CASE REPORT

Cryptococcal Meningitis Disguised As A Stroke: A Case Report

Fatimahtuz Zahrah Muhamad Damanhuri[1,2], Siti Zulaikha Zakariah[1,3], Fatimatulzahra Abdul Ghani[3]

[1] Department of Medical Microbiology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia
[2] Department of Pathology, Hospital Sungai Buloh, Jalan Hospital, 47000 Sungai Buloh, Selangor, Malaysia
[3] Hospital Pengajar Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia

ABSTRACT

We present a case of cryptococcal meningitis initially misdiagnosed as stroke. Our patient is a young man on long-term corticosteroid due to gouty arthritis, who presented with acute onset of left-sided body weakness. Computed tomography of the brain revealed multifocal chronic lacunar infarcts with acute communicating hydrocephalus and cerebrospinal fluid culture isolated *Cryptococcus neoformans*. He was subsequently treated with amphotericin B and fluconazole but passed away due to multiorgan failure. This case report highlights the importance of considering chronic meningitis as a differential diagnosis when encountering stroke in young and immunocompromised patients. *Malaysian Journal of Medicine and Health Sciences* (2022) 18(5): 225-227. doi:10.47836/mjmhs18.5.32

Keywords: Meningitis, Cryptococcal, Stroke, Diagnosis, Differential

Corresponding Author:
Siti Zulaikha Zakariah, DrPath
Email: zulaika@upm.edu.my
Tel: +60397692479

INTRODUCTION

Cryptococcus neoformans is an encapsulated yeast found through the world in soil contaminated with pigeons' droppings and enter the human body most commonly through inhalation of the infectious propagules. It remains the most common opportunistic infection of the central nervous system (CNS) among immunocompromised patients particularly with impaired cell-mediated immunity such as human immunodeficiency virus (HIV), prolonged steroid therapy, malignancy and diabetes mellitus (1). Fungal infections of the CNS can manifest as meningitis, abscesses, granuloma, or infarction (2). Ischemic stroke can arise as a complication of cryptococcal meningitis in up to one-third of cases and carries a high mortality (3). Therefore, the identification of cryptococcal pathogens in cerebrospinal fluid (CSF) testing is essential to guide the diagnosis in a patient who suffered from an acute onset of stroke secondary to cryptococcal meningitis in the high-risk patient (2).

However, as the cryptococcal test is not part of the routine CNS investigation, this case report describes a 34-year-old man with cryptococcal meningitis who was misdiagnosed with an acute ischaemic stroke.

CASE REPORT

We report a case of a 34-year-old man who had been self-medicating himself with regular oral prednisolone for the past two years for gouty arthritis. He was referred to our hospital for acute onset of left-sided body weakness. He was initially diagnosed as left-sided stroke and discharged back to the referring hospital for conservative management. However, he came back to our hospital the following day with additional symptoms of fever and abnormal behaviour. On examination, his pulse rate was 80 beats per min, blood pressure was 146/105 mmHg and afebrile. He was well orientated with coherent speech. Pupils were equal and responsive to light. He had mild left hemiparesis with normal sensory function. The biceps, triceps, knee, ankle and plantar reflexes were symmetrical. Cranial nerve examinations were normal. The motor coordination was smooth. The random blood sugar was high (18 mmol/L). Non contrast-enhanced computed tomography (CT) of the brain showed multifocal chronic lacunar infarcts at the right basal ganglia, right internal capsule and right corona radiata with associated acute communicating hydrocephalus (Figure 1). There was no history of trauma. Upon further questioning, family members revealed that he has been suffering from intermittent fever and headache associated with nausea and vomiting for the past four months. He was admitted for further investigation and management of possible brain abscess, tuberculous meningitis, toxoplasma meningitis and cryptococcal meningitis.

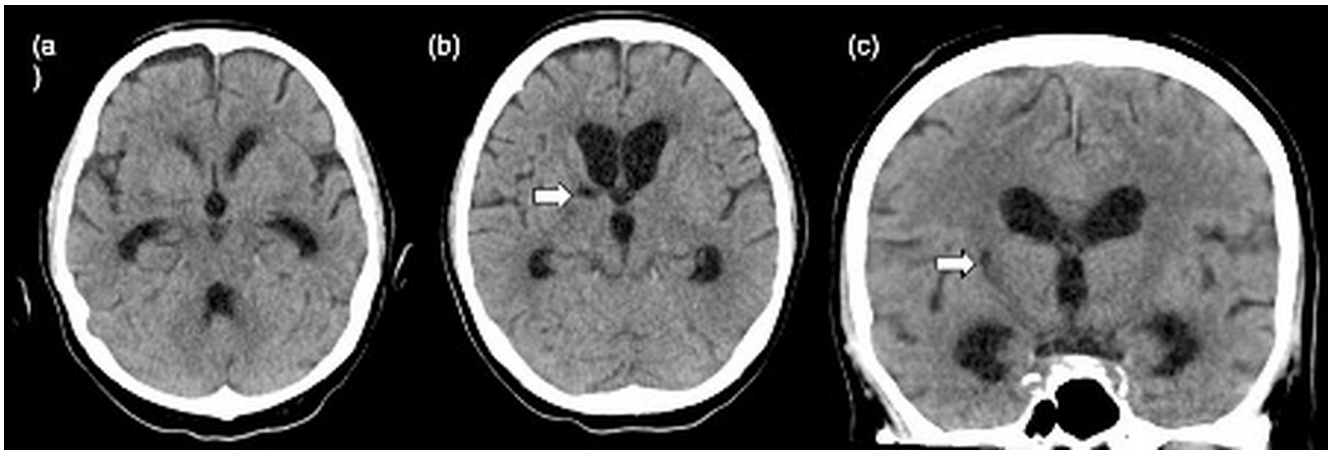

Figure 1: Non-contrast CT of the brain in transverse (a and b) and coronal (c) planes. (a) Generalized ventricular dilatation in keeping with communicating hydrocephalus and (b, c) right basal ganglia chronic lacunar infarctions (arrow). CT = computed tomography.

On the second day of admission, he deteriorated and required intubation. He developed a fever of 38.9oC, exhibited abnormal behaviour, and Brudzinski sign was positive. Repeated CT of the brain showed worsening acute communicating hydrocephalus. His blood sugar level was persistently high. The investigations of serum parathyroid hormone (PTH) was low (<0.583pmol/L) and serum cortisol was high (145nmol/L). He was diagnosed as hypercortisolism secondary to prolonged used of steroid.

The full blood count showed leucocytosis (16 x109/μL), predominantly neutrophils (79%). The HIV screening test was negative. The sputum acid-fast bacilli (AFB) was negative. A lumbar puncture was performed on the third day of admission, normal opening pressure (6 cmH2O) was observed. Analysis of the CSF showed clear fluid with elevated glucose (4.31 mmol/L) and protein level (4.1 g/L). The cryptococcal antigen was positive with a titre of 1:40. The CSF culture grew *Cryptococcus neoformans* after two days of incubation and blood culture was no growth.

Consequently, the patient was treated with intravenous amphotericin B (0.7mg/kg per day) and oral fluconazole. However, due to worsening renal function, the patient was subsequently given intravenous flucytosine 2g bd and oral fluconazole. Serial cultures done after five days of anti-fungal showed clearance of *Cryptococcus neoformans* in the CSF. Nonetheless, the patient's condition did not improve with multiple episodes of failed extubation. He required close monitoring in the intensive care unit for one month and succumbed to death due to multiorgan failure.

DISCUSSION

Ischaemic stroke is a common complication of cryptococcus meningitis among HIV-positive patients, transplant patients and occasionally immunocompetent individuals. The diagnostic challenge in this patient was that the typical presentations of cryptococcal meningitis such as headache, fever, altered mental status and neck stiffness was not apparent in this patient until after the diagnosis of stroke (1). He had symptoms similar to that of an acute ischemic stroke which caused a delay in diagnosing the patient. Cerebrospinal fluid analysis and culture, commonly used to diagnose CNS infection is not a routine investigation for acute ischemic stroke.

Our patient's use of corticosteroid causes suppression of the immune system and reduced cell-mediated immunity leading to increased susceptibility towards Cryptococcal neoformans infection (1). Cerebral ischaemia in cryptococcal meningitis can occur at any stage of the infection either the acute stage, chronic stage or during treatment. The infarction is a result of progressive vasculitis from perforating arteries resulting in thrombosis and occlusion due to fungal invasion along the perivascular spaces of the brain base (4). This patient also had evidence of hydrocephalus which is usually preceded by the diagnosis of cryptococcal meningitis by weeks or months. The hydrocephalus can stretch already-compromised vessels leading to further ischaemia of already compromised areas in the brain.

Commonly reported neuroimaging findings are dilated perivascular spaces, pseudocysts, hydrocephalus and leptomeningeal enhancement. Dilated perivascular spaces are similar to lacunar infarction and located mainly in the basal ganglia, centrum semiovale, corpus callosum, cerebellum, and brainstem. However, in immunocompromised patients, the neuroimaging findings mentioned may overlap with other conditions such as cerebral toxoplasmosis and primary CNS lymphoma since there is currently no pathognomonic radiologic feature that points to fungal CNS infection (5). Microbiological and pathological investigations are still needed to come to a conclusive diagnosis.

The prognosis of cryptococcal meningitis is variable and depends on several factors. Poor prognostic factors

includes Cryptococcus growth from sites other than CSF, altered mentation, elevated intracranial pressure, high CSF cryptococcal antigen titre, papilloedema, chronic use of corticosteroids or other immunosuppressants, absence of headache and low Glasgow coma scale (GCS) score (1). Studies show that certain strains of Cryptococcus may have a high propensity to cause vasculitis and thrombosis (1).

CONCLUSION

This case underscores the need for a complete history and consideration of chronic meningitis as a differential diagnosis when encountering patients with acute stroke with a predisposing immunocompromised state. Missed cryptococcal meningitis diagnosis may lead to improper diagnosis and management, affecting the patient's clinical outcome with increased morbidity and mortality.

REFERENCES

1. Qu J, Zhou T, Zhong C, Deng R, Lь X. Comparison of clinical features and prognostic factors in HIV-negative adults with cryptococcal meningitis and tuberculous meningitis: a retrospective study. BMC Infect Dis. 2017 Jan 10;17(1):51–51. doi: 10.1186/s12879-016-2126-6.
2. Hao Lai C, Yu Lin G, Tay Lee J, Wen Kao H, Han Ho T, Kai Lin Y, et al. A Rare Case of Cryptococcus Meningoencephalitis Presenting with Acute Brainstem Infarction in an Immunocompetent Host. Neuropsychiatry [Internet]. 2017 [cited 2020 Dec 9];07(06). doi:10.4172/Neuropsychiatry.1000285
3. Tarhan B, Mehkri Y, De Prey J, Hu C, Tuna IS, Shuhaiber H. Cryptococcosis Presenting as Cerebrovascular Disease. Cureus [Internet]. 2021 Nov 10 [cited 2022 Jan 21]; doi:10.7759/cureus.19442
4. Vela-Duarte D, Nyberg E, Sillau S, Pate A, Castellanos P, Chastain DB, et al. Lacunar Stroke in Cryptococcal Meningitis: Clinical and Radiographic Features. J Stroke Cerebrovasc Dis. 2019 Jun;28(6):1767–72. doi:10.1016/j.jstrokecerebrovasdis.2018.12.043
5. Tan Z-R, Long X-Y, Li G-L, Zhou J-X, Long L. Spectrum of neuroimaging findings in cryptococcal meningitis in immunocompetent patients in China — A series of 18 cases. J Neurol Sci. 2016 Sep;368:132–7. doi:10.1016/j.jns.2016.06.069