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CASE REPORTS

Cryptic clues: Hemichorea, hypersomnolence, and bilateral thalamic pulvinar calcification in cryptococcal meningoencephalitis

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Abstract

Cryptococcal meningoencephalitis (CME) is a severe fungal infection which although common, is challenging to identify in its early stages particularly in resource limited settings. This case report aims to enhance clinicians' ability to recognise atypical signs of CME, facilitating early diagnosis and treatment. We report here a 63-year-old male with an atypical presentation of CME including subacute hemichorea which eventually became generalised; hypersomnolence, and bilateral pulvinar calcifications. Initial misinterpretation of these findings led to a delay in diagnosis. Despite receiving appropriate treatment, the patient ultimately succumbed to the infection. In conclusion, this case highlights the diagnostic challenges in CME, particularly in patients without classical symptoms like fever or headache. Additionally, it also highlights the potential link between pulvinar calcifications and CME, emphasising the need for further investigation into the potential role of this sign as a diagnostic clue.

Keywords: Central nervous system infections, chronic meningitis, cryptococcosis, cryptococcal meningoencephalitis, chorea, hemichorea, hypersomnolence, calcification, pulvinar

INTRODUCTION

Cryptococcal meningoencephalitis (CME) imposes a substantial global health challenge, impacting individuals with HIV or other immunocompromised conditions, as well those apparently immunocompetent.[1] The burden of this deadly fungal infection is disproportionately higher in resource-limited regions, where the already higher prevalences of CME are exacerbated by poorer access to care. Adding to this conundrum, diagnosing CME in its early phase is challenging, as clinical symptoms may be subtle and neuroimaging is commonly unremarkable. We describe a patient with an atypical presentation of CME with subacute onset chorea, hypersomnolence, and bilateral pulvinar calcifications. We emphasise that while uncommon, these features—when taken in context—can serve as critical diagnostic clues for timely identification and management of CME.

CASE REPORT

A 63-year-old man with long-standing hypertension, diabetes mellitus, and chronic kidney disease (CKD), initially presented to a district hospital with a sub-acute right-sided hemichorea (Video 1). There was no documented fever, headache, or relevant contact/travel history, and no evidence of hyperglycaemia, hyperviscosity, or uremia at presentation. A plain brain CT at presentation revealed ill-defined hypodensities in the left lentiform nucleus, subtle hydrocephalus, and linear hyperdensities in both thalami (Figure 1 a, b). These findings were reported as an acute infarct on the background of age-related cerebral atrophy and calcification, and management for secondary ischaemic stroke prevention was rendered.

However, his condition progressively worsened over the subsequent four months with the development of generalised chorea, hypersomnolence, and diminished verbal output.

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This gradual deterioration culminated in an abrupt reduction in consciousness, requiring emergency intubation upon arrival at our institution.

A repeated brain CT showed communicating hydrocephalus, multiple ill-defined hypodense lesions (predominantly affecting the left basal ganglia), and the same symmetrical linear hyperdensities in both thalami, consistent with pulvinar calcification (Figure 1 c, d). Cerebrospinal fluid analyses revealed high opening pressure (22cmH20), low glucose (1.0 mmol/L), high protein (3.7g/L), lymphocytosis (100 cells), and a high cryptococcal antigen titre (1:1280), confirming the diagnosis of CME. Screening for HIV and tuberculosis was negative. Despite treatment with amphotericin-B and ventriculo-peritoneal shunting, he succumbed fifteen days after admission, prior to a scheduled MRI.

DISCUSSION

This case is particularly notable for the initial presentation of right-sided hemichorea, which progressively generalised, and hypersomnolence—all in the absence of more common symptoms of CME, such as headache.

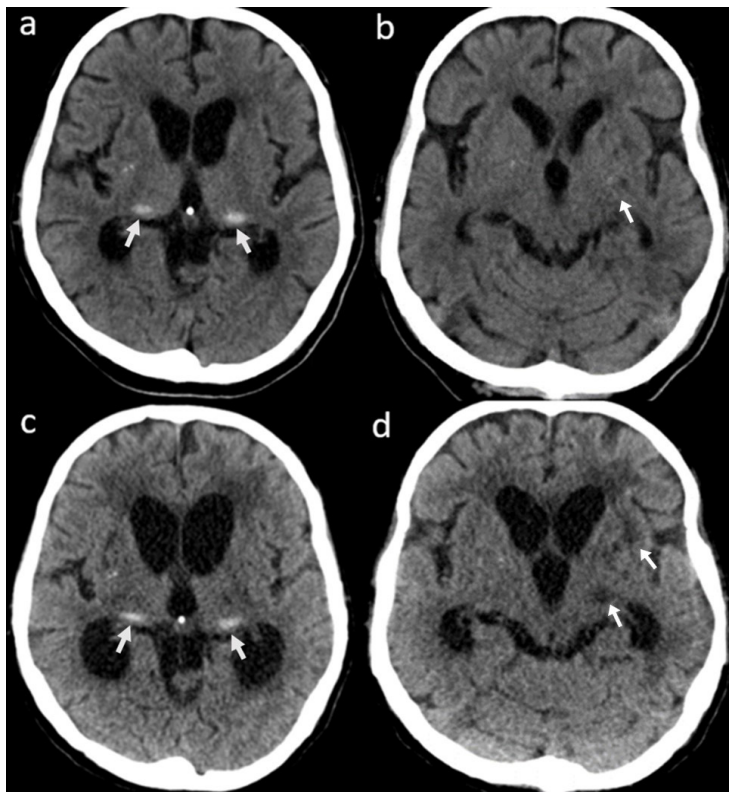

Figure 1. Brain CT images taken during index symptom and at onset of deterioration. All images are plain CT images. (a and b): Acquired from index event during initial presentation for chorea. (a). Bilateral symmetrical hyperdensities over both thalami signifying pulvinar calcification (arrows) are clearly seen along with subtle hydrocephalus. (b). A few ill-defined hypodense lesions most prominently in the left lentiform nucleus (arrow) can be appreciated. These were initially reported as infarcts. (c and d): Acquired four months later during acute deterioration. (c). Bilateral thalamic pulvinar calcification (arrows) are still present and are relatively unchanged. Additionally, the presence of adjacent hypodensities [not previously seen in (a)] suggest further thalamic involvement. Worsening hydrocephalus is appreciated as evidenced by increased dilatation of frontal and occipital horns of the lateral ventricles relative to (a). Periventricular hypodensities seen are likely to represent CSF seepage, suggesting a relatively acute process. (d). previously seen areas of hypoattenuation are slightly more conspicuous and are accompanied by new hypodense lesions (arrows) in the left lentiform nucleus, thalamus, and internal capsule. These may represent cryptococcomas or lacunar infarcts arising from a vasculitic process driven by cryptococcal infection. Further ballooning of the third ventricle indicates worsening hydrocephalus.

Chorea is a rare manifestation of CME. All reported cases describe chorea confined to only one limb/side of the body (hemichorea) and usually associated with a contralateral brain lesion.[2-5] CME has a tendency to affect deep grey matter structures leading to the formation of cryptococcomas or infarcts, both of which may give rise to abnormal hyperkinetic movements.[6] Similarly, in our patient, the left basal ganglia hypodensities observed on neuroimaging, consistent with cryptococcomas, might explain his initial right-sided hemichorea.

The eventual generalisation of his choreiform movements is interesting and might signify the spread of inflammation or the involvement of additional basal ganglia structures bilaterally, as seen in some cases of CME affecting both sides of the brain.[1] Inflammation in the basal ganglia and its associated circuitry could disrupt movement modulation, potentially resulting in generalised motor dysfunction. Additionally, the development of hypersomnolence suggests further thalamic or hypothalamic involvement (Figure 1 c), and may indicate a broader disruption of neural circuits that includes areas controlling sleep and alertness, further complicating the patient's neurological presentation. This empahsises the importance of recognising that CME can present with a range of non-specific symptoms differing from the classic picture.

Neuroimaging findings in CME is highly variable; dilated perivascular spaces are characteristic, while leptomeningeal enhancement and hydrocephalus are more commonly seen in HIV-negative individuals.[1] The bilateral basal ganglia hypodensities and progressive hydrocephalus observed in our patient are well-recognised features of CME.[6] This highlights the potential utility of early neuroimaging in identifying subtle CNS infection markers. However, it is important to note that approximately half of CME patients may present with unremarkable brain CTs.[1]

Existing literature regarding parenchymal calcification (likely a sequela of chronic infection) in CME remains limited[7,8], and pulvinar calcifications, although intriguing, are not established definitive markers of CME. Classically, symmetrical calcifications are more commonly associated with chronic dystrophic changes rather than active infection. A relatively isolated bilateral pulvinar calcification pattern is distinct and uncommon[7]; and is thought to be characteristic of Fabry's disease (FD), where it is attributed to dystrophic calcification resulting from cerebral hyperperfusion in the posterior circulation.[9] Apart from CKD resulting from uncontrolled hypertension, our patient had no classical features of FD (i.e. acroparesthesias, angiokeratomas, hypohydrosis, hearing loss, or cardiomyopathy).

The appreciation of a bilateral pulvinar calcification pattern outside the context of FD is exceptionally rare, and its association with CME, as seen in our patient and one other case report of immunocompetent-CME is noteworthy.[7] In this context, due consideration should be given to alternative pathophysiological mechanisms, such as early inflammatory or ischemic changes. The thalamic pulvinar is supplied by small perforating end-arteries from the posterior choroidal arteries.[9] We hypothesise that the affinity of cryptococcosis towards the perivascular spaces and the choroid plexus (as demonstrated by cases of cryptococcal choroid plexitis) may lead to ischaemia/inflammation in the parenchyma surrounding the inflamed end-arteries, causing subsequent dystrophic calcification in the longer-term.[1] The pulvinar is selectively vulnerable to this process due to its unique end-arterial vasculature and shared vascular supply with the choroid plexus.

Further research into the presence of this sign in larger cohorts of patients with CME and in other chronic CNS infections, such as tuberculosis, neurocysticercosis, toxoplasmosis, and cytomegalovirus, would also be valuable to further investigate this association.

In conclusion, this case highlights the importance of considering CME in the differential diagnosis of patients with atypical clinical presentations such as chorea and hypersomnolence, even in the absence of classical features like headache. While the association between CME and bilateral thalamic pulvinar calcification remains to be elucidated, its presence, particularly in patients without classical FD features, warrants investigation for an infectious aetiology. Appreciation of these clinical and radiological features may help clinicians with timely recognition of CME which is crucial for the initiation of early treatment, prevention of catastrophic complications from a disseminated infection, and significant improvement of patient outcomes.

DISCLOSURE

Ethics: The patient and his next of kin provided informed consent for the use of de-identified data for publication purposes. This study was approved by the National Medical Research Register of

Malaysia (NMRR ID-24-00859-LHP) on the 21st March 2024, and was granted exemption from requiring additional ethics approval as per local protocol.

Conflict of interest: None

Video 1. Video of patient at index presentation. Choreiform movement is appreciated most prominently over his right upper and lower limbs. Additionally, he also exhibits occasional involuntary movements of his trunk and mouth (behind his mask), along with subtle left upper limb parakinesias (scratching, fidgeting, and repeatedly clamping/tucking his left hand into his contralateral axilla) which collectively might suggest possible early generalisation.
http://neurology-asia.org/content/30/2/neuroasia-2025-30(2)-609-v1.mp4

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