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Clinical commentary

Acute bithalamic infarct manifesting as sleep-like coma: A diagnostic challenge

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ABSTRACT

Bilateral thalamic infarction (BTI) typically presents as a sleep-like coma (SLC) without localizing signs, posing a diagnostic challenge that may lead the treating physician to search for toxic or metabolic causes and delay treatment. We review our experience with BTI of different etiologies, and emphasize the critical role of timely imaging, diagnosis, and management in a series of 12 patients with a presentation of SLC and acute BTI who were managed in our Medical Centers from 2006–2015. In 11/12, urgent head CT scans showed normal brain tissue, while diffusion-weighted (DWI) MRI revealed symmetric bilateral thalamic hyperintense lesions with variable degrees of brainstem involvement. In 1/12, CT scans revealed a contralateral subacute stroke from a thalamic infarct 1 month earlier with a unilateral hyperintense lesion on DWI-MRI. From clinical and imaging findings (DWI-MRI, CT angiography and venography), etiology was attributed to embolic causes (cardio-embolism, artery-to-artery mechanism), small vessel disease, or deep sinus vein thrombosis secondary to dural arteriovenous (AV) fistula. Three patients had good outcomes after prompt diagnosis and optimal treatment in <3 hours (intravenous tissue plasminogen activator in two patients cardio-embolic etiology and neuro-endovascular repair in one patient with venous infarction due to a dural AV fistula). The diagnosis was made beyond the therapeutic window in seven patients, who were left with significant neurological sequelae. Higher awareness of BTI presenting as SLC is warranted. Optimal patient management includes urgent DWI-MRI. In cases of BTI, further imaging workup is indicated to provide a comprehensive assessment for etiology. Early diagnosis and prompt, targeted intervention are crucial.

1. Introduction

Acute bilateral thalamic infarction (BTI) may vary in clinical presentation, with symptoms including sleep-like coma (SLC), disorientation, confusion, and hypersomnolence [1]. Ocular movement disorders are common when infarct extends to the rostral midbrain [2]. The presentation of BTI as SLC, without localizing signs, poses a diagnostic challenge and may prevent swift and satisfactory management, since it may lead the treating physician to search for toxic or metabolic causes. Fluctuations in level of consciousness can occur in the first few days [2,3], making the diagnosis more challenging, yet a delayed diagnosis may preclude thrombolysis and obviate the benefit of early endovascular intervention [4]. Furthermore, a rapidly fluctuating level of consciousness varying from a deep SLC to almost complete arousal with few neurological deficits raises the question whether thrombolysis should be administered. We aimed to describe our experience in the management of a series of 12 patients with BTI, and consider the possible etiologies of this unusual clinical situation based on the diagnostic work-up for each patient. In addition, we sought to identify possible cues that may help to achieve an early diagnosis and rapid intervention.

2. Methods

We retrospectively reviewed files of consecutive patients presenting to our two tertiary care, academic medical centers from 2006–2015 to identify patients with thalamic infarction. Patients who presented with SLC and had a final diagnosis of BTI were included in the study. Patients who had BTI in their ischemic territories but whose clinical picture clearly suggested stroke in additional territory (for instance occlusion of the basilar artery) were

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excluded. Both institutional review boards authorized anonymous inclusion of patients with a waiver of informed consent.

The diagnosis of BTI in this series was based on the detection of hyperintense symmetric bilateral thalamic lesions on MRI diffusion-weighted imaging (DWI) with corresponding lesions on the apparent diffusion coefficient (ADC) sequence. Presentation of a SLC was defined after examination by both a vascular neurologist and an emergency department specialist.

Data for demographic information, risk factors, time from symptom onset to hospital arrival, time from arrival until diagnosis, neurological status on admission, and radiological workup were accrued by retrospective review of clinical and imaging files. In all patients, neurological deficits at admission and 90-day follow-up were recorded. Data regarding delayed neurologic sequelae were taken from the electronic files of the hospital outpatient clinics.

Due to the retrospective nature of our study and the dual-hospital setting, there was no routine protocol for the diagnostic work-up or emergency department. However, all 12 patients underwent a thorough neurological examination, noncontrast CT angiography (CTA) and CT venography (CTV), as well as DWI- and apparent diffusion coefficient (ADC) MRI during the diagnostic work-up. Transthoracic echocardiogram (TTE) and electrocardiogram (EKG) monitoring were performed in the stroke unit during hospitalization and all patients underwent 24 h EKG Holter monitoring after discharge. Imaging studies were evaluated by an experienced, fellowship-trained neuroradiologist (RE).

3. Results

A total of 12 patients met inclusion criteria (eight males, mean age 67 years) (Table 1). All 12 were admitted to the emergency room (ER) after a witnessed onset of somnolence. Upon ER arrival, all 12 were in varying degrees of SLC, ranging from a deep state with minimal response to painful stimuli to a light somnolence state that enabled awakening for short time intervals. In all cases, other localizing findings suggestive of acute stroke were scarce or difficult to recognize during SLC. In 11/12, emergent head CT scan showed normal brain tissue but DWI-MRI revealed symmetric bilateral thalamic hyperintense lesions with variable degrees of rostral midbrain (MB) involvement and correlating low signal on the ADC map. The remaining patient (Pat #11), who presented with sequential unilateral thalamic infarcts at a 1-month interval, had a unilateral hyperintense lesion on the DWI-MRI and a contralateral subacute stroke on the CT scan. The presenting characteristics of the 12 patients are summarized in Table 1.

3.1. Etiology

After a full investigation, three etiologies for BTI are proposed in the current series of patients:

1. Embolic (Patients 4–10). Cardio-embolism was presumed in cases of atrial fibrillation (Patients 4, 5, 6), following a very recent mural myocardial infarction (Patient 9), and in a patient with severe left ventricular hypokinesia (Patient 10). An "artery-to-artery" embolic etiology was presumed in cases of severe vertebrobasilar atherosclerosis with a shower of emboli and multiple foci of restricted diffusion in several vascular territories of the posterior circulation on MRI (Patients #7, 8). Normal TEE and EKG Holter monitoring were also required to establish this etiology (Patients 7, 8).
2. Cerebral small vessel disease (SVD) (Patients #1, 2, 3, 11). SVD was considered as the likely etiology only after exclusion of any embolic or large vessel atherosclerotic causes and detection of SVD on MRI. In one case (Patient #11), SVD was the cause of sequential thalamic strokes at a 1-month interval.
3. Deep cerebral venous thrombosis (CVT) (Patient #12). An associated arteriovenous (AV) fistula was seen on digital angiography in this patient.

3.2. Clinical presentation

Six patients without MB involvement presented with relatively light SLC, meaning they were easily arousable, of shorter duration (<1 hour). Six others, who were later shown to have MB involvement, presented with deeper SLC. They could be awakened only with painful stimuli and quickly returned to the SLC state, for longer interludes (>1 hour) (Fig. 1, Table 1). Distinctive features of MB involvement were pyramidal signs (six patients), pupil involvement (five patients), and skew deviation (three patients). Five patients with extensive MB involvement had a distinctive combination of four-limb flaccid paralysis, bilateral Babinski sign, and marked desaturations (<90% SpO2) during sleep. Four of these patients required mechanical ventilation (Patients #1, 3, 5, 10); the remaining patient (Patient #4) showed marked improvement in her respiratory function after treatment with intravenous tissue plasminogen activator (IV-tPA), precluding the need for respiratory support. MB involvement was seen in both SVD and embolic etiologies.

Two patients who were later determined to have cardio-embolic etiology had short-interval transient vertigo (Patients #4, 8), and one (Patient #8) had a vomiting episode, assumed to precede onset of SLC due to "top of the basilar" syndrome with an embolus that spontaneously disintegrated.

In three patients with an embolic etiology, neurological examination initially failed to disclose neurological deficits during SLC. However, once aroused by the examining physician, two patients presented mild cortical deficits (partial hemianopsia with visuospatial neglect and tactile extinction in Patients #7 and 9, respectively) and the third (Patient #5) had dysphasia and right hemiparesis.

One patient (Patient #12) with deep CVT of the straight sinus due to AV fistula had a progressive headache and encephalopathy ending with deep SLC.

3.3. Imaging

Among patients with clinical MB involvement, DWI-MRI studies clearly showed the caudal extension of the infarct to the MB (Fig. 1). Three patients (Patients #5, 7, 8) had multiple foci of restricted diffusion in several vascular territories, characteristic of embolic strokes; in two (#7, 8), severe atherosclerosis of the vertebrobasilar vasculature was seen in addition to posterior circulation emboli. Severe chronic small vessel ischemic changes were seen on MRI and CT scans in patients with SVD (Patients #1, 11). In one patient with BTI attributed to SVD, an acute thalamic infarct was seen with concomitant late subacute contralateral thalamic infarct (Patient #11). Edematous bilateral thalami were seen on MRI in the patient with deep CVT (Patient #12), a finding that was later attributed to an AV fistula that was evident on digital angiography (Fig. 2).

3.4. Reasons for delayed diagnosis and treatment

Diagnosis and treatment were delayed in four patients (#3, 6, 7, 10) who were mistakenly thought to be asleep and had a delayed arrival to the ER. Family members were initially hesitant to disturb their sleep; however, they found patients in awkward positions and noted they began to snore for the first time in their lives. After futile attempts to wake them up, the patients were brought to the ER.