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Case report: Hydrocephalus in tuberculous meningitis patient with HIV

Belinda Layrenshia[1], Martin Firman Suryo[2]
[1]*Tarumanagara University, Indonesia*
[2]*Royal Taruma Hospital, Indonesia*

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Penulis Korespondensi*:
Belinda Layrenshia
Tarumanagara University, Indonesia
belindalayrenshia@gmail.com

ABSTRACT

Meningitis is defined as inflammation of the membranes of the brain and spinal cord that can be caused by various causes, including tuberculosis. Approximately 1% of tuberculosis patients develop tuberculous meningitis. Hydrocephalus is one of the complications of tuberculous meningitis characterized by the accumulation of intracranial cerebrospinal fluid (CSF) under pressure. In this report, we describe a 32-year-old man whose chief complaint was severe headache. The patient reported irritability and also had fever. Meningeal excitatory signs were positive in the patient. It was known that the patient was a human immunodeficiency virus (HIV) patient with tuberculous meningitis. After several days of hospitalization, the patient developed hydrocephalus. The patient had tuberculous meningitis, which caused hydrocephalus as a complication, coupled with his HIV-positive status. The patient received appropriate medical treatment and underwent a ventriculoperitoneal (VP) shunt procedure, which resulted in symptomatic improvement thereafter.

Keywords : Tuberculosis; Meningitis; HIV; Hydrocephalus.

INTRODUCTION

Meningitis is the inflammation of the meninges which are the coverings of the brain and spinal cord (Aksamit & Berkowitz, 2021; Hersi et al., 2021). Meningitis can be caused by infection, immune-mediated, medications or neoplasms (Berkowitz, 2022).

Meningitis can affect people of all ages with bacterial cause being the most common and deadly (Meningitis, 2023). The incidence of meningitis is thought to be around 20 cases per 100,000 people; that accounts for roughly 1.2 million worldwide (Moradi et al., 2021). It is said that there is roughly 100,000 people who develop tuberculous meningitis annually (Manyelo et al., 2021). Tuberculous meningitis occurs in about 1% of all tuberculosis cases (Imran et al., 2022).

Clinical symptoms of meningitis consists of fever, headache and signs of meningeal irritation (Berkowitz, 2022). Meningitis is diagnosed through cerebrospinal fluid (CSF) analysis. This includes white blood cell count, glucose, protein, culture, and in some cases, polymerase chain reaction (PCR). CSF is obtained via a lumbar puncture (LP), and the opening pressure can be measured (Hersi et al., 2021).

One of the complications of tuberculous meningitis is hydrocephalus (Kaur et al., 2022). Hydrocephalus is a pathological state characterised by the accumulation of intracranial CSF under pressure, with or without distension of the cerebral ventricles (Sunderland et al., 2023). This case report will describe the management of hydrocephalus in a patient with tuberculous meningitis.

RESEARCH METHOD

This case report study was conducted on a 32-year-old male patient at Royal Taruma Hospital. This case report will describe the management of hydrocephalus in a patient with tuberculous meningitis.

RESULT AND DISCUSSION

1. Case Report

A 32 year old male was brought to Royal Taruma Hospital at December 30th 2023, with chief complaint of severe headache with a VAS of 7 since 4 days before hospitalization. Headache was felt all over his head and was described as throbbing. Patient confirmed that he experienced fever and felt lethargic. Patient was also very irritable. Complaints of nausea, vomiting and epigastric pain was also confirmed and those started 1 day before the complaints of headache started. Complaints about urination, defecation, respiratory problems, seizures were denied. Any muscle weakness or pain elsewhere were denied. Patient's friend denied any loss of consciousness since the complaint started but would say that his ability to remember events surrounding his hospitalization is blurry. Patient and his friend deny any history of head trauma as well as contact with tuberculosis positive patients. Patient is part of the LGBTQ community. Before coming to our hospital on the 30th of December 2023, patient first seeked treatment at another hospital before being discharged by his own request, patient denies any improvement while being treated there. When examined at 2nd January 2024, patient stated that his headache has been a lot better with a VAS of 3 and complaints of neck stiffness and nausea were absent.

Patient has no history of hypertension, diabetes mellitus, tuberculosis or any similar complaints in the past. Familial history of stroke is confirmed.

Based on physical examination done on 2nd January 2024, the patient was fully conscious (E4M6V5), blood pressure 120/80 mmHg, heart rate 63 times per minutes, temperature 36.5°C and saturation 98%. respiratory rate 20 times per minute. The patients height is 170 cm and weight is 63 kg with BMI 21.80 kg/m2, categorized as normal. Neurology examination showed positive sign on Brudzinski IV, isochoric pupil with a diameter of 3mm on both eyes, positive direct and indirect light reflexes as well as equal ability of both eyes to turn to every direction. Sensoric and motori. function of cranial nerve V and VII showed no abnormality although cranial nerve VI shows abnormality in his left eye where it was not able to move maximally. Motoric function was normotonic-normotrophic with motor strength 5555/5555 5555/5555. Physiologic reflexes were ++/++ on both extremities while pathological reflexes were not found. Sensory examinations were normal.

Several work up were performed including blood tests and imaging modalities. Complete hematologic profile on the 29th of December 2023 showed leukocytopenia (3890/ microliter). Electrolyte panel showed decrease level in sodium (135 mmol/L) and chloride (96 mmol/L). A head MRI with contrast performed on 29th of December 2023 and showed prominent interception on cerebral and cerebellar sulci with a dilation in the ventricular system (particularly bilateral lateral ventricles).

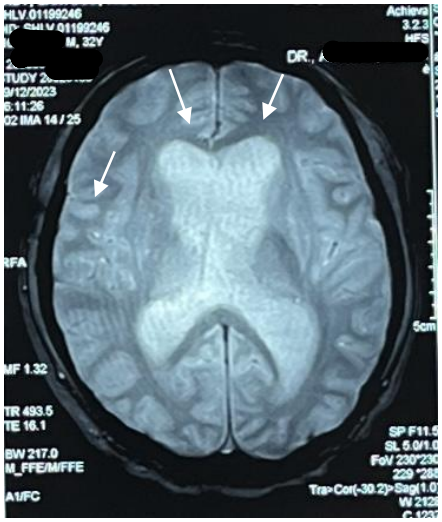

Figure 1. Post-contrast head MRI (Axial view)

Figure 2. Pre-contrast head MRI (Axial view)

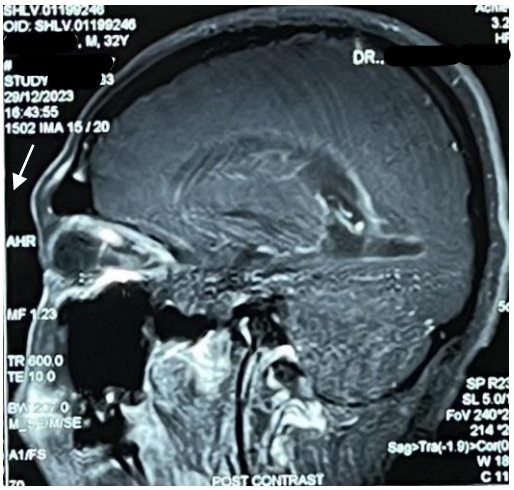

Figure 3. Post-contrast head MRI (Sagittal view)

On 31st December 2023, patient was tested for anti-HIV and was found out to be reactive. Patient was also subjected to spinal tap on the same day and the result was that the cerebrospinal fluid was yellow and cloudy macroscopically; microscopically, there was an increase in cell number (150/microliter) with 97% mononuclear and 3% polymorphonuclear

cells. total protein (279 mg/dL) and decrease in glucose (36 mg/dL). Nonne and Pandy were found to both be positive. Electrolyte panel done at 1st of January 2024 showed normal sodium levels of 139 mmol/L. Indian Ink test done on the CSF on 1st of January 2024 shows negative result.

On the first day, 30th December 2023, patient was treated with ondansentron 3x8 mg, paracetamol 3x1 gram, ketorolac 3x 10 mg, omeprazole 1x1, ceftriaxone 2x2 grams and dexamethasone 3x 10 mg. On the second day, 31st of December 2023, after spinal tap and anti-HIV test was done, an additional therapy of laxatives 1x5ml and TB FDC 1x4 tablet was added. On the third day, 1st of January 2024, natrium docusate ear drop was added to the therapy with a dosage of 2x4 drops/ ear. On the third day of hospitalization, dose of dexamethasone was decreased to 3x5mg. On the fourth day of hospitalization, ondansentron was stopped and paracetamol was given only if necessary.

On the 3rd of January 2024, patient had complaints of profuse projectile vomiting accompanied. Patient was then taken up to CT and it was discovered that there is diffuse cerebral edema.

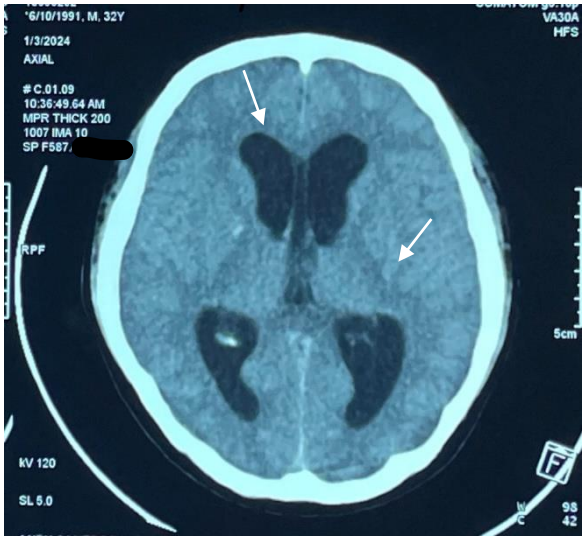

Figure 4. Brain CT of patient before ventriculoperitoneal shunt

Ventriculoperitoneal (VP) shunt procedure was done on the 4th for this patient. Follow up in the next day shows improvement in patient's complaints of vomiting. CT scan on the 9th showed dilatation in the right lateral ventricle and improvement on the left as well as VP shunt tip in the left lateral ventricle.

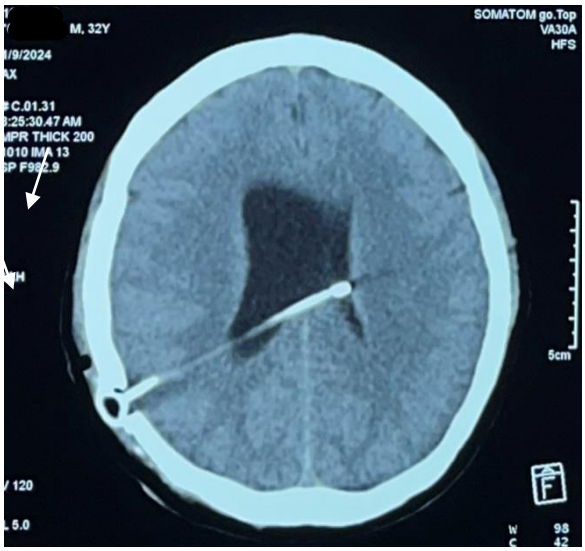

Figure 5. Brain CT scan of patient post VP shunt

2. Discussion

A 32-year-old man was admitted to Royal Taruma hospital due to a four-day history of severe headaches and fever. Patient's friend confirmed that patient has had trouble remembering the sequence of events after the complaint. During the physical examination, the Brudzinsky IV sign was detected. A head MRI with contrast revealed significant abnormalities including notable changes in the cerebral and cerebellar sulci, ventricular system dilation (particularly in the bilateral lateral ventricles).

Additionally, the patient's anti-HIV test came back positive. Analysis of the cerebrospinal fluid (CSF) displayed macroscopic yellow and cloudy appearance. Under microscopic examination, an increased cell count (150/microliter) primarily composed of 97% mononuclear cells and 3% polymorphonuclear cells was observed. The total protein was elevated at 279 mg/dL while glucose levels were decreased to 36 mg/dL. Both Nonne and Pandy tests were positive.

On the 5th day, patient had complaints of profuse projectile vomiting and was taken up to CT where it was discovered that he had diffuse cerebral edema. VP shunt was later done on the patient.

Meningitis is defined as inflammation of the meninges.(Hersi et al., 2021) Meninges are the coverings of the brain and spinal cord. From external to internal, meninges consist of the dura mater, arachnoid, and pia mater.(Aksamit & Berkowitz, 2021) Hydrocephalus is a condition in which there is an accumulation of intracranial CSF under pressure, with or without distension of the cerebral ventricles**.**(Sunderland et al., 2023)

Anerobic Mycobacterium tuberculosis may enter through inhalation and continue with macrophage colonization in the alveolus. In active lung tuberculosis, bacteria will spread to lymph nodes and enter systemic blood flow which would help it reach the central nervous system and build focal infection in the brain parenchym which can be latent or activated later. Pathologically, it will show a focal lesion of granulomatous necrotic focal lesion. The immune system in the brain parenchym is less active compared to other organs and can be seen with the minimal presentation of antigen presenting cells, dendritic cells and major histocompatibility complex II. Infection focus in the subcortical that is activated can burst to the subarachnoid space and release M. tuberculosis into the cerebrospinal fluid and manifest as tuberculous meningitis.(Imran et al., 2022) There are two stages of tuberculous meningitis; bacterial seeding of the meninges and subpial regions of the brain with formation of tubercles that then rupture and discharge of bacteria to the subarachnoid space. In 1985 in the Unites States, there was an increase of cases of tuberculous meningitis due to the emergence of HIV in which tuberculosis is one of the first clinical manifestations of HIV. (Ropper et al., 2019)

In the history taking of meningitis patients, one must consider if the patient has had any close contact exposures, incomplete vaccinations, immunosurpression, age (younger than five, older than 65), alcohol use, recent travel, sexual contact, animal contact and recent neurosurgery intervention.(Hersi et al., 2021)

Tuberculous meningitis has an onset of 5-10 days and there are no difference in manifestations between patients with HIV and non.(Imran et al., 2022) Early manifestations of tuberculous meningitis may include low-grade fever, malaise, headache, lethargy, confusion and stiff neck with positive Kernig and Brudzinski signs in which these symptoms develop less rapidly than bacterial meningitis, usually within a week or two, sometimes longer. In young children and infants, symptoms may include hyperiritability and apathy; however stiff neck may not be as prominent. Because of its chronic nature, several cranial nerve palsies and papilledema may be present at the time of diagnosis. Patients who suffer from fungal meningitis are said to have similar clinical features as those in tuberculous meningitis. In tuberculous meningitis, there is usually evidence of tuberculosis elsewhere in the body. (Ropper et al., 2019)

According to the Medical Research Council (MRC) in the year 1948, there are 3 stages of severity of tuberculous meningitis that may predict prognosis. First degree is patient with full awareness (Glasgow coma scale/ GCS 15) with no focal neurological deficit. Second degree is patients with GCS of 11-14 or GCS of 15 with focal neurological deficit. Third degree is patients with GCS of less than or equal to 10 with or without focal neurological deficit.(Imran et al., 2022)

Meningitis is diagnosed through cerebrospinal fluid (CSF) analysis. This includes

white blood cell count, glucose, protein, culture, and in some cases, polymerase chain reaction (PCR). CSF is obtained via a lumbar puncture (LP), and the opening pressure can be measured. (Hersi et al., 2021)

Patients with tuberculous meningitis can experience slightly increased pressure within CSF analysis. Cell number usually falls between 50-500/mm3. Initially, PMNs and MNs will be equal in number but it will soon be dominated by MNs after several days. Protein content is usually between 100-200 mg/dL with decreased glucose levels (below 40 mg/dL but rarely as low as bacterial). Protein content may be higher is CSF flow is blocked around the spinal cord. (Ropper et al., 2019) Definitive diagnosis of tuberculous meningitis is obtained if there are any acid-fast bacili in the CSF, positive culture of M. tuberculosis on the CSF or nucleic acid workup shows positive sign on patient who shows clinical signs of tuberculous meningitis.(Imran et al., 2022)

Additional testing can be done according to suspected etiology. (Hersi et al., 2021) For suspected mycobacterial etiology, CSF Acid-fast bacili smear and culture can be done. (Hersi et al., 2021) However, Acid-fast bacili smear in CSF analysis has a low sensitivity of 10-20%. Gold standard workup is the culture of CSF in tuberculous meningitis cases but it takes 2-8 weeks to perform and is not sensitive enough to rule out tuberculous meningitis. (Imran et al., 2022) Tuberculin skin test may be ordered for children with suspected tuberculous meningitis. (Ropper et al., 2019) PCR (Xpert) may be performed with those suspected of tuberculous meningitis.(Berkowitz, 2022)

In tuberculous meningitis cases, neuroimaging may reveal hydrocephalus with meninges enhancement, basal area enhancement, tuberculoma and infarct.(Imran et al., 2022) Inflammatory exudate in tuberculous meningitis is produced in the subarachnoid cisterns and the skull base which will cause inflammation and lead to vasculitis, vasospasm, periarteritis or even necrotizing panarteritis of affected vessels. These may jeopardize arterial blood flow, hence ischemia and cerebral infarct.(Yiek & Wong, 2022)

The decision to treat tuberculous meningitis is not dependent on culture results if the probability of tuberculous meningitis is high. In general, tuberculous meningitis is probable if symptoms has lasted for 7 days or more with CSF pleocytosis with CSF to blood glucose ratio of less than 50%, neuroimaging that is characteristic of tubercuous meningitis (hydrocecphalus, tuberculoma) or chest x-ray that reveals miliary tuberculosis.(Imran et al., 2022) Treatment of tuberculous meningitis generally consists of 2 months of a four-drug regimen (isoniazid, rifampin, pyrazinamide, and ethambutol or streptomycin) followed by an additional prolonged course of isoniazid and rifampin.(Aksamit & Berkowitz, 2021; Berkowitz, 2022) The prolonged course witll be 10 months. Isoniazid, pyrazinamid and ethambutol all have acceptional capability to go through the blood brain barrier. Rifampin has poor ability to go through to the central nervous system but is still one of the drugs used in meningeal tuberculosis due to the high mortality of patients who are resistant to it. Streptomycin is not recommended in patients with HIV as it has to be administered intramuscularly.(Imran et al., 2022)

Corticosteroids (dexamethasone) are often added during the initial 2 months.(Aksamit & Berkowitz, 2021; Berkowitz, 2022) Patients who are HIV positive may not show as much benefit as HIV negative in the usage of corticosteroids. Dosage of dexamethasone differs according to the MRC degree of the patient.(Imran et al., 2022)

In patients with coexisting HIV infection who are not already on antiretroviral therapy, it may be necessary to defer initiation of antiretrovirals until after an initial period of treatment of tuberculous meningitis due to the risk of immune reconstitution inflammatory syndrome (IRIS). (Aksamit & Berkowitz, 2021; Berkowitz, 2022)

Tuberculosis meningitis can result in hydrocephalus, strokes, epilepsy, cognitive decline, neurological impairments, and cranial nerve issues. (Kaur et al., 2022) Hyponatremia may result from meningeal tuberculosis due to adrenal insufficiency, syndrome of inappropriate secretion of antidiuretic hormone (SIADH) and cerebral wasting syndrome (CSWS).(Imran et al., 2022)

SIADH causes a dysregulation in the release of antidiuretic hormone or gain-of-function mutations in the V2 vasopressin receptor in the renal tubule. SIADH may be diagnosed if the patient meets 2 criteria of the following(Cui et al., 2019):

a. No signs of hypovolemia (dry mucosa, tachycardia, hypotension or postural hypotension)

b. No laboratory evidence of dehydration (elevated hematocrit, hemoglobin, serum albumin, blood urea)
c. Normal oppositive fluid balance with absence of weight loss
d. Central venous pressure of >6 cm of water

CSWS has an unclear pathophysiology but some have suggested that there may be sympathetic neural input to the juxtaglomerular apparatus can reduce sodium reabsorption and decrease renin and aldosterone release or natriuretic peptide theory that suggests atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) increases sodium excretion and urine volume. CSWS is characterized by negative sodium balance with volume depletion (Cui et al., 2019).

The accumulation of intracranial CSF under pressure is called hydrocephalus (Sunderland et al., 2023)**.** The disruption of CSF flow may be caused by the inflammatory infiltrate within the subarachnoid space or the ventricular pathways. This may result in hydrocephalus. Hydrocephalus can be communicating, which is caused by abnormal flow through the basal cisterns causing impairment in absorption of CSF or non-communicating, which is usually a later complication due to obstruction at the level of the fourth ventricle causing blockage of CSF circulation within the ventricular system (Davis et al., 2018).

Among these two, communicating hydrocephalus is more common and can be managed medically however may require intervention if progressing, although some studies suggest that early diversion in patients may result in btter outocme (Davis et al., 2018; Garg & Gupta, 2021). The medical management can consist of antitubercular therapy, steroids and diuretics. Medical management is given in hopes that this will subside pathological processes, such that of basal exudates, that may result in hydrocephalus (Garg & Gupta, 2021).

Anti-tubercular therapy includes a four drug regimen of isoniazid 5 mg/kg (4-6 mg/kg), rifampin 10 mg/kg (8-12 mg/kg), pyrazinamide 25 mg/kg (20-30mg/kg) and ethambutol 15 mg/kg (15mg-20mg/kg) due to its antibacterial and anti-inflammatory property. However, suggestions to replace ethambutol with streptomycin 15 mg/kg (12-18mg/kg) has been made.(Garg & Gupta, 2021)

Steroids have been found to improve survival without impacting functional outcomes of patients with more than 14 years of age. The common dose of intravenous dexamethasone would be 0.2 mg/kg/day in divided doses (Garg & Gupta, 2021).

If the patient develops clinical signs of increased intracranial pressure (altered mental status, neurologic deficits, non-reactive pupils, bradycardia), conservative interventions to maintain cerebral perfusion include elevating the head of the bed to 30 degrees, inducing mild hyperventilation in the intubated patient or osmotic diuretics such as 25% mannitol or 3% saline. (Hersi et al., 2021) Other options of diuretics would be furosemide or acetazolamide. It is said that other than decreasing intracranial pressure and improving cerebral perfusion pressure, it can help with antitubercular therapy delivery to the central nervous system.(Garg & Gupta, 2021)

Noncommunicating hydrocephalus requires rapid intervention.(Davis et al., 2018) Modified Vellore Grading (MVG) of tuberculous meningitis with hydrocephalus is used to assess the rate of failure of a CSF diversion procedure. The scoring are as follows:(Aranha et al., 2018)

a. Grade 1: GCS 15 with headache, vomiting, fever and no neurological deficits
b. Grade 2: GCS 15 with neurological deficit
c. Grade 3: GCS 9-14 with or without neurological deficit
d. Grade 4: GCS 3-8 with or without neurological deficit

CSF diversion techniques such as ventriculoperitoneal shunts (VPS), endoscopic third ventriculostomy (ETV) and external ventricular drain (EVD) are the mainstay of surgical treatment for hydrocephalus. (Yiek & Wong, 2022)

VP shunt is a surgical procedure that involves insertion of a catheter that connects brain ventricle to the peritoneal cavity (Kurniawan & Zulfariansyah, 2020). ETV is a procedure where a small ostium is created in the floor of the third ventricle to alleviate symptoms of hydrocephalus (Farag et al., 2022). EVD is a temporary device placed into the lateral ventricles of the brain to facilitate external CSF drainage as well as to monitor CSF pressure (Lele et al., 2017).

Historically, ventriculoatrial shunt was the treatment of choice in the 1970s before being replaced by VP shunt in the 1980s. ETV was introduced in the 1990s and proved to

have some advantages over VP shunts which include reducing the risk of infection and blockage as well as avoiding abdominal pseudocyst formation (Yiek & Wong, 2022). Shunt infection is more commonly caused by gram (-) bacili followed by S.aureus, S.epidermidis dan Staphylococcus haemolyticus (Nataprawira et al., 2022). Other advantages of ETV may include the absence of tissue reaction to foreign body, shorter surgery duration with fewer incisions, avoiding tuberculous peritonitis, eliminate CSF overdrainage and reduce rate of long-term complications (Aranha et al., 2018). Other than that, ETV can be done on patients whose CSF cell contents exceeds 100 cells/mm^3 unlike with VP shunt which risks obstruction of shunt if done in that condition and will require shunt revision surgery (Aranha et al., 2018; Yiek & Wong, 2022). ETV is said to bring CSF circulation to previously inaccessible and normal areas of absorption, hence clearing exudates (Aranha et al., 2018).

EVD placement is recommended for 7 days for patients with poor prognosis (MVG grade 3-4) as a preliminary procedure before VP shunt. If patient shows improvement that enables them to move 1 MV grade up VP shunt shall be done.(Yiek & Wong, 2022) Even with that as the case, EVD placement is associated with higher risk of ETV or VP shunt failure due to the fact that patient's general condition is usually in the worse side before procedure (Aranha et al., 2018).

Despite that, patients with severity grade of MRC 3 or MVG of 3 and 4 show poor prognosis despite shunting. It is also said that HIV positive patients show worse prognosis than those HIV negative ones (Davis et al., 2018; Yiek & Wong, 2022). Decision of treatment or procedure will depend on patient's clinical condition, surgeon experience and expertise, as well as endoscopy resource (Yiek & Wong, 2022).

Meningitis may originally be caused by an infection localized anywhere in the body (Vasudeva, 2023). Patient had complaints of nausea and vomiting as well as fever before the complaints of headache started which may suggest an infection in the gastrointestinal tract preceding meningitis. Patient is also part of the LGBTQ community therefore rendering him vulnerable to the possibility of being HIV positive which could be one of the risk factors of meningitis, especially tuberculosa or fungal (Hersi et al., 2021; Ropper et al., 2019).

Patient's complaints of headache are consistent with symptoms of meningitis. This is due to the stimulation of dural nociceptors surrounding these structures as a result of meningeal irritation. As a result of infection, a systemic inflamation will arise and may result in the increase basal metabolic rate, inducing fever. Inflammation near the brain parenchyma may interfere with normal CNS function, hence patient's confusion (Yu, 2022).

Although neuroimaging is not definitive for the diagnosis of meningitis, it is still useful to eliminate conditions such as brain abscess, etc (Aksamit & Berkowitz, 2021). This patient was found to have some dilatation in his intracranial structure that would be suggestive of an inflammatory process. Patient has also tested positive for anti-HIV which is one of the risk factors of meningitis (Hersi et al., 2021). Patient's CSF analysis result shows high cell count and protein content with decreased glucose level and dominantly mononuclear cells with negative Indian ink stain. This may be highly suggestive of tuberculous meningitis (Aksamit & Berkowitz, 2021; Berkowitz, 2022; Ropper et al., 2019).

Patient is initially treated with anti-emetics, anti-pyretic, antibiotics and corticosteroids. This is in line with protocol of when meningitis is being considered.(Aksamit & Berkowitz, 2021; Berkowitz, 2022) Patient was then given TB FDC once it was confirmed that he was HIV positive which is also common practice. This is due to delaying therapy having an adverse effect on the HIV patient's prognosis if tuberculous meningitis is considered, especially those dominantly mononuclear cells in CSF analysis and negative Indian ink stain (Pormohammad et al., 2018). Patient was not administered any anti-retrovirals until tuberculous meningitis is resolved to avoid IRIS (Aksamit & Berkowitz, 2021; Berkowitz, 2022).

Patient then experienced an increase in intracranial pressure with signs of projectile vomiting. Patient then underwent VP shunt. VP shunt is one of the mainstay CSF diversion methods in hydrocephalus cases in tuberculous meningitis. Even though in literatures mentioned in this paper stated that ETV is more recommended, choice of procedure or treatment of patient should also consider surgeon's experience and expertise as well as endoscopic availability (Aranha et al., 2018; Davis et al., 2018; Yiek & Wong, 2022).

CONCLUSION

A 32 year old man was diagnosed with tuberculous meningitis and suffered hydrocephalus as a complication of it. Patient is also an HIV positive patient. Patient was given adequate medical therapy and VP shunt procedure was done on the patient. Afterwards, patient showed improvement of symptoms.

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