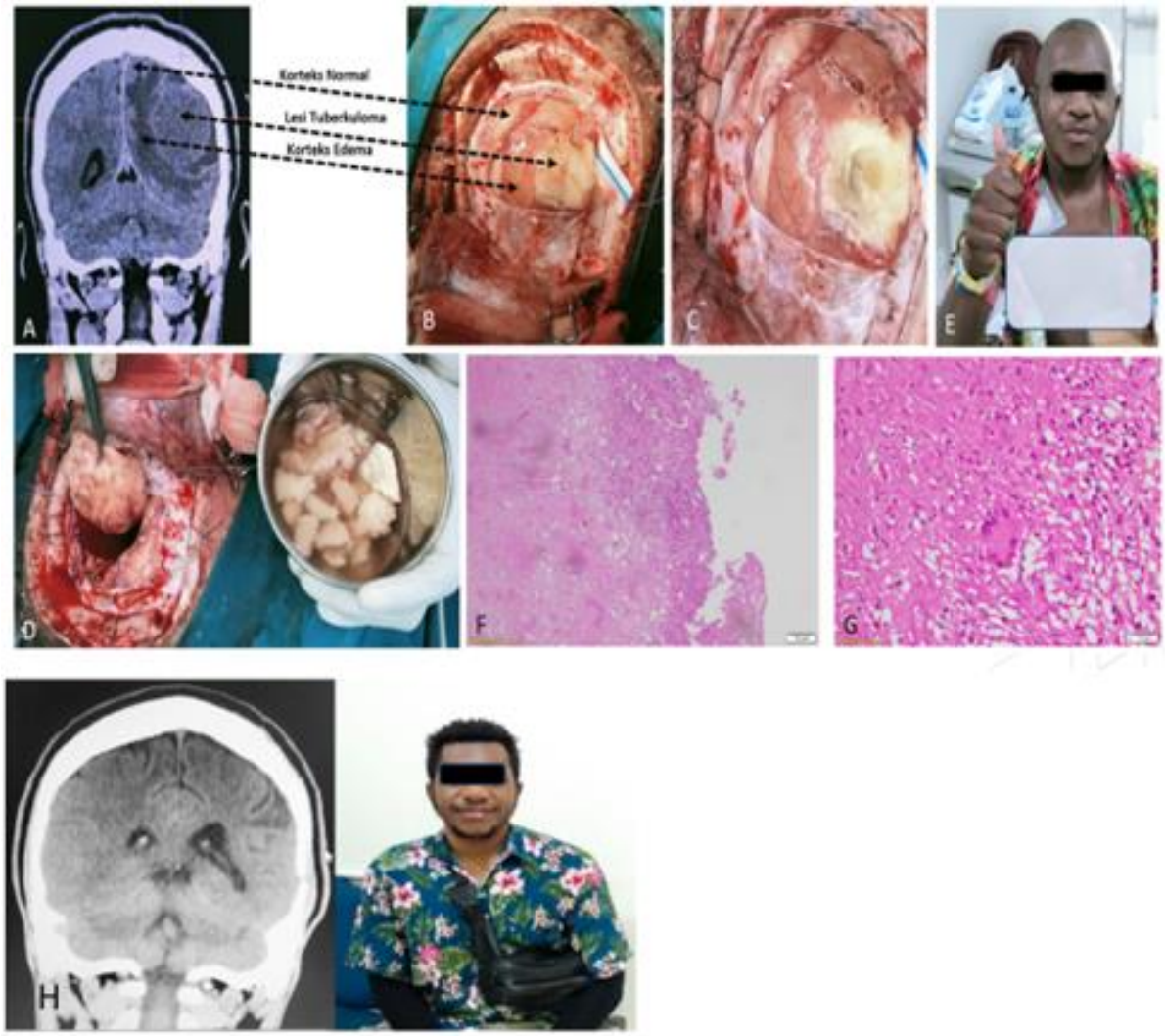

Figure 1. Tuberculoma patients who are managed according to the tuberculosis management of surgery and drugs regiment.

(A) Pre-operative CT scan photo of a well-defined mass, caseous lesion with a solid appearance in the center of the lesion

(B),(C),(D) Intraoperative photo of a patient undergoing craniotomy

(E) Clinical photo of the patient on the first day after surgery

(F) (G) Microscopic photos of histopathology examination results at 100x magnification (F) and 200x magnification (G) show cellular images consistent with tuberculosis infection in brain tissue.

(H) Head CT scan and clinical photos 7 months after surgery and 6 months after tuberculosis drugs programme.

Discussion

Early diagnosis and treatment of cerebral tuberculosis are essential to prevent mortality and morbidity. (5) Several studies have reported that cerebral tuberculosis is an uncommon manifestation of tuberculosis, accounting for only 0.2% of brain mass biopsies. (3) A definitive diagnosis of tuberculosis in this patient was obtained from the results of pathological anatomical examination of abnormal lesion tissue from surgery. The highest incidence of cerebral tuberculosis is in those aged <30 years, dominated by male gender. Brain tuberculosis is usually a single lesion in the brain but is often found in multiple lesions (more than 2 lesions). The size of the tuberculoma lesion ranges from 1 mm to 12 cm. (2) In this 22-year-old male patient, the single lesion, tuberculoma, even measured 7 cm. Based on the review of Manyelo et al.(2021), the pathogenesis of tuberculosis follows the general framework of the pathogenesis of tuberculosis meningitis as follows. First, aerosol droplets containing MTB bacteria are inhaled into the lungs, infecting alveolar macrophages and forming granulomas. MTB bacilli that escape from the (primary) granuloma cause bacteremia and then spread to the brain through the bloodstream. In the blood-brain barrier (BBB) area, MTB bacteria that successfully escape then infect microglial cells and activate the release of cytokines and chemokines, causing further damage to the BBB and allowing the influx of other uninfected immune cells into the brain tissue. This condition will then result in the formation of a “rich focus” granuloma. At some point, this rich focus will rupture, causing bacteria to be released and enter the subarachnoid cavity, then allowing the spread of infection to the cerebrospinal fluid and meninges. The release of bacteria into the meninges and cerebrospinal fluid will cause meningeal inflammation and the formation of thick exudate. This thick exudate is capable of precipitating the signs and symptoms of meningitis. (6) Our patient, based on the anamnesis and chest X-ray, did not show a history of previous pulmonary TB infection. Perez-Malagon et al. (2021) stated that 75% of tuberculoma patients started with pulmonary tuberculosis infection 6-12 months previously, and the remaining 25-30% had no history of pulmonary tuberculosis infection. (7)

Consideration of surgical therapy in these patients is based on consideration of a single lesion measuring >3 cm in a non-eloquent area. A CT scan shows signs of increased intracranial pressure and clear neurological deficits. (7,8) The diagnostic approach to tuberculoma using neuroimaging results a CT scan of the head shows that tuberculoma is an iso- or hypodense lesion, accompanied by

peripheral thickening and central isodense; 10% have calcification. The dominance of peritumoral edema surrounds the lesion capsule and most lesions are avascular. (9,10,11) According to Mukherjee et al.(2015), in patients with focal seizures accompanied by images of solitary or multiple ring-enhancing lesions on a CT scan or MRI of the head, brain magnetic resonance spectroscopy (MRS) needs to be performed to find an image of increased lipid components to confirm the diagnosis of tuberculoma. (12) If early detection is earlier and it is known that the size of the lesion is still small (<2 cm), then the patient will likely not undergo craniotomy surgery. (7) This patient received OAT for 9 months after lesion resection. WHO recommends the same regimen for 2 months consisting of rifampicin, isoniazid, pyrazinamide, and ethambutol, followed by 10 months of rifampicin and isoniazid for the management of tuberculous meningoencephalitis. However, in this patient, using the FDC category I regimen for 9 months, the patient has shown significant clinical improvement. (9-14) Post-surgery patients should not lose control (loss of follow-up) and continue to take medication regularly until finished. In this regard, health workers involved in the DOTS program for tuberculosis patients must also be equipped with the ability and understanding related to good tuberculosis management. This is because the evaluative approach and follow-up of tuberculosis patients are likely to be slightly different from those that would be carried out on normal pulmonary tuberculosis patients.

Conclusion

Management of large tuberculoma (>3 cm) with clear neurological deficit symptoms requires a combination of surgical intervention and OAT administration for 9 months, showing excellent clinical improvement in patients. Early clinical detection and diagnostic CT scan examination of the head in pulmonary TB patients who show neurological deficits are important steps to obtain good outcomes for tuberculoma patients. Specific education for all first-line and advanced health workers related to tuberculoma, especially in Papua, which has a high prevalence of TB, needs to be carried out optimally.

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Conflict of Interest

The author declares that this article has no conflict of interest. This manuscript was written without any financial assistance from commercial agencies or other non-profit sectors.

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