Improvement of Complete Oculomotor Cranial Nerve Palsy with Pupillary Involvement in Patient with Tuberculoma, a Rare Case

ABSTRACT

Introduction: Tuberculosis infection that spread to the CNS is a sign of severe case of TB, accounting for 5-10% from all extrapulmonary TB. One of the most rare manifestation of CNS TB is tuberculoma, accounts for 1% from all CNS TB. Tuberculoma lesion in the cranial will affect neurological functions, depending on its location.

Purpose: The puprose of this study is to present a case of unilateral complete oculomotor cranial nerve palsy with pupilary involvement due to tuberculoma.

Case Report: A 20 year old female came with chief complaint dropped right eyelid since two months ago. There was no pain around eye, headache, nausea, or vomit. Ophthalmological examination showed exotrophia 7 degree, limitation of ocular motility, ptosis, and iridoplegia of the right eye. Patient previously had history of pulmonary tuberculosis medication for six months that already finished two months ago. CT scan revealed multiple tuberculoma of cerebral with the largest tuberculoma $\pm$ 0.9 mm on the brainstem. Patient was diagnosed with complete oculomotor nerve palsy with pupillary involvement of the right eye due to multiple tuberculoma. Patient was treated with oral methylprednisolone, oral mecobalamine, calcium and vitamin D supplementation. For the brain tuberculoma, anti tuberculosis drug regimen was given.

Conclusions: Apropiate history taking, physical and ophthalmological examinations, and imaging are needed to diagnose the etiology of a patient with oculomotor nerve palsy. Hematogenous spread of *Mycobacterium tuberculosis* to the CNS causing tuberculoma formation. Anti tuberculosis drug regimen are needed, whereas steroid therapy can be given as an adjuctive therapy.

Keywords: Tuberculoma, Oculomotor nerve palsy, Pupillary involvement.

I. INTRODUCTION

Tuberculosis (TB) is a contagious infection that caused by rod shaped bacili *Mycobacterium tuberculosis*. It can infected either pulmonary organ or extrapulmonary, including central nervous system. Tuberculosis infection to the central nervous system (CNS) is a sign of severe and rare form of TB. Central nervous system infection due to *Mycobacterium tuberculosis* accounts for 5-10% of all extrapulmonary tuberculosis. Manifestation of CNS TB including meningitis, cerebritis, abscesses, spinal tuberculous arachnoiditis, and tuberculoma. Intracranial tuberculoma accounts only for 1% from total CNS TB.[1,2]

Tuberculoma is an enlargement of tubercle in the brain parenchyma without any rupturing into the subarachnoid. Tuberculoma formed due to haematogenous spread

or adjacent spread from meningeal or vertebral. Tuberculoma of central nervous system can form in any site. Cerebrum and cerebellum are the most common site of tuberculoma location, especially frontal and parietal lobe for adult and infra-tentorial involvement for pediatric group.[2–4]

Oculomotor nerve palsy can be caused by neoplasm, trauma, ischemic lesion, and life-threatenig aneurysm. Anatomically, the lesion components are divided into infranuclear (peripheral), nuclear, internuclear, and supranuclear. It may be sparred the pupillary function or with pupillary involvement. A pupillary involvement in complete oculomotor nerve palsy should be evaluated carefully to exclude the etiology of aneursym. Intracranial tuberculoma may be present with focal neurological deficit, including oculomotor nerve palsy, with or without any systemic clinical manifestation. Treatment of choice of intracranial tuberculoma is tuberculosis drugs regimen with steroid, and surgical interventions for refractory case.[2,3,5,6] This case report is aimed to describe a complete occulomotor nerve palsy with pupillary involvement that caused by a rare intracranial tuberculoma.

II. CASE REPORT

Twenty years old woman came to Neuro-opthalmology outpatient clinic Cicendo Eye Hospital 5th November 2020 with a chief complaint of dropped right eye (RE) eyelid since two months ago. Dropped eyelid did not change with activity or rest. The complaint was accompanied with double vision, horizontal diplopia that lessen when one eye is closed. History of blurred vision, red eye, headache, nausea or vomit were denied by the patient. There were no history of trauma, limb weakness, fever, cough, sneezing or shortness of breath in this patient. Patient had a history of pulomonary tuberculosis infection eight months ago and had been treated with anti tuberculosis drug regimen for six months. The lung tuberculosis medication had been stopped two months ago by the internist.

General examination of this patient showed fully alert consciousness, blood pressure 96/70 mmHg, respiratory rate 20x/min, pulse 71 bpm, temperature 36.9 C, and body weight was 35 kilograms. Visual acuity of the RE was 0.2 pinhole 0.5 and the left eye (LE) was 0.3 pinhole 0.63 on the snellen chart. Both eye showed 1.0

visual acuity with patient's correction spectacles. Primary position of the eye showed exotrophia 7 degree. Eyeball movement of the right eye were reduced to the superior (-4), medial (-2), and inferior (-1), but there was no reduction of motility to lateral (0) or pain on eyeball movement. Left eye ocular motility showed full range of motion and no pain during eye movement (Figure 1).

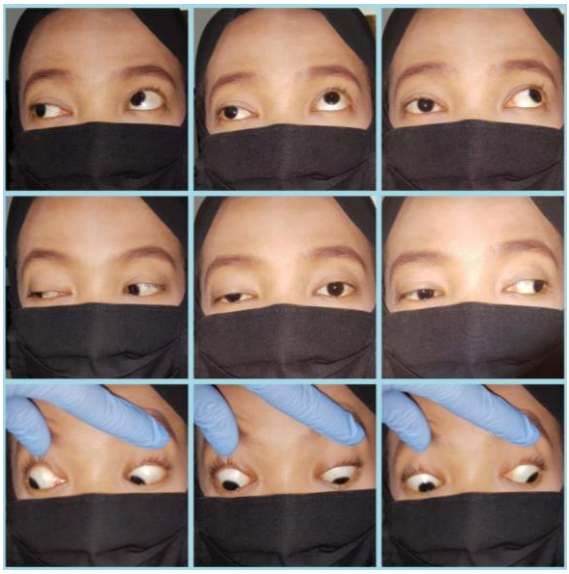

Figure 1. Nine cardinal position of the patient at the first time visit.

Anterior segment examination of the RE showed ptosis of the eyelid with margin to reflex distance (MRD) 1 was -1 mm, MRD 2 was 7 mm. The total interpalpebral fissure (IPF) were 6 mm with 10 mm levator function (LF). Conjunctiva, cornea, and anterior chamber were within normal limit. Direct and indirect pupil reflex of the right eye were reduced, with no reverse relative afferent pupillary defect (reverse RAPD) on the left eye, suggesting iridoplegia of the right eye. Lens and funduscopy were within normal limit. Ophthalmological examination of the left eye showed normal findings, with MRD 1 was 4 mm, MRD 2 was 7 mm, IPF 11 mm and LF 12 mm. Pupillary light rexlex direct and indirect of the left eye showed normal reflexes.

Color vision, contrast sensitivity and amsler grid for both eyes were within normal limit. Neurological examinations showed full motoric function for superior and inferior extremities and there was no any other cranial nerve function abnormalities. Funduscopy, optical coherence topography (OCT), and Humphrey

examinations for both eye were within normal limit (Figure 2). Computed tomography (CT) scan of head and orbita 11th November 2020 revealed homogenous isodens lesions on the left and right cerebral with the largest diameter was about ± 0.9 mm at the brainstem with contrast enhacement on its wall. This lesion suggesting multiple tuberculoma at the right and left cerebral, with the largest tuberculoma at the brainstem (Figure 3).

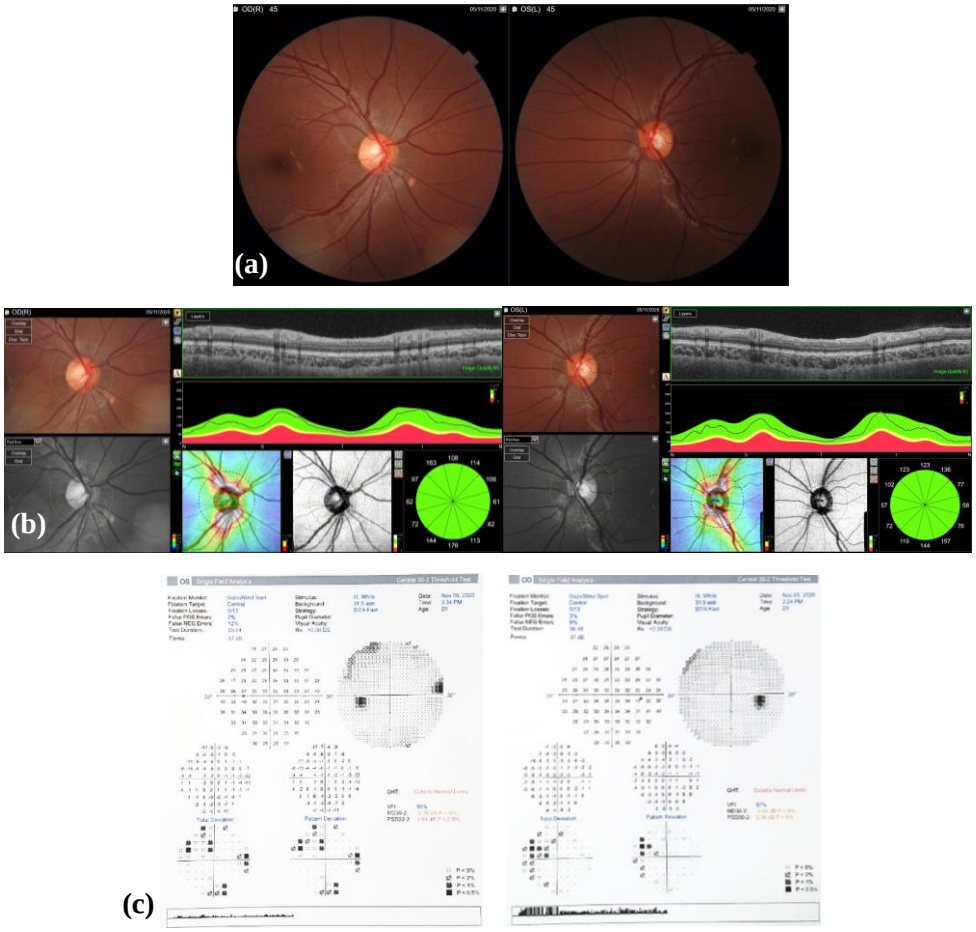

Figure 2. (a) Funduscopy examination; (b) OCT examination; (c) Humphrey examination

The patient was diagnosed with complete third (oculomotor) cranial nerve palsy of the right eye with pupillary involvement due to multiple brain tuberculoma and resolved pulmonary tuberculosis. Treatment management of the patient were oral methylprednisolone 1 mg/kg body weight, oral mecobalamine 500 mcg once daily, oral lansoprazole 30 mg bid, calcium and vitamin D3 supplementation three times

a day. The patient also consulted to the neurology and pulmonary department for tuberculosis diagnosis evaluation and management.

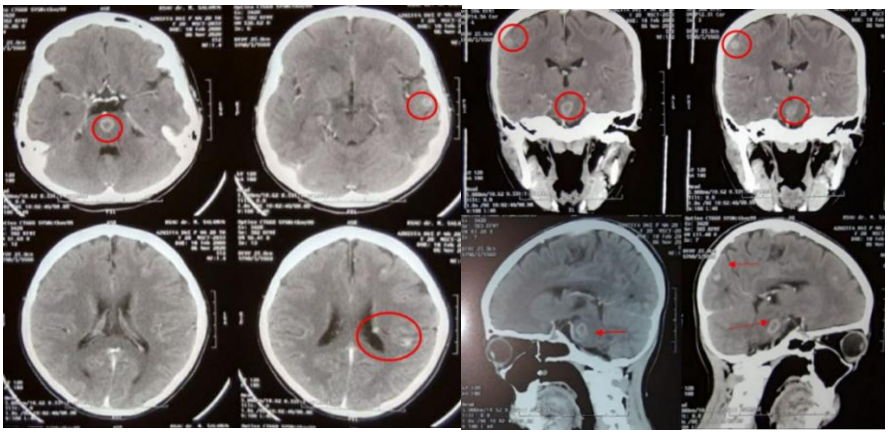

Figure 3. CT scan: Multiple tuberculoma of cerebral and brainstem.

At one week follow up visit, the patient showed some improvement of dropped eyelid. The diplopia also reduced with improvement of right eyeball range of motion. Full range of motion to the inferior and lateral, with some reduction to superior (-3) and medial (-1). Examination of MRD 1 was 3.0 mm, MRD 2 7.0 mm, and IPF was 10 mm (Figure 4). The patient continued the treatment regiment from Neuro-opthalmology unit with tappering off Methylprednisolone dosage every one week.

(a) (b)

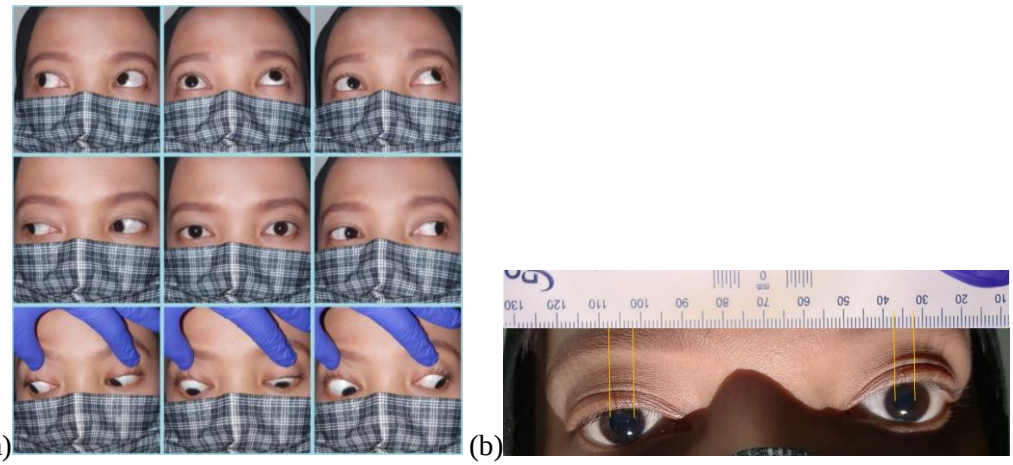

Figure 4. Examinations at one week follow up: (a)Ocular motility, (b)Pupillary diameter in dim light.

The Neurology department refered the patient to the Directly Observed Treatment Shourtcourse (DOTS) outpatient clinic at Hasan Sadikin Hospital

Bandung. The patient was given tuberculosis drug regimen or *Obat Anti Tuberkulosis* (OAT) for the next 9 months from DOTS outpatient clinic. The anti tuberculosis drug regimen consist of Ethambutol 750 mg once a day, Rifampicin 900 mg once a day, Isoniazid 300 mg once a day, and Pyrazinamide 1500 mg once a day.

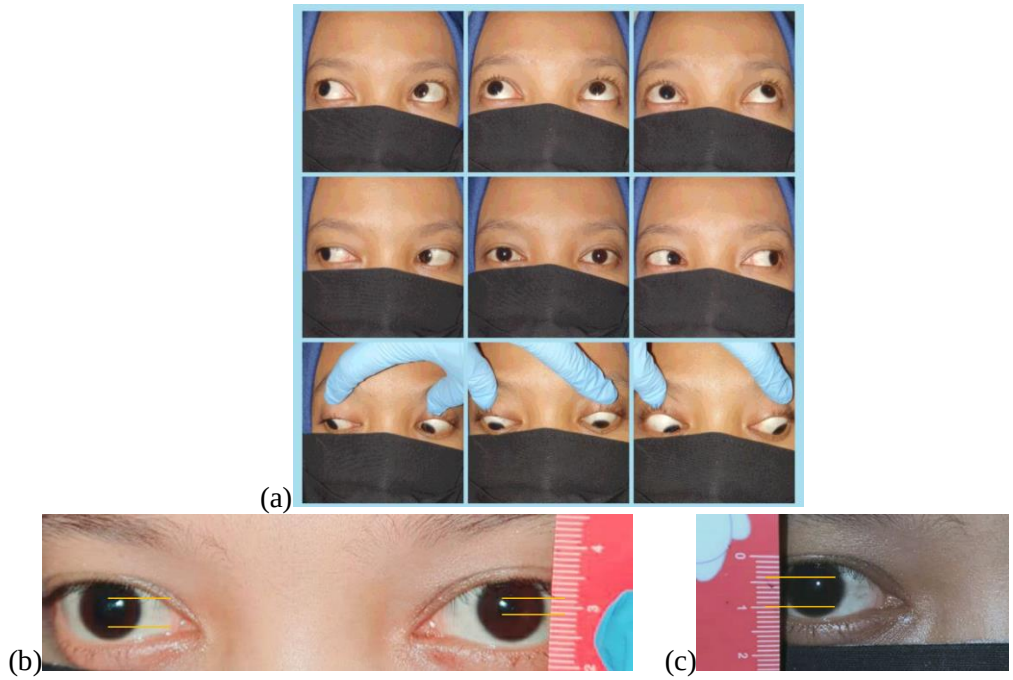

Figure 5. Examinations one month follow up: (a) ocular motility, (b) pupilary diameter in the bright, (c) RE pupillary diameter in dim light.

One month follow up examination revealed improvement sign and symptoms of the patients. Hirshberg examination was orthotrophia, with slight limitation of the right eye ocular motility, -1 to the superior and no limiatation to the medial, lateral and inferior. The pupil diameter of the right eye was 6.0 mm in the dark, and 5.0 mm in the light. The pupil diameter of the left eye was 5.0 mm in the dark and 2.0 mm in the light (Figure 5). Six weeks follow up examination showed there was still limitation right eye ocular motility to superior (-1), anisocoria with pupil sizes of the right eye were 6.0 mm in dim light, and 5.0 mm in bright light whereas the left eye were 5.0 mm in dim light and 2.0 mm in bright light. The patient continued the anti tuberculosis medication, Methylprednisolone oral tappered off, Mecobalamine 500 mcg once daily, Calcium and vitamin D supplementations three times a day, and Lansoprazole 30 mg twice a day. The patient instructed to get follow up visit

every one month. Prognosis of this patient *quo ad vitam ad bonam, quo ad functionam*, and *quo ad sanationam* were *ad bonam*.

III. DISCUSSION

Extensions of Mycobacterium tuberculosis bacteria to the CNS can lead to a rare and severe form of tuberculosis, known as cerebral tuberculoma. Mycobacterium tuberculosis spread hematogenously to the highly oxygenated organs like brain, or proximity expansion of a meningeal or tubercular TB. Enlargement of tubercles in the brain parenchyma will form tuberculoma. Cerebral tuberculoma accounts for 1% from all CNS tuberculosis and had a high morbility and mortality rate. Manifestations of intracranial tuberculoma including headache, fever, seizure, hemiplegia, papilledema, cranial nerve palsies, and other clinical symptoms of increased intracranial pressure. Some non specific feature of intracranial tuberculoma such as fatigue, malaise, weight loss, and loss of appetite. From the history taking and examination of this patient, the patient did not showed any non spesific complaint. There was no fatigue, malaise weight loss, or loss of appetite. But the patient had a history of previously pulmonary tuberculosis infection.[2–4]

Imaging of CNS tuberculosis may appear as low-dens or isodens lesion on the intial stage that can changed to encapsulated iso-dens or hypodense lesion with peripheral ring enhancement (target lesion). From CT scan of this patient, we found multiple homogenous isodens lesions on the left and right cerebral with the largest diameter was about $\pm$ 0.9 mm at the brainstem with contrast enhacement on its wall that suggesting multiple tuberculoma. Multiple lesion are seen in only 15-33% of CNS tuberculoma cases and mostly in endemic area. Involvement of frontal and parietal lobe usually occur in adult patient, whereas infra-tentorial involvement occur in children.[2–4]

Oculomotor nerve palsy can occured due to lesion to the oculomotor nucleus, oculomotor nerve fascicle, oculomotor nerve in subarachnoid space, oculomotor nerve in cavernous sinus and superior orbital fissure or oculomotor nerve in the orbit. The manifestation of oculomotor nerve palsy including dysfunction of somatic muscles (superior, inferior, medial rectus, inferior oblique, and levator

palpebra superioris) and autonomic muscles (pupillary spinchter and ciliary). Complete oculomotor nerve palsy comes with ptosis, ocular motility limitation in adduction, supraduction, and infraduction with the eye position deviated to downward and outward. The patient in this case report came with exotrophia eye position, unilateral ptosis, and ocular motility limitation to the superior, medial, and inferior. The patient right eye pupil also showed reduced both direct and indirect light reflexes.[7,8]

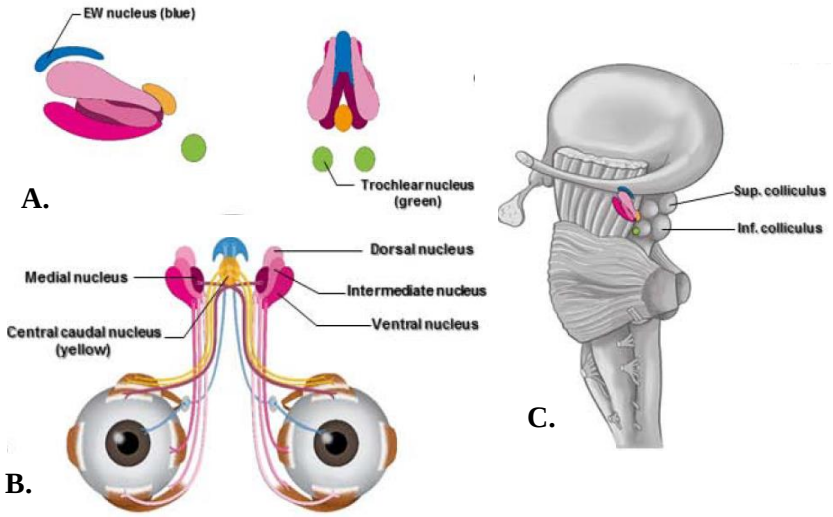

Figure 6. Oculomotor nerve complex at brainstem; A. Lateral and superior view of oculomotor nuclear complex. B. Schematic motor neuron for the extraocular muscle innervation. C. Oculomotor complex at the most ventral part of periacueduct gray at the level of superior colliculus.
Source: Park, HaeKwan et al[9]

Lesion that damaged the oculomotor neucleus are relatively uncommon and bilateral, with or without caudal (pupillary) subnucleus involvement. Bilateral ptosis produced due to both levator palpebra superioris muscle innervated by a single central caudal nucleus of oculomotor nerve complex (Figure 6). Lesion to the oculomotor nerve fasicle can resulted in complete or incomplete oculomptor nerve palsy, and this is cannot be differentiate from lesion outhside the mid brain. Lesion to the oculomotor nerve in subarachnoid space may be present with: (1) Isolated pupil dilatation with reduced/no light reflexes, (2) Ophthalmoplegia with pupilary involvement, or (3) Ophthalmoplegia with normal pupil. Isolated oculomotor nerve palsy with pupillary involvement mostly casued by intracranial

aneurysm. Particulary patient with intracranial aneurysm has a history of sudden severe pain in or around the eye. Since aneurysm is one of a life threatening condition, it is important to consider an intracranial aneurysm as a differential diagnosis of isolated oculomotor nerve palsy that comes with pupillary involvement. Lesion to the oclomotor nerve in cavernous sinus and superior orbital fissure will present with sphenocavernous syndrome, usually without any visual loss. Lesion of oculomotor nerve in the apex of orbit will manifest as proptosis, opththalmoplegia, and visual loss. In this patient, lesion in the brainstem resulted in total ophthalmoplegia and ptosis of the right eye. There was also pupillary involvement that cause midriasis pupil and reduced pupillary reflexes to the direct or indirect light reflexes.[7–9]

Management of cerebral tuberculoma based on United States Centers for Disease Control and Prevention (CDC) started with initial intensive phase for two months consist of isoniazid, rifampin, pyrazinamide and ethambutul). The treatment continued with isoniazide and rifampin for the next 7-10 months. Sharma et al recommend anti tuberculosis medication fot one and a half year is sufficient for brain tuberculoma. Mohammadian et al mentioned that treatment of CNS Mycobacterium tuberculosis is a four-drug regimen including rifampin, isoniazid, pyrazinamide, and ethambutol or rifampin, isoniazid, pyrazinamide with either fluorquinolone or aminoglycoside, administred daily for two months. The treatment then followed by isoniazid and rifampin for the rest course of 18 months. The patient got anti tuberculosis drug regimen from DOTS outpatient clinic Hasan Sadikin Hospital consist of isoniazid, ethambutol, pyrazinamide and rifampicin for the next following nine months.[2,3,10,11]

Steroid as an adjunctive therapy can be given to the patients with TB meningitis, basilar enhancement on radiographic findings, intracranial tuberculoma, high cerebrospinal fluid protein (>500 mg/dL), and worsen clinical symptoms after starting TB therapy. In tuberculoma, steroid indicated in cases associated with extensive perilesional edema. For the patients who did not responsive to the medication, or the patients with obstructive hydocephalus, midline shift, and compressions of the brainstem or spinal cord, surgical intervention can be

considered. In this patient, oral steroid Methylprednisolone are given 1 mg/kgBW that tappered off every week in order to reduce the perilesional edema. The patient showed improvement in ocular motility and eyelid ptosis with steroid medication at initial phase before oral anti tuberculosis drug regimen are given.[1–3,11]

IV. CONCLUSIONS

Lesion to the oculomotor nerve form the nucleus to the occulomotor nerve fiber in the orbit can cause oculomotor nerve palsy. Complete oculomotor nerve palsy with pupillary involvement is one of emergency and life threatening condition because its commonly caused by intracranial aneurysm. Apropiate history taking, examinations, and imaging are important to find the etiology of complete oculomotor nerve palsy. It is important to keep a broad differential diagnosis of oculomotor nerve deficit, including suspicion to the risk of TB, especially in patient with previous history of pulmonary TB. Multi-department approach are important to gain the best outcome for the patient, not only management therapy from ophthalmologist, but also neurologist and pulmonologist.

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