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Mycobacterium tuberculosis Infection in the Central Nervous System Mimicking Metastatic Process

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ABSTRACT

Mycobacterium tuberculosis (MTB) infection is a global health issue. Tuberculosis (TB) on the central nervous system (CNS) is a severe form of the disease which entails mortality rate of 15-40%. CNS TB infection results from lymphohematogenous spread and could mimic metastases, thus, diagnosis often becomes difficult. Microbiology and histology examinations are very important for the diagnosis to be made. In this article, we report a 29-year-old immunocompetent male patient with atypical extra-pulmonary TB. Magnetic resonance imaging (MRI) results showed multiple lesions in the brain parenchym, duramater, calvaria and vertebrae, which mimics the metastatic process. Granulomatous lesions and MTB were found through the fine needle aspiration biopsyand histopathological examination. The present of MTB was also confirmed with the GeneExpert examination. In conclusion, establishing a definite diagnosis for multiple CNS TB that mimics metastasis is difficult. Beside from clinical manifestation and radiology, histopathology analysis have an important role in establishing a diagnosis in this case. Detection of MTB bacteria on culture is a gold standard to diagnose TB. Treatment of multiple CNS TB should consist of oral anti tuberculous (OAT) category 2.

Keywords: Tuberculosis, MTB, CNS TB,metastasis, Indonesia

Introduction

Tuberculosis (TB) is a granulomatous disease caused by *Mycobacterium tuberculosis*(MTB), a gram-positive rod that grows slowly. TB is an endemic in developing countries. According to WHO, there are about 9.2 million new cases of TB and 1.7 million deaths due to TB annually. In 2008, according to data from the National TB control program in India, 18% of the total cases of TB were extrapulmonary TB.[1,2] Meanwhile, the TB prevalence rate in Indonesia in 2014 was 297 per 100,000 population. Since 2004, extrapulmonary TB cases have increased by 3% compared to the previous year, where 30% pleural effusions, 10% abdominal TB, 8% bone TB, 47% lymph node TB, 2% TB meningitis and 3% TB in other organs.[2] TB cases in the central nervous system (CNS) are categorized as extrapulmonary TB cases and often presents with broad symptoms and non-specific clinical features that resemble the symptoms of other neurological diseases.[3]

CNS TB is an uncommon manifestation and accounts for 5–10% of all cases of extrapulmonary TB. CNS TB causes high mortality and morbidity rates. In a prospective cohort study in Canada from 1971 to 2001, it was concluded that the manifestations of CNS TB consisted of tuberculoma meningitis, tuberculoma of the brain, tuberculoma brain abscess, encephalopathy TB, spinal TB and spinal tuberculoma.[3]

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In this article, we presented a case of the manifestation of TB in the central nervous system that resembles metastasis, where no classical TB symptoms were found (through anamnesis) and imaging and histopathology tests showed contradicting results.

Case Illustration

The patient was a 25-year-old male with complaints of weakness in both legs since September 2018. Weakness initially started on the right side of the leg, then spread to the left leg a week later. Symptoms gradually worsened and when presented to the hospital the patient was unable to move both legs. Examination revealed that patient suffered from upper motor neuron paraplegia. The patient also complained of thickness from the navel to the feet, unbearable defecation and micturition, back pain as well as a left-sided headache. The patient initially had a cherry-sized lump on the left side of his head since June 2018, which then continued to grow to the size of a tennis ball. According to patient's medical records, patient had 2 seizures in January 2019, no history of trauma, no history of long-standing cough. Fig 1 shows the reported disease course of the patient.

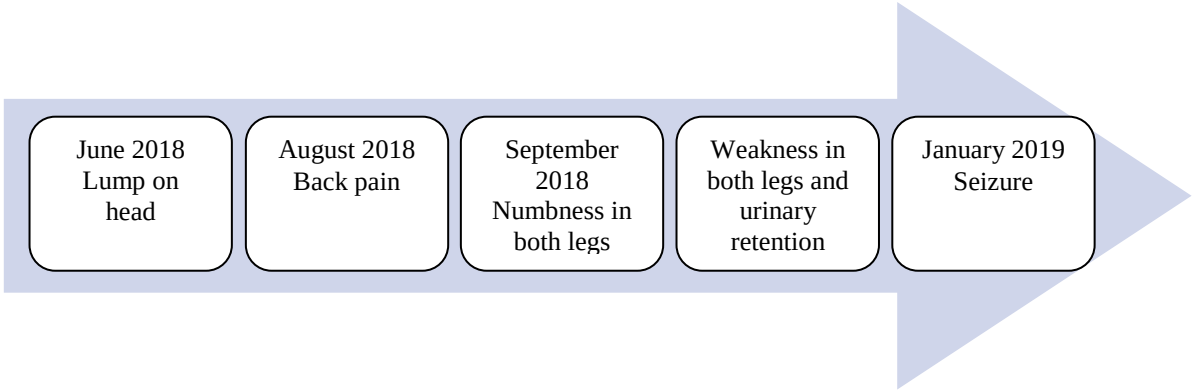


Figure 1. Disease course of patient

Results of patient's head MRI with contrast showed a solid lesion that absorbed the contrast in the form of a ring on the convexity of the left parietal lobe that extended to the left parietal skull bone with perifocal edema around it and destroyed the left parietal calvaria bone, which can be metastasis. Spectroscopic MRI images showed an increase in the intralesional choline/creatinine ratio and an increase in perilesional lactate lipids.

The patient underwent a biopsy of the tumor mass, duramater and calvarial bone. Macroscopic soft tissue with size of 1.3x0.9x0.5cm -5x3.5x1.7 cm was obtained. The soft tissue showed a white-gray color with a firm and spongy consistency, while the bone tissue appeared as a whitish lesion with a hard and solid consistency. The microscopic image showed fibrocollagenous connective tissue that contained many granulomas consisting of collections of epithelioid cells surrounded by lymphocytes. Some granulomas were accompanied by Langerhans cells. There were no signs of malignancy. In excised bone tissue, tissue regions infiltrated by lymphocytes and histiocytes formed granulomas. There were no signs of malignancy and through ZN staining, BTA bacteria was found. According to the anatomical pathology examination of the parenchyma, granulomatous inflammation and MTB bacteria were found in the parenchyma, duramater and calvaria.

Results of thoracolumbar MRI with contrast showed destruction of the lamina, transverse processes, spinous processes, and pedicles on the cervical vertebrae with soft tissue bulging consistent with TB.[4,5] These findings suggest that metastasis processes. Suspected mass in the center of right lung was also identified. CT-scan of the thorax with contrast showed a

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malignant lung mass with size 3.5x2.6x2.8 cm in the center of the right lung with lymphadenopathy in the right upper-lower paratracheal and subcarinal, as well as multiple metastases in the spine and sternum body (AJCC staging 8th 2017:T2aN2M1c), and bilateral pleural effusion hepatomegaly. Meanwhile, according to fibreoptic bronchoscopy examination, brushing cytology, pus cytology, broncho alveolar lavage (BAL), aspiration biopsy and forceps biopsy, no signs of malignancy were found. Tumor marker results: LDH 253, CEA 4.22 AFP 0.1 and CA-125 24.0.

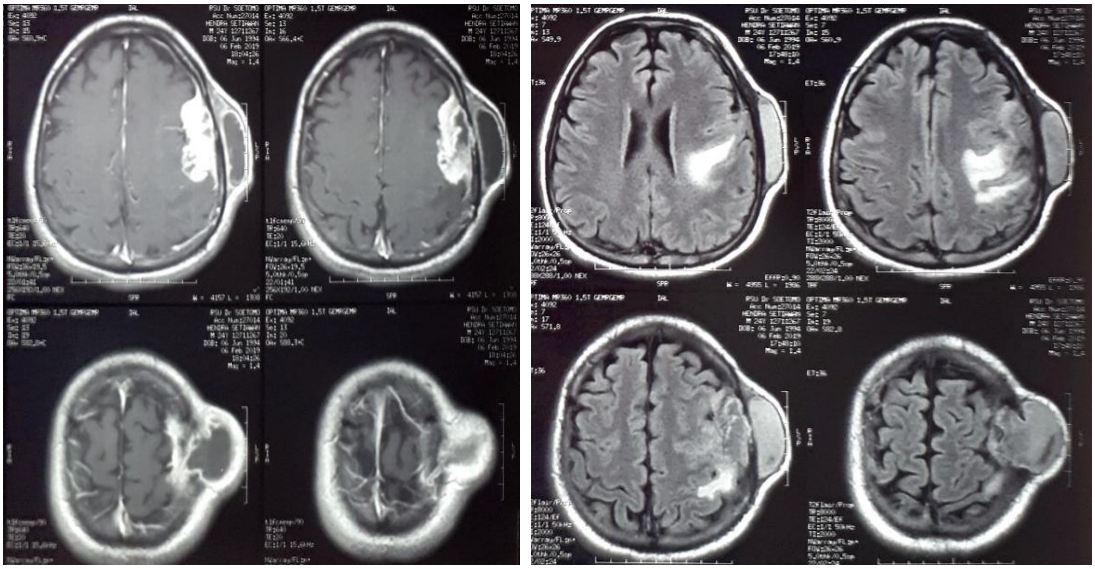


Figure 2. Axial MRI of the head with Rim enhancing contrast. Solid lesion in the convexity of the left parietal lobe that extends to the scalp of the left parietal region with perifocal edema surrounding it, destroying the left parietal calvaria.

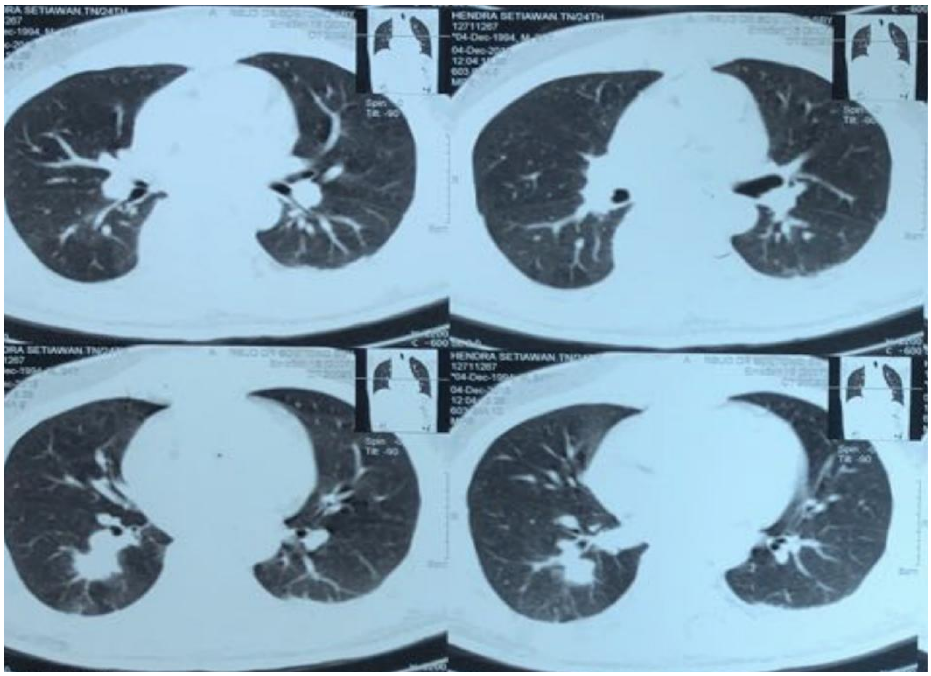


Figure 3. CT-scan of the thorax with contrast suggested malignant lung mass with size of 3.5x2.6x2.8 cm in the center of the right lung with lymphadenopathy in the right upper-lower paratracheal and subcarinal as well as multiple metastases in the spine and body of the sternum (staging AJCC 8th 2017:T2aN2M1c). Bilateral pleural effusion hepatomegaly.

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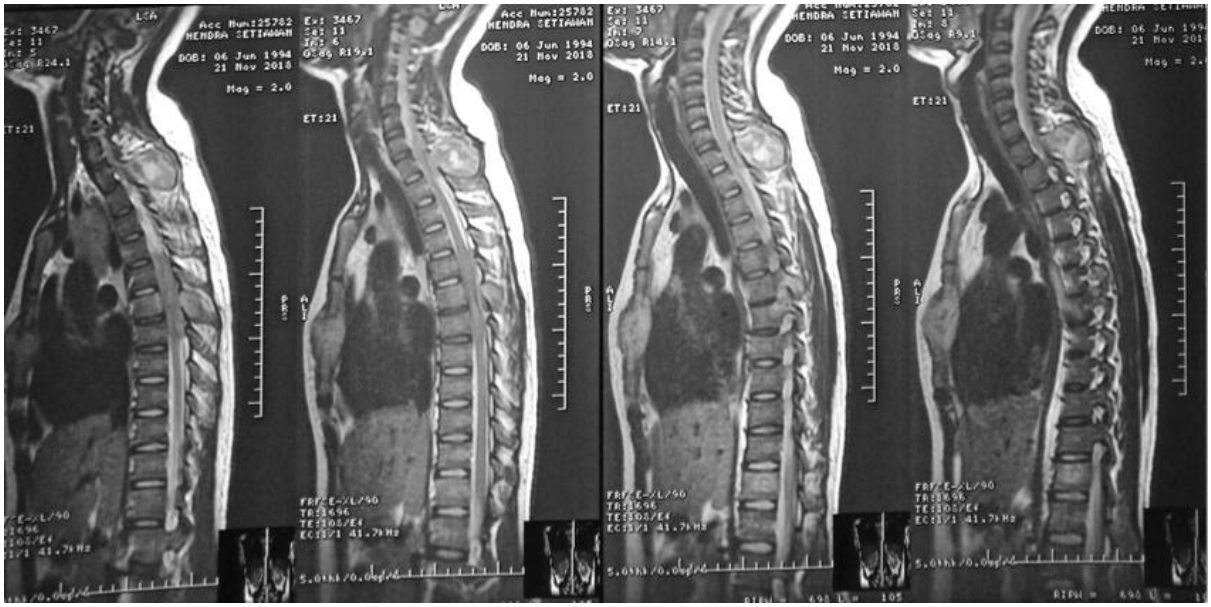


Figure 4. Thorax CT-scan showing destruction of the lamina, transverse processes, spinous processes, and pedicles on the cervical vertebrae is apparent accompanied by soft tissue bulging suggesting metastasis. Incidental finding: suspected mass in the center of right lung.

Discussion

TB is the major cause of infectious morbidity and mortality worldwide, especially in Southeast Asia. The involvement of extrapulmonary TB, where in this case with CNS TB manifestations in an immunocompetent person, causes difficulties in diagnosis and causes many differential diagnoses. In a retrospective study at the Department of Pathology of the Northem Institute of India from 2001 to 2009, results showed that the demographic characteristics of CNS TB were associated with gender, with more males (64.4%) than females (35.5%). In the same study, most CNS TB cases were found in patients ranging from 20-40 years of age with a total of 43.7% in that age group. Meanwhile, demographic data based on the location of lesions in CNS TB patients were mostly supratentorial (90.47%), having a major predilection in the frontal and parietal regions. In CNS TB, the involvement of the left hemisphere is the highest, with percentage of 55%. Meanwhile, 30% of cases include the involvement of the right hemisphere and 15% in both hemispheres.[1]

The case reported in this research occurred in a male patient aged 29 years with a lesion located supratentorial in the left parietal lobe, which is in accordance with the demographic data described above. However, this case is considered rare as the lesion was not only present in the parenchyma of the brain but extended to the duramater and destroyed the calvaria in the left parietal region, which resembles metastasis. This is supported by the spectroscopic examination, where results showed an increase in the intralesional choline/creatinine ratio and an increase in perilesional lactate lipids, therefore described as metastatic lesions by radiologists. Anatomical histopathological examination was then performed and results showed granulomatous inflammation and the presence of Mycobacterium tuberculosis.

There was a similar case reported by Chamberlin *et al.* in 2018.[7] In that case, TB infection attacked various organs such as the lungs, pleura, bilateral testes, spinal and cerebri. However, unlike the case in this study, the spread of the lesion did not expand and damage the scalp and calvaria.

Macroscopic soft tissue with size of 1.3x0.9x0.5cm -5x3.5x1.7 cm was obtained from the mass in the patient's head. The soft tissue was white-gray in color and had solid and spongy consistency. Meanwhile the bone tissue showed whitish lesions surrounding the center hole with a solid and firm consistency. Microscopically, the bone tissue showed fibrocollagenous connective tissue containing many granulomas consisting of a collection of epitheloid cells surrounded by lymphocytes. Some granulomas were accompanied by Langerhans datia cells. There were no signs of malignancy. In the bone tissue, regions of tissue with infiltration of inflammatory cells of lymphocytes and histiocytes forming granulomas were found. Even so, there were no signs of malignancy and through ZN staining, BTA bacteria was found. According to the anatomical pathology examination, granulomatous inflammation and MTB bacteria were found on the parenchyma, duramater and calvaria.

Another manifestation of CNS TB in the case in this study was spinal TB. The thoracolumbar vertebrae is the most common region of infection in spinal TB, although other regions of the vertebrae can be affected. Spinal TB attacks the anterior portion of the vertebral body to the intervertebral disc, which is characterized by the destruction of the end plate. The posterior elements are usually also affected. Spread to the intervertebral disc instantly occurs, which reveals erosion of the anterior vertebral body caused by a soft tissue abscess. The anatomical distribution of the vertebral vessels is related to age. In adults, the highly vascularized vertebra is the angle of the vertebral body adjacent to the endplate and is therefore the most common site of initial infection. Subsequently, the infection spreads to the endplate of the opposite side of the vertebra, the disc space, the spinal arch and under the anterior or posterior longitudinal ligaments, leading to expansion of the infection to several adjacent or separate vertebral segments.[4] This is different compared to the case reported in this study, where the cervicothoracolumbar MRI radiological image showed damage in the lamina, transverse process, spinous process and pedicle of the cervical vertebrae accompanied by soft tissue bulging, where in general the above findings lead to metastasis.[4,5]

In the case in this study, pulmonary manifestation, which is the most common form of TB infection, was also found. However, clinical respiratory symptoms such as coughing up blood, prolonged cough and shortness of breath were not found. However, CT scan of the thorax + contrast showed the presence of a malignant lung mass with size of 3.5x2.6x2.8 cm in the center of the right lung with lymphadenopathy in the upper-lower right paratrachea and subcarina with multiple metastases in the spine and the body of sternum as well as bilateral pleural effusions. These findings resemble metastasis.

CT-scan of the thorax in patients with lung metastasis usually shows a solitary lesion with nodule size >2-3 cm, speculated edges and absorbs contrast with punctate calcification as well as bronchovascular invasion (air bronchogram is present). Meanwhile in pulmonary tuberculoma images, multiple lesions with a round or polygonal shape with flat edges is accompanied by satellite nodules and do not absorb contrast.[5] This is inconsistent with the radiological images of the patient reported in this research. The histopathological results showed granulomatous inflammation and tuberculosis. GeneExpert examination found that rifampicin-sensitive MTB.

The patient reported in this research is an immunocompetent individual, as evidenced by an absolute CD4 count of 503. TB usually reacts differently in immunocompromised patients and immunocompetent patients. In immunocompromised patients, disseminated extrapulmonary TB generally occurs, no restriction area is present, multibacillary occurs and patients are often resistant to first-line therapy.[8]

There is a theory that states that the cause of disseminated TB in immunocompetent individuals is the energy level in that individual, where the body's defense mechanism lacks reactions against foreign substances and consists of induction of peripheral lymphocyte tolerance due to the human leukocyte Ag phenotype. Another theory states that this may be caused by intercurrent infections, which are infections that occur during the course of another disease and modifies the course of other diseases, usually in conditions of chronic viral infections such as CMV, hepatitis C and HHV2, which cause deficiency of cytotoxic NK cell activity due to chronic viral infection, resulting in temporary immunosuppression against TB bacteria resistance.[8]

Conclusion

In establishing the diagnosis of multiple CNS TB that is similar to the description of metastasis is not easy. In addition to clinical and radiological manifestations, histopathological analysis plays an important role in establishing the diagnosis in this case. The detection of MTB bacteria from bacterial culture examination is the gold standard for diagnosing TB. The high mortality rate in CNS TB is caused by late diagnosis and inadequate treatment for TB and its complications. This case report is expected to add information related to CNS TB disease that exists in Indonesia.

References

1. Lapausa, M.R., Saldana, A,M., Asensio, A.N., 2015. Extrapulmonary Tubercolosis: An Overview, Rev Española SanidPenit, p. 3-11.
2. Mubeen, B., Ul Rasool, M., Hamid, S., Haq, S., Hameed, R., Khursheed, N., Baba, K.M., 2015. A Clinical Study to See the Relationship between CNS Tuberculosis and Various Demographic Factors in a Population Attending a Tertiary Hospital in Northern India, Journal of Medical Science and Clinical Research, p. 3997-4007.
3. Rock, R.B., Olin, M., Baker, C.A., Molitor, T.W., 2008. Peterson, P.K., Central Nervous System Tuberculosis: Pathogenesis and Clinical Aspects, Clinical Microbiology Reviews, p. 243-261.
4. Rivas-Garcia, A., Sarria-Estrada, S., Torrents-Odin, C., Casas-Gomila, L., Franquet, E., 2013. Imaging Findings of Pott's Disease, European Spine Journal, p. 567-578.
5. Totanarungroj, K., Chaopotong, S., Tongdee, T., 2012. Distinguishing Small Primary Lung Cancer from Pulmonary Tuberculoma using 64-slices Multidetector CT, Journal of the Medical Association of Thailand, p. 574-582.
6. Castro-Gago, M., Gelabert, M., 1992. Central Nervous System Tuberculosis, Pediatric Neurology, p. 240.
7. Chamberlin, K., Orfanos, S., Mukherjee, A., Moy, E., Koganti, M., Khan, W., 2018. A Case of Disseminated Tuberculosis Mimicking Metastatic Cancer, Respiratory Medicine Case Reports, p. 239-241.
8. Kaur A, Kucheria M, Gupta R. Extensive Multisystemic Disseminated Tuberculosis in an Immunocompetent Patient, J Clin Aesthet Dermatol.2018;11(9);42-46