LARGE IMMUNOLOGICAL CEREBRAL VASCULITIS, ENCEPHALITIS, AND MULTIPLE INFARCTION CAUSED BY MYCOBACTERIUM TUBERCULOSIS INFECTION IN YOUNG ADULTS : A RARE COMPLICATION OF TUBERCULOSIS)

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ABSTRAK
Tuberkulosis Neurovaskular-serebral adalah kondisi yang jarang terjadi, ditemukan pada sekitar 1% dari total kasus komplikasi tuberkulosis. Infeksi ini dapat menyebabkan vaskulitis serebral tidak hanya melalui invasi langsung, tetapi juga melalui deposisi kompleks imun. Kasus ini menjelaskan tentang vaskulitis serebral luas dan infark yang disebabkan oleh tuberkulosis pada dewasa muda. Seorang wanita muda berusia 21 tahun datang ke unit gawat darurat dengan keluhan bicara tidak jelas sejak satu hari sebelumnya. Pasien menggigil dan tidak merespons saat diajak berbicara. Pemeriksaan fisik menunjukkan tekanan darah 101/65 mmHg, nadi 80x/menit, suhu 36,7°C, dan saturasi oksigen (SpO2) 97%. Pemeriksaan neurologis menunjukkan GCS 456, tanda meningeal (+). Pemeriksaan laboratorium awal menunjukkan Hb 9,6 g/dl; HCT 29,8%; neutrofil 84,9%, limfosit 7%, SGOT 29 U/L, SGPT 51 U/L. Pemeriksaan rontgen dada menunjukkan dugaan tuberkulosis milier paru. Pemeriksaan dahak menunjukkan hasil positif DNA MTB dan sensitif terhadap rifampisin. Pemeriksaan serologis HIV tidak menunjukkan kelainan. Hasil CT scan kepala dengan kontras menunjukkan infark multipel pada hemisfer bilateral dan nukleus lentiform bilateral dari korpus kalosum bilateral. Pasien didiagnosis dengan vaskulitis serebral luas, ensefalitis, dan infark multipel yang berhubungan dengan infeksi tuberkulosis. Pasien mendapat pengobatan FDC (fixed dose combination) untuk tuberkulosis, antikonvulsan, mecobalamin, PPI, dan steroid dosis tinggi. Kasus ini tergolong langka, terutama sebagai komplikasi tuberkulosis yang menyebabkan vaskulitis serebral luas dan ensefalitis pada pasien dewasa muda. Deteksi dini merupakan kunci penting dalam memberikan pengobatan yang tepat kepada pasien.

Kata kunci : ensefalitis, infark, meningitis, tuberkulosis, vaskulitis serebral

ABSTRACT
Cerebral Neurovascular tuberculosis is rare condition that occur in 1% of total case in complication of tuberculosis. This infection can cause cerebral vasculitis not only by direct invasion, but by immune complex deposition. This case explain about large cerebral vasculitis and infarction caused by tuberculosis in young adult A 21 year old young woman came to the emergency room with complaints of incoherent speech one day before. The patient shivering and does not respond when spoken to. Physical examination showed BP: 101/65, pulse: 80x/minute, temperature: 36.70C and SPO2 97%. Neurological examination: GCS 456, meningeal sign (+). Initial laboratory examination showed Hb 9.6 g/dl; HCT 29.8%; Neutrophils 84,9%, lymphocytes 7%, SGOT 29 U/L, SGPT 51U/L. Chest x-ray examination showed suspicion of miliary pulmonary TB. Sputum examination showed positive results for MTB DNA and sensitivity to rifampicin. HIV serological examination did not reveal any abnormalities. The results of a Head CT scan with contrast showed multiple infarctions in the bilateral hemisfer and bilateral lentiform nuclei of the bilateral corpus callosum. The patient was diagnosed by large cerebral vasculitis, encephalitis, multiple infarction related tuberculosis infection. The patient received FDC of tuberculous, anticonvulsant, mecobalamin, PPI, and high dose steroids. This case is relatively rare, especially in complications of tuberculosis which causes extensive cerebral vasculitis and encephalitis in young adult patients. Early detection is an important key to providing appropriate treatment to patients.

Keywords *: cerebral vasculitis, infarction, tuberculosis, encephalitis, meningitis*

INTRODUCTION

Tuberculosis is one of disease with high prevalance in the world. Indonesia become number 2 of highest prevalence with 1.060.000 cases in 2024. Meanwhile, the mortality rate of tuberculous is 134.000 cases per year. A rare manifestation of tuberculous is Central Nervous System Tuberculous / CNS-TB and one of it is cerebral vasculitis tuberculous. Cerebral vasculitis tuberculosis is rare condition that occur in 1% of total case in complication of tuberculosis (Daniel, *et. al.,* 2019). Vasculitis can affect blood vessels including cerebral vascular. Cerebral vasculitis tuberculosis accounts for 12.5% of secondary cerebral vasculitides (Chen, *et. al.*, 2014). Vasculitis can cause by tuberculous infection by immune complex deposition or direct invasion by Mycobacterium tuberculous. Cerebral vasculitis associated by meningitis and encephalitis. Tuberculous meningitis (TBM) has a poor prognosis, and survivors often have severe disabilities (Daniel, *et. al.,* 2019). This case explain about large cerebral vasculitis and multiple infarction caused by tuberculosis in young adult who experienced tuberculous treatment in 5 years recently.

CASE REPORT

Table 1. Initial Laboratory Examination

Parameter	Nilai lab pasien	Satuan	Nilai normal
	Eritrosit		
RBC	4,65	10^6/uL	4 -5,5
Hb	9,6	g/dL	12-16
HCT	29,8	%	37-54
MCV	64,2	fL	80-100
MCH	20,6	Pg	27-34
MCHC	32,1	g/dl	32-36
	Leukosit		
White blood cells	6,83	10^3/uL	4.000-10.000
Limfosit	7,0	%	20-40
Neutrofil	84,9	%	45-70
Eosinofil	0,9	%	0,5-5
Basofil	0,3	%	0-1
Monosit	6,9	%	3-12
	Liver function		
SGOT	29	U/L	0-37
SGPT	51	U/L	Pr: 0-32
	Renal Function		
Creatinin	0,48	Mg/dl	Pr: 0,45-0,75
UREA	13	Mg/dl	10-50

A 21 year old young woman came to the emergency room of RSUD dr. Koesnadi Bondowoso with main complaints of incoherent speech one day before. The patient shivering and does not respond when spoken to. Physical examination showed BP: 101/65, pulse: 80x/minute, temperature: 36.7^{0}C and SPO2 97%. Neurological examination: GCS 456, meningeal sign (+). Initial laboratory examination showed Hb 9.6 g/dl; HCT 29.8%; Neutrophils 90%, lymphocytes 7%, SGOT 29 U/L, SGPT 51U/L (Table 1). Chest x-ray examination showed suspicion of miliary pulmonary TB (Image 1). Sputum examination showed positive results for MTB DNA and sensitivity to rifampicin. HIV serological examination did not reveal any abnormalities. The results of a Head CT scan with contrast showed multiple infarctions in the bilateral frontal, temporal, and parietal lobes and bilateral lentiform nuclei of the bilateral corpus callosum (Image 2). The patient was diagnosed by large cerebral vasculitis, encephalitis, and multiple infarction related tuberculosis infection. The

patient received FDC of tuberculous, anticonvulsant, neuroprotectant, PPI, and high dose steroids. Patients showed clinical improvements in 7 days after comprehensive treatment.

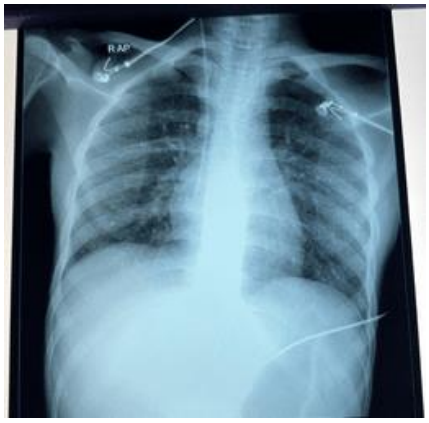

Figure 1. Chest X-Ray Examination Showed Suspicion Of Miliary Pulmonary TB

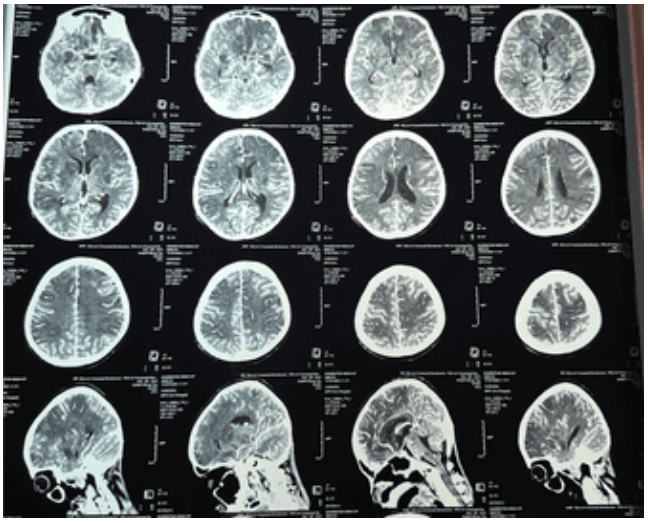

Figure 2. Head CT Scan With Contrast Showed Multiple Infarctions In The Bilateral Frontal, Temporal, and Parietal Lobes and Bilateral Lentiform Nuclei Of The Bilateral Corpus Callosum

DISCUSSION

Tuberculosis is a infectious disease that have high prevalance worldide. Tuberculosis prevalence noted about 1.060.000 cases per year in the world. Tuberculosis have various manifestation. Usually, tuberculosis affected pulmonal and called pulmonary tuberculosis (Roy, *et. al.,* 2023). Eventually, tuberculosis can affected another organ called extrapulmonary tuberculosis. Tuberculosis meningitis (TBM), vasculitis, and infarction are among extrapulmonary tuberculosis that have a rare prevalence in the world. About <1% of tuberculosis cases classified as TBM and vasculitis cases. TBM frequently presents with non-specific symptoms in the early stages and is diagnosed in the later stages of the illness when brain damage has already occurred (Erdemli, *et. al.,* 2020).

In this case, a young woman presented with incoherent speech one day before. The patient complaint shivering and physical examination showed BP: 101/65, pulse: 80x/minute, temperature: 36.7^0C and SPO2 97%. Neurological examination: GCS 456, meningeal sign (+). Initial laboratory examination showed Hb 9.6 g/dl; HCT 29.8%; Neutrophils 90%, lymphocytes 7%, SGOT 29 U/L, SGPT 51U/L. patient showed neurological deficits with positive meningeal sign that suggest Meningitis and increased in neutrophil indicated infection in patient. On another examination, Chest x-ray showed suspicion of miliary pulmonary TB.

Sputum examination showed positive results for MTB DNA and sensitivity to rifampicin. HIV serological examination did not reveal any abnormalities. This examinations showed positive results of tuberculosis infections and no other co infections.

Cerebral vasculitis caused by mybacterium tuberculous refers to inflammation of the vascular in cerebral that caused by some mechanism. The exact mechanism of cerebral vasculitis is still not known. Various possible mechanisms proposed include immunogenic reaction to the bacilli, deposition of immune complexes, and direct invasion by tubercular bacilli in the vessels. On other hand, mechanism of infarct caused by tuberculosis infection consist of multiple stages. The initial risk for acute infarcts is attributed to vasospasm and less commonly to vascular thrombosis; while, infarcts in the later stage of the disease are attributed to proliferative lesions causing luminal compromise due to thickening of the vessel wall (Wang, *et. al.,* 2015).

Other mechanism that explain about pathogenesis of tuberculous meningitis is microglia infection. Microglia in cerebral parecnchyma are the principal CNS cells infected by *M. tuberculous*. *M. tuberculous* is recognized by microglial cells via innate immune and neuro-specific receptors, including pattern recognition receptors. Activation of microglia leads to secretion of a number of cytokines that induce leading pro-inflammatory response through NAPDH oxidase-dependant reactive oxygen species (ROS) generation. This condition stimulate inflammatory response that induce Tumor Necrosis Factor (TNF). TNF-a production in the CNS also increases permeability of BBB and thus influc other immune mediator in the CNS (Davis, *et. al.,* 2019; Isabel & Rogerio, 2014).

The patient was diagnosed by large cerebral vasculitis, encephalitis, and multiple infarction related tuberculosis infection. This diagnosis made by various clinical approach from neurological examination and other adjuvan examination (Wilkinson, *et. al.,* 2017). The results of a head CT scan with contrast showed multiple infarctions in the bilateral frontal, temporal, and parietal lobes and bilateral lentiform nuclei of the bilateral corpus callosum. This results indicated a large vasculitis and multiple infarction caused by active pulmonary tuberculosis. The diagnosis of tuberculous meningitis and encephalitis become more challenging. Combination of multiple diagnostics approach will increasing accuracy of diagnostic. Real-time PCR, hold promising results for TB diagnosis but need optimization for early detection of TBM. Moreover, CSF IGRA is also used but unable to differentiate between active and latent TB (Manyelo, *et. al.,* 2021; Méchaï & Bouchaud, 2019). On addition, Magnetic Resonance (MR) based vessel wall imaging (VWI) also can identify intracranial vasculitis (Vanjare, *et. al.,* 2021) In this case, diagnostic made by neurologist by combination of diagnostics approach sucah as physical and neurological examination, real-time PCR, thorax plain photo, and Head CT Scan (Ahlawat, *et. al.,* 2020). Recent studies on CSF biomarkers provide a better understanding of the inflammatory cascade and neuromarkers of brain damage and suggest potential for novel host-directed therapy (Donovan, *et. al.,* 2020; Wasserman & Harrison, 2023).

The neurocritical care of tuberculous meningitis are predominantly focus on diagnosis, inflammatory processes, and antituberculosis theraphy (Donovan, *et. al.,* 2019). The patient received Fixed Drug Combination (FDC) of tuberculous, anticonvulsant, neuroprotectant, PPI, and high dose steroids. Patients showed clinical improvements in 7 days after comprehensive treatment. This treatment corresponding to WHO Guidelines treatments for tuberculous meningitis. WHO consider three aspects to successful management: in TBM patients: (i) effective antimicrobial treatments, (ii) controlling the host inflammatory response, and (iii) supportive interventions to reduce raised intracranial pressure (Davis, *et. al.,* 2018). WHO suggest that tuberculous meningitis and vasculitis without HIV infection should given antituberculous theraphy that include rifampicin 10 mg/kg/day, Isoniazid 5 mg/kg/day, pyrazinamide 25 mg/kg/day, ethambutol 15 mg/kg/day. Dexamethasone suggest to given

0,3mg/kg/day and withdrawn after 6 weeks (Lin, 2025; Mezochow, *et. al.*, 2017; Prasad, *et. al.*, 2016). After the patient showed good clinical response to treatment, an evaluation should be carried out after 8 weeks. Culture mycobacterium tuberculosis should be done after 8 weeks. Host directed therapies like aspirin may be appropriate in patients with high vasculitic burden and evidence of ongoing ischemic events where corticosteroids have failed (Huynh, *et. al.*, 2022).

CONCLUSION

This case is relatively rare, especially in complications of tuberculosis which causes extensive cerebral vasculitis and encephalitis in young adult patients. Early detection is an important key to providing appropriate treatment to patients. Another research is needed to exploring various diagnostic approach based on novel technology for improving diagnosis accuracy.

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