INVOLVEMENT OF TUBERCULOUS MENINGITIS PATIENT WITH HOSPITAL ACQUIRED PNEUMONIAE (Case Report)

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ABSTRACT

Meningitis is a global public health problem. The causes can be viruses, bacteria, fungi and parasites. Meningitis is an infectious disease that cannot be overcome and is still a problem in developing countries. As a developing country Indonesia, Tuberculosis has a high number of cases throughout the year. Tuberculous meningitis (TB) is an infection byMycobacterium tuberculosisabout meningor brain parenchyma resulting variety morbidity and mortality. A 39 years old woman came to the emergency room at Drs. H. Amri Tambunan complained of seizures 1 day ago with a duration of more than 1 hour. Seizures are found throughout the body. Also a fever was found 1 day today. Shortness of breath and cough were found for the past 3 days. Decreased appetite has been observed for the past 1 week. There was no history of nausea and vomiting. Os post VP shunt installation on May 29th, 2023. Female patient, 39 years old, with a diagnosis of Tuberculous Meningitis with Hospital Acquired Pneumoniae has been hospitalized from 9 to 20 September of 2023. And also outpatient treatment at the Pulmonology Departement is recommended.

Keyword: *Tuberculous Meningitis, Hospital Acquired Pneumoniae*.

INTRODUCTION

Meningitis is a global public health problem. Meningitis is an infectious disease that cannot be overcome and is still a problem in developing countries. Globally, it is estimated that there are 500,000 cases with 50,000 deaths every year. WHO noted that up to October 2018, 19,135 suspected cases of meningitis were reported with 1,398 deaths along the meningitis belt (Case Fatality Rate/CFR 7.3%). Of the 7,665 samples examined, 846 samples were positive for N. meningitis bacteria (SMITH, 1964).

Tuberculous meningitis (TB) is an infection by Mycobacterium tuberculos is about mening or brain parenchyma. Tuberculous meningitis (MTB) is one of the most life-threatening forms of extrapulmonary tuberculosis. Due to the high risk of mortality, tuberculous meningitis requires fast and appropriate treatment, namely by administering antituberculosis drugs and corticosteroids (Slane VH & Unakal, 2022).

Although it is a preventable and curable disease, tuberculosis is the leading cause of death worldwide due to its infectious etiology. About one third of the world's population is thought to be infected with MTB. Tuberculous meningitis carried a fatal prognosis before the development of anti-tuberculous drugs, and remains the number one cause of death and disability in MTB-infected children.

Pneumonia is an inflammation of the lung parenchyma, from the alveoli to the bronchi, bronchioles, which can be contagious, and is characterized by consolidation, thereby disrupting the exchange of oxygen and carbon dioxide in the lungs. A more practical

classification for Pneumonia is according to the nature of its acquisition, as is often used, namely Community-associated Pneumonia (CAP), Hospital-associated Pneumonia (HAP) or Health care-associated Pneumonia (HCAP) and Ventilator-associated 3 Pneumonia (VAP) (Jain et al., 2023).

HAP is the second most common cause of infection among hospital patients, and the main cause of death due to infection (mortality-rate around 30-70%), and an estimated 27-50% are directly related to pneumonia. Clinical manifestations of pneumonia are fever, chills, sweating, cough (productive, or non-productive, or production of mucoid and purulent sputum), chest pain due to pleurisy and shortness of breath (Monegro et al., 2023).

CASE REPORT

A 39 years old woman came to the emergency room at Drs. H. Amri Tambunan complained of seizures 1 day ago with a duration of more than 1 hour. Seizures are found throughout the body. Also a fever was found today. Shortness of breath and cough were found for the past 3 days. Decreased appetite has been observed for the past 1 week. There was no history of nausea and vomiting. Os post VP shunt installation on May 29th, 2023. Patient admitted that he was no longer working so his daily activities were only at home. Patient admitted to the hospital with pulmonary TB on treatment. Family history of similar disease or symptoms was denied. History of hypertension and DM was denied. The condition of defecation and urination is within normal limits. The patient often looks weak and sometimes does not want to eat because she has no appetite.

Family History of Disease : -
History of Drugs Use : -
Allergy History : -

PRESENT STATUS

Sensorium Status : Somnolent
Blood pressure : 110/70 mmHg
Pulse Frequency : 160 x/minute
Respiratory Frequency: 30 x/minute
Temperature : 39.2 °C
Oxygen Saturation : 90 %
Weight : 55 kg
Height : 160 cm

ORGAN ANAMNESIS

Heart

Short of breathness : (+)

Respiratory Tract

Cough : (+)
Sputum : white (+), bleeding <200ml

Digestive Tract

Appetite : Decreased (+)

Anthropmetric Examination

Weight : 44 Kg
Height : 167 cm
BMI : 21,5 (Normal)
Dietary Habit : Good

PHYSICAL EXAMINATION

Head

Eye : Light Reflex (+/+)
Face : Looks lethargic

Thorax

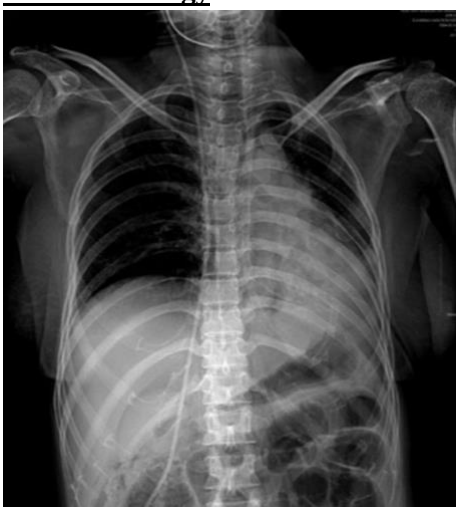
Auscultation : SP: Bronchial (+/+) in both lung fields, ST: Ronchi (+/+) in lung basal

Abdomen

Inspection : Symmetrical
Palpation : Soepel, mass (-), epigastric tenderness (+)
Percussion : Timpani
Auscultation : Peristaltic (+)

SUPPORTING INVESTIGATION

Chest Radiology



Interpretation :

Consolidation in right pericardium → Pneumonia

Full Blood Count

WBC	11.16 10^3/uL
RBC	4.37 10^6/uL
HGB	11.9 g/dL
HCT	35.4 %
MCV	81.0 fL
MCH	27.2 pg
MCHC	33.6 fL
PLT & F	402 fL
RDW-SD	38.5 %
RDW-CV	13.1 %
PDW	6.9 %
MPV	8.0 %
P-LCR	9.9 %
PCT	0.27 %
NRBC	0.3 %
NEUT	76.3 %
LYMPH	18.5 %
MONO	4.8 %
EO	0.0 %
BASO	0.4 %
IG	1.1 %
RET	2.04 %
IRF	9.7 %
LFR	90.3 %
MFR	8.8 %
HFR	0.9 %
RET-He	28.8 pg
IPF	0.8 %

Glucose, HbA1C, Ureum, Creatinin, Uric acid, and Electrolyte

Glucose	341 mg/dL
HbA1C	4,9
Ureum	37 mg/dL
Creatinin	0,6 mg/dL
Uric Acid	11,2 mg/dL
Natrium	133 mEq/L
Kalium	3.1 mEq/L
Chloride	87 mEq/L

Liver Function Test

SGOT	110 U/L
SGPT	115 U/L
Alkaline Phosphatase	124 U/L
Total Bilirubin	0.62 mg/dL
Direct Bilirubin	0.30 mg/dL

HBsAg, and Anti HCV

HbsAg	Negative
Anti HCV	Negative

Arterial Blood Gas

pH	7,370
pCO2	25,4 mmHg
pO2	203 mmol/L
BEECF	-11 mmol/L
HCO3	14,7 mmol/L
TCO2	15 mmol/L
SO2	100 mmol/L
LAC	>20.00 mmol/L

CRP, D Dimer, and Procalcitonin

CRP	198.1 mg/L
D DIMER	4.0 mg/L
Procalcitonin	119.3 ng/ml

Head CT Scan

Interpretation:

Communicating hydrocephalus with VP shunt installed, Encephalomalacia at Right Corona Radiata, Nucleus Caudatus and Right Nucleus Lentiformis

Antibiotic Sensitivity Testing

Antimicrobe	Mic	Outcome
Benzylpenicillin	0.25	R
Oxacillin	≤ 0.25	S
Gentamicin	≤ 0.5	S
Ciprofloxacin	≤ 0.5	S
Levofloxacin	≤ 0.12	S
Moxifloxacin	≤ 0.25	S
Erythromycin	≤ 0.25	I
Clindamycin	≥ 8	R
Dalfopristin	1	S
Linezolid	2	S
Vancomycin	≤ 0.5	S
Tetracycline	≤ 1	S
Tigecycline	≤ 0.12	S
Nitrofurantoin	≤ 16	S
Rifampicin	≤ 0.5	S

Trimethoprim	≤ 10	S
Fosfomycin	30	S

S : Susceptible / sensitive
I : Indetermidiate
R : Resistant

DIAGNOSE

Tuberculous Meningitis on treatment + Hospital Acquired Pneumoniae + DILI + Hypocalemia

FOLLOW UP

September 9th, 2023

S : Seizure (dur: >1hour), Fever (+), Cough (+), Short of breathness (+), Decreased appetite
O : GCS (E4V2M2), BP: 110/70 mmHg, HR: 160x/i, RF: 30x/i, SpO2: 90%, Temp: 39,2ºC
A : Status Epilepticus + Hemiparesis ec Meningoencephalitis
P : IVFD NaCl 0,9%, KSR 1x600mg, Loads of 9 amps Phenytoin + NaCl 0,9% 32cc in 3 hours, Later on Phenytoin 3x100mg tab, Depakote 2x250mg, Folate Acid 1x1 tab, Inj Paracetamol 1fl/8hrs

September 15th, 2023

S : Focal seizures
O : BP: 80/40 mmHg, HR: 127x/I, RF: 26x/I, SpO2: 98% with NRM 10L/I, Temp: 37,2ºC
A : Tuberculous Meningitis + DILI
P : Therapy continues with additional Norphagen 2amp/12hrs, Sucralfate syr 3xCth2

September 20th, 2023

S : Worsening condition, fever (+)
O : Sens: Coma, ECG: Bradyarrhythmia, BP: 80/50 mmHg, HR: 150x/i, RF: 21x/i, SpO2: 80% and intubated with ett number 8 connected to ventilator, Temp: 39,4ºC
A : Tuberculous Meningitis + DILI + Hypokalemia
P : Inj Epinephrine 1amp/3-5min, RJPO 30:2 + Manual bagging, ROSC (-), and Patient stated die at 14.15 WIB.

RESULTS AND DISCUSSION

Tuberculous Meningitis

Tuberculous meningitis (MTB) is inflammation of the lining of the brain (meninges) caused by the bacteria *Mycobacterium tuberuclosis*. The inflammatory process occurs and spreads through the subarachnoid space around the brain, spinal cord and ventricles. Primary infection appears in the lungs and can spread lymphogenously and hematogenously to various areas of the body outside the lungs (Pemula et al., 2016).

Epidemiology

In general, tuberculosis (TB) is a global infection with a high prevalence caused by the bacteria M. tuberculosis. Indonesia is the country with the second highest number of tuberculosis cases after India with 10% of the total cases worldwide. Data from the World Health Organization (WHO) shows that the incidence rate of tuberculosis in Indonesia in 2015 reached 395 cases per 100,000 people (Sulistyowati et al., 2019).

Etiology

Tuberculous meningitis is a serious form of infection caused by M. tuberculosis. Rod-shaped bacteria, 0.4-3μm in size, are not motile, and do not form spores. Mycobacterium is obligate aerobic so it has a predilection for tissues with high oxygenation such as the apex of the lungs, kidneys and brain. M. tuberculosis bacterial infections of the central nervous system include tuberculous meningitis, intracranial tuberculoma, spinal tubercular arachnoiditis and tuberculous encephalopathy (Jain et al., 2023).

Risk Factors

Risk factors for tuberculous meningitis include:

1. Age (children > adults)
2. HIV co-infection
3. Malnutrition
4. Violence
5. Use of immunosuppressive agents.

Clinical Manifestations

Patients with tuberculous meningitis will experience typical signs and symptoms of meningitis (meningitis triad) such as headache,

fever and neck stiffness which can be accompanied by focal neurological deficits, behavioral changes and decreased consciousness. Non-specific symptoms include malaise, anorexia, fatigue, and myalgia.(Seid et al., 2023)

The course of tuberculous meningitis consists of 3 stages, namely:(Gupta & Munakomi, 2023)

1. Stage I (Early Stage)
   Non-specific prodromal symptoms are apathy, irritability, lightheadedness, malaise, fever, anorexia, vomiting, abdominal pain.
2. Stage II (Intermediate)
   Symptoms become clear, such as "drowsy", mental changes, signs of meningeal irritation, paralysis of nerves III, IV, VI.
3. Stage III (advanced stage)
   Patients experience decreased consciousness, namely stupor or coma, seizures, hemiparesis, and involuntary movements are found.

Pathogenesis

The pathogenesis of this disease is thought to occur in two stages. In the early stages, bacteremia causes M. tuberculosis bacilli to spread from the primary infection in the lungs to the brain. Bacilli can cross the blood brain barrier (BBB) and blood cerebrospinal fluid barrier (BCSFB) due to viral virulence factors. As a result of the formation of a small subpial or subependymal focus of metastatic caseous lesion known as Rich's focus.(Davis et al., 2018)

In the second stage, Rich's focus grew bigger until it ruptured. Tuberculous meningitis occurs due to the release of M. tuberculosis bacilli into the meningeal space from subependymal or subpial lesions (especially in the Sylvian fissure). Inflammatory exudate pushes against structures at the base of the brain, nerves and blood vessels in this area.(Davis et al., 2018)

Decreased cerebral perfusion generally poses a risk for ischemia, infarction, and poor patient outcomes. The spread of disease through the spinal canal can manifest as arachnoiditis, tuberculoma, and accumulation of exudate.(Jipa et al., 2017)

Diagnostic Criteria

Fulfill the criteria for anamnesis, physical examination, and imaging and cerebrospinal fluid examination:(Seddon et al., 2019)

1. History: Malaise, anorexia, fever, worsening headache, mental changes, decreased consciousness, seizures, and one-sided weakness.
2. Physical examination: Check vital signs and thorough physical examination. Neurological examination includes GCS examination, neck stiffness examination, cranial nerve examination (cranial nerve paralysis II, III, IV, VI, VII, VIII), motor strength (hemiparesis).
3. Laboratory examination: Routine laboratory examination in tuberculous meningitis typically, an increased, normal or low leukocyte count can be found and the count shifts to the left,
4. Cerebrospinal fluid analysis

Differential Diagnosis

1. Bacterial Meningitis
2. Viral Meningitis
3. Encephalitis
4. Brain Abscess

Supporting Examinations

Supporting examinations that can be carried out include:(Seddon et al., 2019)

1. Microbiological examination
   The definitive diagnosis of tuberculous meningitis is the result of microbiological examination of cerebrospinal fluid specimens either microscopically with Ziehl Neelsen staining to view acid-fast bacilli (AFB) or culture with solid or liquid media as the gold standard examination.
2. Polymerase Chain Reaction (PCR)
   Since 2010 WHO has recommended the use of the Xpert MTB/RIF device. The molecular examination program with Xpert MTB/RIF is still registered for sputum specimens.
3. Imaging examination
   Radiological examination in the form of a CT scan is not very specific in describing abormalities obliteration of the basal cisterns

by mild isodense or hyperdense exudate is the most common finding.

Complications

1. Hydrocephalus and Increased Intracranial Pressure
2. Hyponatremia
3. Tuberculoma
4. Stroke and Vasculitis

Therapy

Table 1. WHO Therapy Recommendation

First-line drugs for treatment of drug sensitive TBM in adults		
Drug	WHO-recommended daily dose	WHO-recommended duration
Rifampicin	10 mg/kg (range 8–12 mg/kg); max 600 mg	12 months
Isoniazid	5 mg/kg (range 4–6 mg/kg); max 300 mg	12 months
Pyrazinamide	25 mg/kg (range 20–30 mg/kg)	2 months
Ethambutol	15 mg/kg (range 15–20 mg/kg)	2 months
Second-line drugs for treatment of TBM in adults		
Levofloxacin	10–15 mg/kg	Throughout treatment
Moxifloxacin	400 mg	Throughout treatment
Amikacin	15 mg/kg; max 1 g. IV or IM.	Intensive phase only
Kanamycin	15 mg/kg; max 1 g. IV or IM.	Intensive phase only
Capreomycin	15 mg/kg; max 1 g. IV or IM.	Intensive phase only
Ethionamide or prothionamide	15–20 mg/kg; max 1 g.	Throughout treatment
Cycloserine	10–15 mg/kg; max 1 g	Throughout treatment
Linezolid	600 mg	Throughout treatment
Other drugs used in treatment of multi-drug-resistant TB but of uncertain benefit in TBM		
Clofazimine	100 mg OD	No recommended duration
p-Aminosalicylic acid	200–300 mg/kg	No recommended duration
Bedaquiline	Not determined	New drug. Limited availability.
Delamanid	Not determined	New drug. Limited availability.

Hospital Acquired Pneumoniae

Pneumonia is an inflammation of the lung parenchyma, from the alveoli to the bronchi, bronchioles, which can be contagious, and is characterized by consolidation, thereby disrupting the exchange of oxygen and carbon dioxide in the lungs. A more practical classification for Pneumonia is according to the nature of its acquisition, as is often used, namely Community-associated Pneumonia (CAP), Hospital-associated Pneumonia (HAP) or Health care-associated Pneumonia (HCAP) and Ventilator-associated Pneumonia (VAP).(Papadakis et al., 2012).

Etiology

The pathogens that cause nosocomial pneumonia are different from community pneumonia. Nosocomial pneumonia can be caused by non-multidrug resistance (MDR) germs, for example *S. pneumoniae, H. Influenzae, Methicillin Sensitive Staphylococcus aureus* (MSSA) and MDR germs for example *Pseudomonas aeruginosa, Escherichia coli,*

Klebsiella pneumoniae, *Acinetobacter spp* and Gram positive like Methicillin Resistance Staphylococcus aureus (MRSA) (Ranes et al., 2010).

Risk Factors

The risk factors for pneumonia are divided into 2 parts:(Monegro et al., 2023)

1. Factors related to endurance Chronic diseases long hospital stay, coma, use of sleeping pills, smoking, endotracheal intubation, malnutrition, advanced age, steroid treatment,
2. Exogenous factors are:
   a. Surgery
   b. Use of antibiotics
   c. Respiratory therapy equipment Contamination
   d. Insertion of a nasogastric tube/tube
   e. Hospital environment

Pathophysiology

In rare cases, pneumonia can occur due to hematogenous spread of infection, for example tricuspid endocarditis, or through widespread infection from pleural infections or mediastinal cavity infections. HAP, VAP, HCAP may occur through microaspiration or contamination of respiratory therapy equipment, as well as weak host (Qu et al., 2022).

Colonization of the pharynx increases due to: exogenous factors and endogenous factors from patient. Within 48 hours of hospital admission, 75% of seriously ill hospital patients will have microbial colonization of their upper airway, originating from the hospital environment. Weak cellular and mechanical defense mechanisms in the lungs of hospitalized patients increase the risk of infection (David et al., 2017).

Diagnosis

According to the criteria from The Centers for Disease Control (CDC-Atlanta), the diagnosis of nosocomial pneumonia is as follows:(Liu et al., 2015)

1. Pneumonia onset that occurs 48 hours after admission to hospital.
2. The diagnosis of nosocomial pneumonia is made on the basis of; Chest x-ray: there is a new or progressive infiltrate, Add 2 of the following criteria: body temperature > 38 C, purulent discharge, leukocytosis.

Therapy

- Empiric antibiotic treatment for HAP, without high risk of mortality and has no risk factors for MRSA, one of the following:(*Panduan Tata Kelola Hospital Acquired Pneumonia*, 2009)
- Cefepime, Levofloxacin, Imipenem, Meropenem, Piperacillin-tazobactam

Without high risk of mortality but has MRSA risk factors One of the following:

- Cefepime, Levofloxacin, Ciprofloxacin, Imipenem, Meropenem, Aztreonam, Piperacillin-tazobactam, plus
- Vancomycin
- Risk of mortality or history of IV antibiotic use in the last 90 days

Choose 2 from below (avoid β-lactams)

- Piperacillin – tazobactam, Cefepime, Levofloxacin, Ciprofloxacin, Amikacin, Gentamicin, Tobramycin, Imipenem, Meropenem, Aztreonam, plus
- Vancomycin or Linezolid

Prevention

The prevention for HAP (Sopandi et al., 2018):

- Prevention of oropharynx and stomach colonies
- Prevention of lower respiratory tract aspiration
- Prevention of exogenous inoculation
- Optimizing the patient's body defenses

CONCLUSION

Tuberculous meningitis is the most common life-threatening form of neurological extrapulmonary tuberculosis. Diagnosis can be made by the triad of meningitis and clinical suspicion of tuberculosis (Prochaska & Benowitz, 2016).

TB meningitis is a deadly type of TB because it involves the central nervous system. The pharmacological therapy used is first-line

TB in the form of rifampicin, isoniazid, pyrazinamide, and ethambutol, additional corticosteroids in the form of dexamethasone, and additional third-class cephalosporin antibiotics (Sulistyowati et al., 2019).

Pneumonia is an inflammation of the lung parenchyma, from the alveoli to the bronchi, bronchioles, which can be contagious. Hospital-acquired pneumonia (HAP) is pneumonia that occurs 48 hours or more after the patient is admitted to hospital. Health care-associated pneumonia (HCAP) is pneumonia that occurs in members of the public (who are not hospitalized), who have extensive contact with health care (Christian et al., 2016).

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