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ASSESSMENT OF CRYPTOCOCCAL MENINGITIS CONCURRENT WITH MULTIDRUG-RESISTANT TUBERCULOUS MENINGITIS: A CASE REPORT

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ABSTRACT

Cryptococcal meningitis is an infection that attacks the tissue lining the brain and spinal cord, caused by the fungus Cryptococcus neoformans. This infection mainly occurs in individuals with a weakened immune system, such as people with HIV/AIDS. The spread of this fungus into the central nervous system can result in serious conditions, even fatal if not treated quickly and appropriately. Objective: to present a rare and complex case report of a patient with concurrent cryptococcal meningitis and multiresistant tuberculous meningitis, as well as evaluate the management strategies used in the patient's care. Method: Case study was conducted through a comprehensive approach including health history assessment, physical examinations, psychosocial analysis, customized nursing assessment forms, electronic medical record reviews, laboratory diagnostics, imaging studies, and multidisciplinary consultations to ensure accurate diagnosis and effective interventions Mrs. R, a 33 year old woman with a final diagnosis including Pneumonia with aspiration mechanism, Cryptococcal Meningitis, Grade II MDR TB Meningitis complicated by arteritis, as well as several other conditions including Hyponatremia, hypochloremia, and hypocalcemia due to insufficient intake, Chronic Suppurative Otitis Media (CSOM) and Typhoid Fever. Results: The patient was diagnosed with aspiration pneumonia, cryptococcal meningitis, multiresistant tuberculous meningitis, as well as other conditions such as hypernatremia, hypokalemia, hypocalcemia, chronic suppurative otitis media, and typhoid fever. Despite treatment, the patient's condition worsened, leading to respiratory failure and death from aspiration pneumonia. Conclusions: This case report highlights the diagnostic and therapeutic challenges in managing concurrent cryptococcal meningitis and multiresistant tuberculous meningitis. This emphasizes the importance of a comprehensive approach in diagnosis and management in patients with complex concurrent infections, even without HIV. This case also emphasizes the need for further research and improved strategies for managing rare and complex infections such as this.

Keywords: case study; cryptococcal meningitis; definite meningitis

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INTRODUCTION

Cryptococcal meningitis is an infection that occurs in the tissue lining the brain and spinal cord, known as the meninges(medlineplus.gov, 2022). This infection is caused by the fungus Cryptococcus neoformans. This disease is a serious complication that can occur in individuals with a weakened immune system, especially in those living with HIV/AIDS. When the immune system is not functioning as it should, pathogenic organisms such as the fungus Cryptococcus neoformans have a greater chance of spreading and causing serious infections.(Su et al., 2024). Cryptococcal Meningitis is caused by penetration of the fungus Cryptococcus neoformans into the central nervous system due to inhalation of airborne spores

spread in the environment.(Erturk Sengel et al., 2021)after spreading from the lungs to the brain(cdc.gov, 2024).

Risk factors that play a role in increasing the likelihood of cryptococcal meningitis include immunodeficiency status such as HIV/AIDS, use of immunosuppressants(Raman Sharma, 2010), and contact or exposure as well as high environmental humidity factors(Ministry of Health, 2019). Cryptococcal meningitis is an important opportunistic infection that causes more than 100,000 HIV-related deaths each year.(Pescador Ruschel MA & Thapa B, 2023).To be precise, around 152,000 cases and caused around 112,000 deaths. Even with the recommended antifungal regimens available such as amphotericin B, flucytosine, and fluconazole. Within 10 weeks, mortality is still around 25-30% 10. Cryptococcal infections are estimated to occur in 5 to 30% of the population in Indonesia. The Department of Parasitology, Faculty of Medicine, University of Indonesia recorded a significant increase, namely 21.9%, in patients with HIV(Paramitha & Ritarwan, 2022).

Serious complications of cryptococcal meningitis include increased intracranial pressure(Jjunju et al., 2023), inflammation of the brain that causes nerve damage, and the possibility of death if not treated immediately and adequately(medlineplus.gov, 2022). The importance of conducting this case report lies in the need for appropriate and effective treatment of patients with concurrent cryptococcal meningitis and multidrug-resistant tuberculous meningitis. Cases like this are rare and complex, considering the presence of two serious infections occurring simultaneously in one patient. Therefore, through this case report, we aim to evaluate the management given to a patient with concurrent cryptococcal meningitis and multidrug-resistant tuberculous meningitis to provide further insight into the management of this more complex case.

METHOD

This study adopts a case study approach to comprehensively describe the selected case. We selected one participant, Mrs R, a 33-year-old woman who is being treated at Dr Hasan Sadikin General Hospital in Bandung diagnosed with aspiration pneumonia, cryptococcal meningitis, multiresistant tuberculous meningitis, as well as other conditions such as hypernatremia, hypokalemia, hypocalcemia, chronic suppurative otitis media, and typhoid fever. Participants were chosen based on inclusion criteria relevant to our research objectives. Data were collected through comprehensive nursing assessments and a review of the patient's medical records. Nursing assessments encompassed health history, physical evaluations, and analyses of the patient's psychosocial condition. We utilised customised nursing assessment forms as the primary instrument, alongside analysing the patient's electronic medical records for diagnostic information and interventions performed. Data analysis was conducted descriptively, focusing on patterns, themes, and trends emerging from the case.

Data collection involved comprehensive nursing assessments and detailed reviews of the patient's medical records that includes her disease progression, physical examination, supporting examinations, and clinical management. The data collection process begins with anamnesis, where the doctor or nurse gathers information about the current and past medical history, including the main complaints, symptoms experienced, and the patient's general condition. Following this, a direct physical examination is conducted by the doctor. This examination includes vital signs, internal status of the head, thorax, abdomen, extremities, and neurological status. We systematically organised the data to encompass the physical, psychological, and social aspects of the patient's condition. The study adheres to research ethics principles, including patient data confidentiality and obtaining ethical clearance from

relevant institutions before data collection. Subsequently, supporting examinations are carried out, which include various laboratory tests such as haematology, urea, creatinine, sodium, potassium, quantitative CRP, random glucose, as well as imaging examinations like a head CT scan to assess the patient's internal condition. The patient's condition is monitored regularly to observe progress and response to treatment. The collected data is then thoroughly reviewed to determine the appropriate diagnosis and management plan. In Mrs R's case, this information is crucial to ensure that the treatment is suitable and effective for her clinical condition.

RESULTS

The study focused on a single participant, a 33-year-old Female patient Mrs. R, came with the main complaint of headache that lasted for 5 days, accompanied by fever, shortness of breath, and decreased consciousness. Physical examination revealed signs of meningitis, such as stiff neck and legs, as well as other neurological symptoms including total pupillary mydriasis and cranial nerve disorders. Patients also experience increased blood pressure, fever, and oxygen saturation which decreases significantly. The final diagnosis included Pneumonia with an aspiration mechanism, Cryptococcal Meningitis, grade II MDR TB Meningitis complicated by arteritis, as well as several other conditions including Hyponatremia, hypochloremia and hypocalcemia due to insufficient intake, Chronic Suppurative Otitis Media (CSOM) and Typhoid Fever. Despite treatment, the patient's condition worsened, leading to respiratory failure and death from aspiration pneumonia. The patient's main complaint was headache, with a history of pain since 5 days before the consultation. The pain is described as stabbing, affecting the entire head and neck, worse with fever, and relieved by medication. The patient had no history of seizures, projectile vomiting, or impaired consciousness. However, he reported double vision since 1 week previously, reduced hearing in the right ear, and a history of foul-smelling green discharge from the ear. The patient has no history of diabetes, hypertension, high cholesterol, or uric acid stones, and no history of heart disease or kidney disease. He also had no history of minor strokes (TIA), and no history of sexual relations with multiple partners or drug abuse.

On physical examination, the patient was conscious and responsive and quite interactive. His vital signs include blood pressure 130/90 mmHg, heart rate 108 bpm, respiratory rate 20 breaths per minute, temperature 37.8°C, and oxygen saturation (SpO2) 99% with room air. Internal examination showed normal cranial nerves, except for paresis of CN VI on the right side and central paresis of CN VII on the right side. The Rinne and Weber tests showed conductive hearing loss in the right ear, and the Schwabach test showed short hearing, which also indicates conductive hearing loss. Motor function was normal at 5/5, without spasticity. Sensation and vibration remain intact. Physiological and pathological reflexes are negative. Interventions during patient care include several medical steps taken to treat the patient's condition. The patient was treated for eight days in the inpatient care unit (IPD) before being transferred to the intensive care unit (ICU). During treatment, the patient was given oxygenation using a non-rebreather mask (NRM) with a flow rate of 15 liters per minute, which increased the patient's oxygen saturation to 95%. Initially, the treatment plan involved Ceftriaxone, Amphotericin B, Paracetamol, rehydration, calcium gluconate, Calcium Carbonate, and hospitalization in the Intensive Care Unit (HCU). However, the treatment plan was later updated to include additional medications including anti-tuberculosis drugs, Bedaquillin, Linezolid, Levofloxacin, Clofazimine, and Cycloserine, as well as correction of hypokalemia with KCl. Laboratory examination results showed various abnormalities, including leukocytosis, thrombocytopenia, anemia, as well as electrolyte abnormalities such as hyponatremia, hypokalemia, and hypocalcemia. Cerebrospinal fluid examination shows

signs of bacterial infection, while other tests confirm the diagnosis and provide additional information about the patient's condition.

Thus, the care provided to patients includes appropriate antimicrobial treatment, supportive therapy, and correction of electrolyte abnormalities. The patient was admitted with initial diagnoses that included partially treated suspected bacterial meningitis, communicating hydrocephalus, CSOM, and typhoid fever. The patient received treatment with amphotericin, which indicated suspicion of fungal infection. After the amphotericin drip was completed, the patient's blood pressure was measured to be 188/104, indicating a hypertensive response to the intervention. Next, the patient was intubated with manual bagging while waiting for ICU availability. The patient remained conscious and followed commands, with 99% saturation using manual bagging ETT. The patient also experienced several episodes of cardiac arrest and respiratory arrest, which were followed by three cycles of cardiopulmonary resuscitation and administration of epinephrine. The patient experienced return of spontaneous circulation (ROSC), indicating a response to the intervention. In addition, patients receive physical examinations and other supporting examinations, and there are indications that consultations with other doctors or relevant specialists are carried out in the treatment process. Overall, these interventions demonstrate the medical efforts made to stabilize the patient's condition and prevent further complications. Unfortunately, the patient's condition continued to worsen, ending in the patient's death due to respiratory failure due to aspiration pneumonia.

DISCUSSION

Cryptococcal meningitis is a relatively rare disease, and most healthy people are not at risk of developing cryptococcal meningitis(Muzazu et al., 2022). This disease is most common in people who have a weakened immune system. People who are more at risk for developing cryptococcal meningitis often have one of the underlying conditions such as HIV, AIDS, diabetes, leukemia, liver cirrhosis, or have had an organ transplant.(Muzazu et al., 2022). Cryptococcal meningitis is most likely to occur in people who have a low CD4 count. CD4 cells, also known as T cells, are a type of white blood cell that is vital to the immune system(Frank et al., 2019). People with HIV and AIDS often have low CD4 counts, so they are much more likely than other people to develop cryptococcal meningitis. However, in this case, the patient's test results did not show the presence of HIV(Frank et al., 2019).

Cryptococcal meningitis is an infection caused by the fungus Cryptococcus neoformans or Cryptococcus gattii. Cryptococcal infections usually occur in individuals with weakened immune systems, especially in patients with HIV/AIDS infection. In theory, this disease generally attacks the central nervous system, especially the brain and spinal cord(Liu et al., 2012). However, different clinical presentations can make diagnosis more difficult. In this case, the patient presented with complaints of constant headache, fever, and neurological symptoms such as cranial nerve paresis GBM Ophthalmoplegia ODS CN VII central right paresis CN VIII rinne AC < BC, weber lateralization to the left, shortened swabach). Cases of cryptococcal infection in patients without HIV can also occur, although they are rare. It is necessary to review the risk factors that might cause cryptococcal infection in patients with this case, such as a history of systemic disease that weakens the immune system or use of immunosuppressive drugs. Another unique thing is that the patient was also diagnosed with Definite MDR TB meningitis grade II with complications of arteritis and paresis of the cranial nerves. Tuberculosis (TB) is a bacterial infection that generally attacks the lungs, but can also attack other parts of the body, including the brain.

In this case, assessment of meningeal tuberculosis was carried out by examination of cerebrospinal fluid (Lumbal Puncture) which showed the following results: Traumatic, clear, Dripping rapidly, Cells 287 (PMN:MN=25.8:74.2), Protein 196, CSF:serum glucose ratio=26 :160=16%, BTA not found, and Gram negative. The results of this examination indicate the possibility of MDR grade II tuberculous meningitis with complications of arteritis and entrapment of NIII ODS, NVI ODS. In line with the theory that the assessment of tuberculous meningitis is carried out by obtaining cerebrospinal fluid (CSF) for analysis. Typically, CSF shows low glucose, increased protein, and a slightly increased white blood cell count with a lymphocytic predominance. However, there are various sophisticated new modalities for testing specific antigens and antibodies for TB using PCR. This innovation can be a recommendation in the future for establishing a diagnosis. Despite advances in the development of better and more accurate MTB diagnostic modalities, confirmation via culture in CSF remains the standard globally(Kashyap et al., 2019).

The patient was also diagnosed with typhoid fever, which generally causes typical symptoms such as high fever, abdominal pain and skin rashes. However, in this case, the presentation of typhoid fever becomes more complex because it is accompanied by neurological conditions and other disorders. Overall, this case shows how a common disease such as typhoid fever can have a unique and complex presentation when co-occurring with other conditions such as cryptococcal meningitis, tuberculous meningitis, and other complications. This emphasizes the importance of careful observation and treatment by the medical team to manage these complex and rare cases. Neurological status examination Cryptococcal meningitis in this case was assessed using various examinations, such as neurological status examination, lumbar puncture, and head CT scan. The results of the neurological status examination showed cranial nerve paresis, while the lumbar puncture showed no signs of meningitis. Apart from that, the results of the CT scan of the head also showed no signs of meningitis, infarction, SOL/neoplasm, or intracranial bleeding. In theory, examination of brain images can show signs of inflammation or structural abnormalities. Thus, the assessment of cryptococcal meningitis in this case shows inconsistent results, and requires further examination for a more accurate diagnosis. The diagnosis of cryptococcal meningitis in this patient was based on clinical symptoms, physical examination, and laboratory test results which showed the presence of Cryptococcus fungal infection in the cerebrospinal fluid. Even though the CT scan of the head showed no signs of meningitis, this does not rule out the possibility of a fungal infection. Therefore, the diagnosis of cryptococcal meningitis remains based on relevant clinical and laboratory findings(Kashyap et al., 2019).

In this context, to ensure a more precise and comprehensive diagnosis for the patient, several additional examinations need to be considered. First, serology tests for other viruses such as hepatitis B and C may be required if there is a risk of infection related to the patient's history. Second, if blood culture results are not positive, cultures from alternative sources of infection such as pleural fluid or cerebrospinal fluid can be taken, especially if there are atypical symptoms or an inappropriate response to therapy. Third, additional radiological examinations such as a CT scan or MRI may be needed if the previous results do not provide a clear picture or there is an inappropriate development of symptoms. Fourth, further evaluation of the function of organs such as the kidneys and liver may be necessary to rule out drug toxicity or related organ complications. Fifth, immunological examination may need to be considered to evaluate the patient's immunological status, including the number and function of immune cells and immunoglobulin levels. Sixth, if there is a suspicious lesion or swelling, a tissue biopsy may be necessary to confirm the correct diagnosis, especially if other examination results do not provide a clear picture. This additional examination aims to gain a

more complete understanding of the patient's condition and assist in better disease management planning. Additionally, in the case of non-HIV patients with cryptococcal infection, it is important to consider a broad differential workup, including other diseases or conditions that may mimic the infection, such as tuberculosis, histoplasmosis, or cerebral neoplasms. Lastly, even if the patient is HIV negative, searching for the underlying cause of cryptococcal infection remains important, highlighting the importance of examining infectious causes such as immune disorders or systemic disease as predisposing factors.

CONCLUSION

The presented case report provides a comprehensive analysis of the management and challenges associated with rare and complex concurrent infections, namely cryptococcal meningitis and multiresistant tuberculous meningitis in a non-HIV patient. These cases highlight the importance of a comprehensive diagnostic approach, including consideration of immunologic abnormalities or systemic diseases that may predispose individuals to such infections. Despite aggressive medical intervention, the patient's condition worsened, resulting in a fatal outcome. This highlights the difficulty in managing such concurrent infections and the need for early diagnosis and effective treatment. The authors emphasize the need to expand the differential diagnosis to include cryptococcal infection in patients presenting with neurological symptoms, even in the absence of HIV. This case report provides a valuable lesson for healthcare providers, especially in areas where tuberculosis and cryptococcal infections are endemic, to be vigilant and consider the possibility of concurrent infections that may complicate patient care. Overall, the case report contributes to the medical literature by documenting a rare and challenging case of concurrent cryptococcal meningitis and multiresistant tuberculosis. It provides insight into the diagnostic and therapeutic challenges involved and emphasizes the importance of a multidisciplinary approach to patient management. Additionally, it proposes further research and improved strategies to manage these complex infections to improve patient outcomes.

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