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Artery of Percheron Stroke as an Unusual Cause of Hypersomnia: A Case Series and a Short Literature Review

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Abstract

The thalamus and the mesencephalon have a complex blood supply. The artery of Percheron (AOP) is a rare anatomical variant. Occlusion of this artery may lead to bithalamic stroke with or without midbrain involvement. Given its broad spectrum of clinical features, AOP stroke is often misdiagnosed. Usually, it manifests with the triad of vertical gaze palsy, memory impairment, and coma. In this article, we report three cases of bilateral thalamic strokes whose clinical presentations were dominated by a sudden onset of hypersomnia. We also reviewed last 5 years' publications related to the AOP strokes in males presenting sleepiness or equivalent terms as a delayed complication. The AOP stroke may present a diagnostic challenge for clinicians which should be considered in the differential diagnosis of hypersomnia.

Keywords

hypersomnolence, Percheron infarction, bithalamic

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The thalamus is an egg-shaped structure of gray matter on the human diencephalon (Khanni et al., 2018). Its vascular supply is complex and presents multiple anatomical variants. The artery of Percheron (AOP), which is a rare anatomical variant, is characterized by a solitary common arterial trunk arising from the posterior cerebral artery (Lamboley et al., 2011). Occlusion of this artery is rare and may lead to a bilateral paramedian thalamic infarction with or without midbrain involvement (Lamot et al., 2015). This uncommon ischemic stroke syndrome, with its broad spectrum of clinical presentations, is often misdiagnosed and therefore represents a diagnostic challenge for physicians. Acute hypersomnia is an unusual complication of this stroke (Bollu et al., 2017). Here, we report three cases of bithalamic stroke whose clinical presentations were dominated by altered mental status, mainly consistent with hypersomnia. We also briefly report the results of the published cases/case series (2015–2020 period) of male patients presenting an AOP stroke.

Cases

The Ethics Committee of Farhat Hached Teaching hospital waived the need for ethics approval for the publication of the case series' retrospectively obtained and anonymized data. However, written informed consents were obtained from the three patients for the publication of their cases.

Case 1

A previously healthy 73-year-old man presented to the emergency department with altered consciousness. On admission, his signs were within normal range. On the neurological examination, the patient had a fluctuant consciousness state fully reversible under pain stimuli, excessive daytime sleepiness, and nocturnal agitation. He

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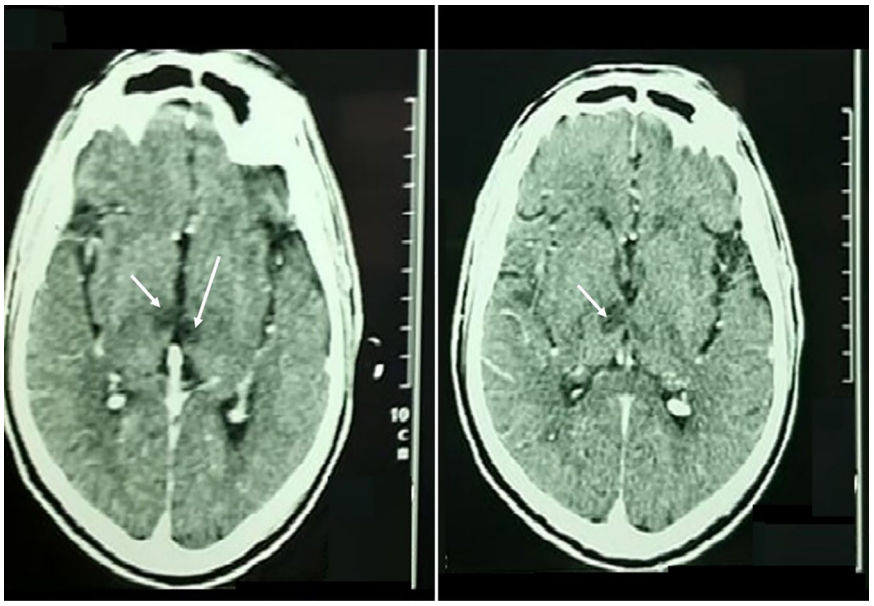

Figure 1. Head computed tomography scan illustrates bilateral thalamic hypodensities (arrows) compatible with an ischemic stroke.

had neither sensitive nor motor focal signs. All blood tests (e.g., electrolytes test, complete blood count [CBC], and liver function tests) were normal. A head computed tomography (CT) performed 2 hr after the symptoms onset was normal. This situation misled to an initial diagnosis of a coma secondary to viral encephalitis. Forty-eight hours after admission to the intensive care unit, a new brain CT scan showed bilateral thalamic hypodensities in the paramedian territory (Figure 1). Further evaluation aiming at identifying the stroke etiology revealed a rapid atrial fibrillation at electrocardiogram without abnormalities on Doppler ultrasound and transthoracic echocardiography, findings consistent with an embolic mechanism or a heart-brain syndrome. Treatment with anticoagulation (enoxaparin) and amiodarone was started. Two weeks later, there was a marked improvement in the clinical condition (somnolence and behavioral impairment). The patient was transferred to the cardiology department.

Case 2

A 43-year-old man with a past medical history of hypertension was brought to the emergency department after 20-hr of unarousable sleepiness. There was no recent history of drug abuse, head injury, trauma, or seizure. On the physical examination, the patient was afebrile and his blood pressures were high at 230/120 mmHg. On the neurological examination, the patient had a Glasgow coma scale of 7 points (2, 2, and 3 points for ocular, verbal, and motor components) requiring invasive mechanical ventilation. No other abnormalities were noted (neither meningeal syndrome nor focal neurological deficit). On admission, the infectious, toxic, and metabolic encephalopathy tests (e.g., CBC, blood urea nitrogen, creatinine, plasma glucose, liver function tests, and urine drug screen) were normal. Initial CT scan was normal. Twenty-four hours later, a new brain CT scan revealed bilateral paramedian thalamic hypodensities, which were not present on the first CT examination (Figure 2). A 9-lead electrocardiogram showed a right bundle-branch block. A transthoracic and transesophageal echocardiogram, carotid, and vertebral Doppler ultrasound revealed no abnormalities. There was a gradual improvement in the patient's clinical state. A detailed neurological examination after extubation revealed fluctuating arousal, complete vertical gaze palsy, thalamic aphasia, and behavior changes with agitation and increased impulsivity. The aforementioned psychiatric disorders were managed with haloperidol. Two weeks after hospitalization, the patient was discharged and referred to a neurologist.

Case 3

An 82-year-old man with a past medical history of hypertension, diabetes mellitus, and myocardial infarction presented to the emergency department with a brief loss of consciousness, followed by drowsiness episodes which were initially neglected and then worsened in a crescendo pattern. On the physical examination, the patient was sleepy, apathetic, and

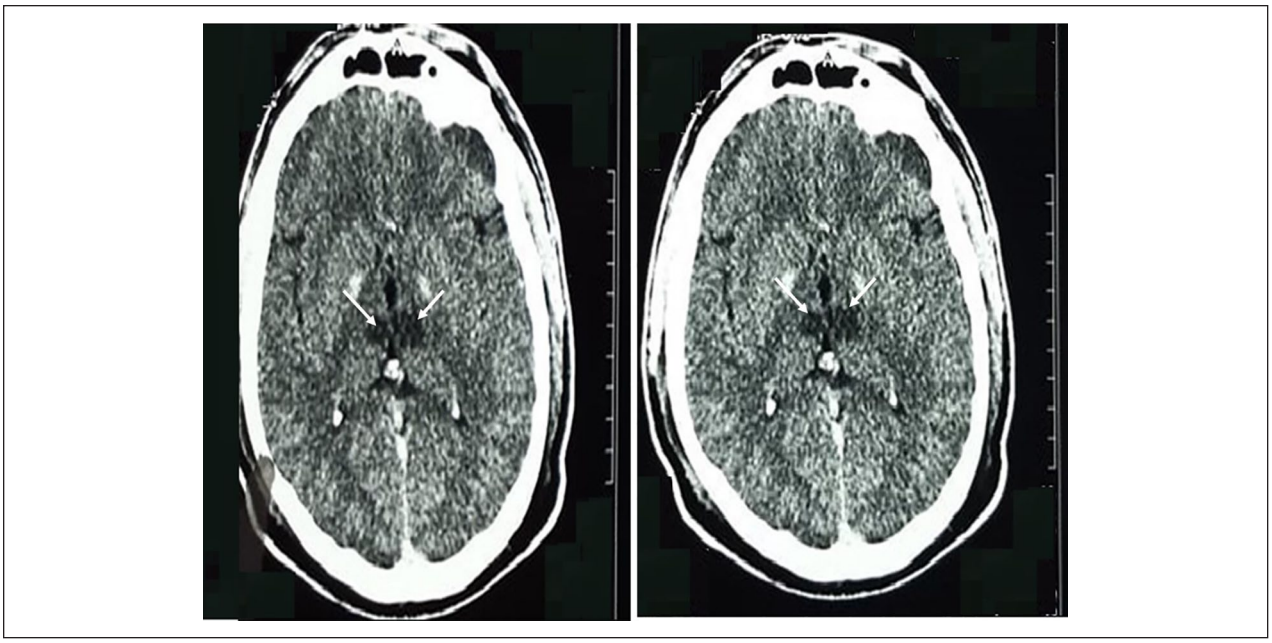

Figure 2. Head computed tomography on an axial view illustrates an ischemic stroke (arrows) in the paramedian artery territory of both thalami.

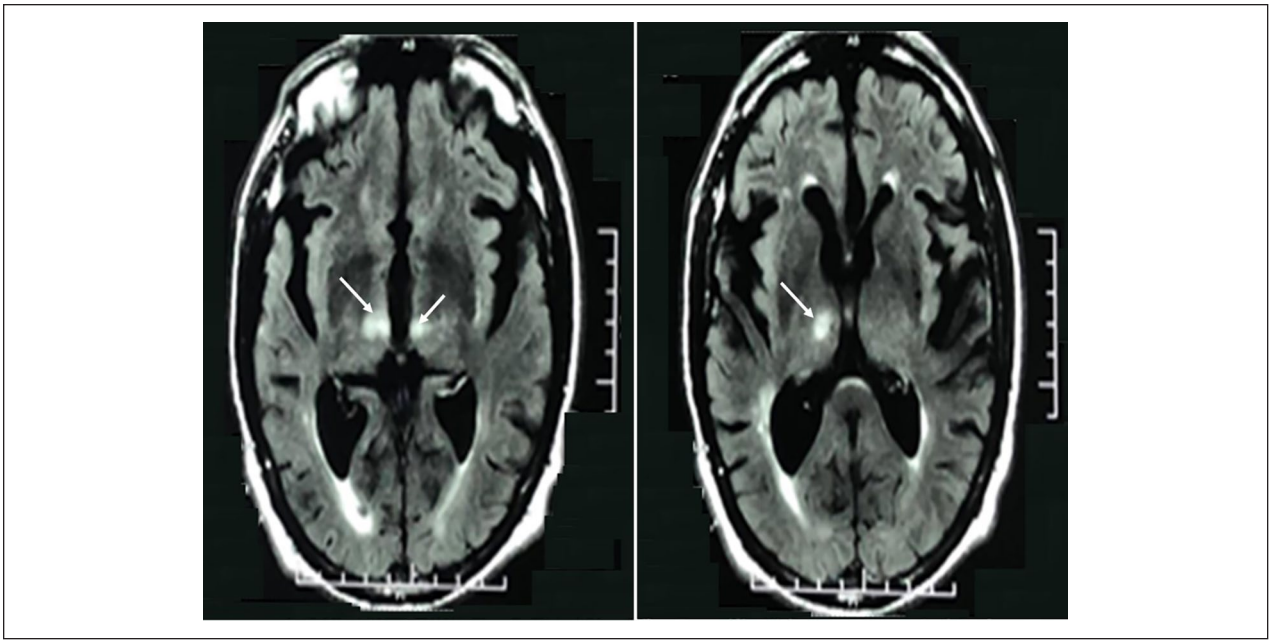

Figure 3. Axial T2-weighted magnetic resonance imaging of the brain illustrates hyperintense bilateral lesions of the paramedian thalami (arrows) compatible with an acute ischemic stroke.

presented no other abnormalities. Results of the routine blood tests (e.g., electrolytes test, blood urea nitrogen, creatinine, plasma glucose, and CBC) were within the normal range. During the hospital course, the patient presented many periods of irrepressible need for sleep, and he was unable to stay awake and alerted during the major daytime waking episodes. Brain magnetic resonance imaging (MRI) showed bilateral paramedian thalamic infarcts (Figure 3). Doppler ultrasound and transthoracic echocardiography were unremarkable. A significant improvement in hypersomnolence during the hospital stay was noted and the patient was discharged on day six following the stroke.

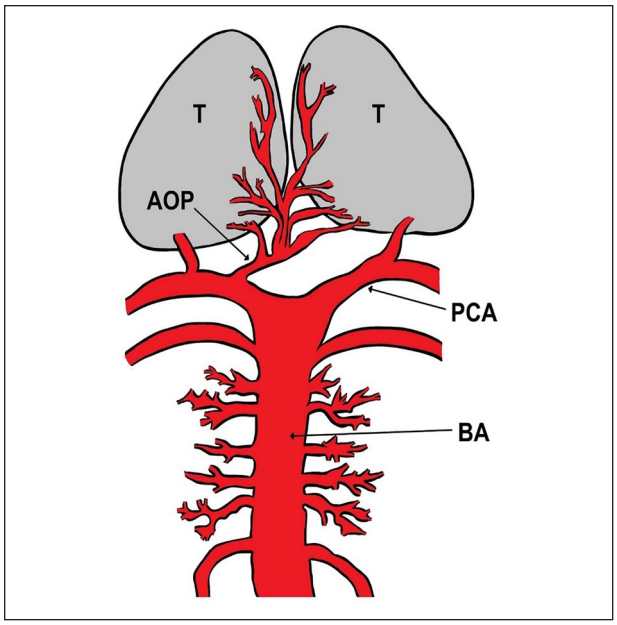

Figure 4. Artery of Percheron (AOP) illustration.
BA = basilar artery; PCA = posterior cerebral artery; T = thalamus.

Discussion

The AOP was first described by Gerard Percheron in 1973 (Agarwal et al., 2014; Caruso et al., 2017). This artery arises from the proximal posterior cerebral arteries and supplies both the paramedian thalami and the mesencephalon (Figure 4). AOP is a rare anatomical variant that is present in 4%–12% of the population (Arauz et al., 2014; Kaya et al., 2010; Kocaeli et al., 2013; Uz, 2007). The prevalence of bilateral thalamic infarction caused by AOP occlusion is unknown since it is often misdiagnosed (Arauz et al., 2014). It "seems" that AOP stroke represents 0.1% to 2.0% of ischemic strokes and 4% to 18% of thalamic infarcts (Agarwal et al., 2014; Caruso et al., 2017; Garcia-Grimshaw et al., 2018; Lamot et al., 2015). There is no predilection as regards sex, race-ethnicity, and age in the reported cases of AOP stroke in literature. According to Garcia-Grimshaw et al. (2018), the aforementioned data depend on the etiology of the AOP stroke. Firstly, the latter can occur at any age, but it is particularly common in patients after their 30s mostly between 60 and 70 years (Lin et al., 2018). Secondly, there is a slight male predominance with a male to female ratio of 3:2 (Hermann et al., 2008; Stamm et al., 2018; Suzuki et al., 2016).

On May 27, 2020, a personal literature review based on a 2015–2020 PubMed search [key items: "artery of Percheron" AND ("case report" OR "case-series")] found 73 papers published in English language (30, 37, and 6 papers included females, males, and both sexes, respectively). Among the 37 studies including only males, 13 reported sleepiness or equivalent terms (i.e., hypersomnolence, drowsiness, or excessive daytime sleepiness) as a delayed complication of an AOP stroke (Table 1; Afana et al., 2019; Aryan et al., 2016; Bailey & Khadjooi, 2016; Goico & Mikesell, 2018; Harisuthan et al., 2018; Ince & Asan, 2018; Kamasak et al., 2015; Khanni et al., 2018; Oliveira et al., 2018; Shah & Ali, 2018; Vasconcellos et al., 2016; Zelante et al., 2015; Zhou et al., 2015).

The shape of the infarct can deduce the presence of AOP stroke because this anatomical variant typically causes bilateral paramedian thalamic-mesencephalic infarction (Agarwal et al., 2014; Lopez-Serna et al., 2009). The risk factors of AOP stroke are similar to those of ischemic ones. The two most frequent risk factors are microangiopathy and cardiac embolism (Arauz et al., 2014; Garcia-Grimshaw et al., 2018). The clinical presentations of AOP stroke are extremely variable. The most common clinical features are bilateral vertical gaze palsy (65%), memory impairment (anterograde and retrograde amnesia) (58%), and coma (42%; Garcia-Grimshaw et al., 2018; Lamboley et al., 2011; Lamot et al., 2015). The remaining clinical features reported in the literature include hypersomnolence (29%), akinetic mutism, and behavioral disorders (apathy, agitation, and aggressiveness; Agarwal et al., 2014; Caruso et al., 2017; Garcia-Grimshaw et al., 2018; Lamboley et al., 2011; Lamot et al., 2015; Lazzaro et al., 2010).

In the three reported cases, we found some of the clinical features reported in the previous series, including hypersomnia, coma, vertical gaze palsy, and neuropsychiatric disorders (Table 1). Altered mental status is a classic manifestation of AOP stroke and can range from hypersomnia to coma (Table 1). However, hypersomnia is rarely reported as a first complaint (Cases 1 and 3) since it is usually misdiagnosed as coma or it is lately diagnosed after recovery from coma (Case 2; Bassetti et al., 1996; Hammersley et al., 2017; Hermann et al., 2008; Oliveira et al., 2018). Hypersomnolence (i.e., excessive daytime sleepiness and/or prolonged sleep) in bithalamic stroke is explained by the crucial role of the thalamus in sleep regulation and in maintaining arousal. Hypersomnolence has been attributed to the interruption of noradrenergic and dopaminergic impulses from the ascending reticular activating system to the thalamus (Bassetti et al., 1996; Bollu et al., 2017; Goyal et al., 2012). Sleep-wake disturbances are more pronounced in bilateral than in left-sided or right-sided thalamic infarcts (Hermann et al., 2008). Sleep needs have been reported to remain increased after this stroke (Goyal et al., 2012; Hermann et al., 2008). Unfortunately, we have no follow-up information about the three patients after their discharge.

Table 1. Results of the 13 Cases/Case-Series, Published During the 2015–2020 Period, Including Males Suffering From an Artery of Percheron (AOP) Stroke and Reporting Sleepiness or Equivalent Terms (Such as Hypersomnolence, Drowsiness, or Excessive Daytime Sleepiness) as a Delayed Complication.

Authors	Number of cases (age/country)/ main complaints	Medical imagery	Conclusion
Afana et al. (2019)	$n = 1$ (39 Yrs, State of Palestine) Coma Slurred speech Hypersomnia Loss of interest Right-sided ptosis Vertical gaze palsy Diminished light reflex Amnesia Right upper limb paralysis	Brain CT scan Brain CTA Brain MRI	• This experience demonstrates the need for surgeons performing anterior cervical discectomy with fusion (ADCF) procedures to be aware of this potential complication • There are many other prophylactic treatments of this complication such as maintaining appropriate cervical positioning during surgery or prevention of postoperative dehydration • Care should be taken to avoid intimal disruption of the vertebral artery by overly dilating the intervertebral space
Khanni et al. (2018)	$n = 1$ (59 Yrs, Haiti) Hypersomnolence	Brain CT scan Brain MRI	• Acute AOP strokes continue to present a diagnostic challenge for clinicians in the acute setting owing to the diversity and inconsistency in presentation, frequent lack of localizing signs, and poor resolution on initial imaging • This has implications for treatment and prognosis, especially in settings offering tissue plasminogen activator (tPA), where early detection and intervention significantly impact functional outcomes for patients • It may not be cost-effective to perform a complete stroke workup on all patients presenting with vague, atypical symptoms, but clinicians should keep thalamic pathology on the differential diagnosis given its involvement in many diverse neurological roles • Maintaining a high suspicion for thalamic infarct, with AOP stroke as one etiology, and a low threshold for MRI in patients presenting acutely with otherwise
Oliveira et al. (2018)	$n = 1$ (56 Yrs, Brazil) Excessive daytime sleepiness Memory impairment Left-sided weakness	Brain MRI	• Awareness of the clinical and neuroimaging features of the AOP stroke syndrome is essential for timely diagnosis and appropriate management
Goico and Mikesell (2018)	$n = 1$ (72 Yrs, United States) Somnolence Vertical gaze palsy	Brain MRI with DWI	• Suspect AOP stroke in a patient with a decreased conscious level, ophthalmologic signs, and cardio-embolic risk factors • Early diagnosis is best obtained with a brain MRI with DWI • Treatment of AOP stroke depends on the pathophysiologic mechanism • Prognosis is subject to the extent of infarction but considered relatively good with regard to mortality and permanent deficits

(continued)

Table 1. (continued)

Authors	Number of cases (age/country)/ main complaints	Medical imagery	Conclusion
Shah and Ali (2018)	*n* = 1 (39 Yrs, United Kingdom) Hypersomnolence	Brain CT scan Brain MRI	• In a patient presenting with drowsiness/somnolence, a posterior circulation stroke should be considered if no evidence of other more common causes is found • A CT head must be followed by an MRI to confirm the diagnosis and subsequent focus should be on eliciting risk factors and careful evaluation for etiologies • The present case is the only one reported to have just dysfunction of arousal/ conscious and no other focal neurological findings
Harisuthan et al. (2018)	*n* = 1 (45 Yrs, India) Dizziness Diplopia Ocular movement abnormalities Hypersomnolence	Brain CT scan Brain MRI	• In an emergency setting, sudden dip in sensorium with localizing neurology findings to midbrain and thalamus (e.g., coma and vertical gaze palsy) could be due to multiple causes • Embolic stroke of the proximal AOP should be one of the differentials • Anytime the initial imaging is normal, perform a follow-up head CT or MRI as early, to make the correct diagnosis • If the diagnosis was made within the stroke window period, thrombolytic therapy could still be done, and the outcome can be fairly good
Ince and Asan (2018)	*n* = 1 (41 Yrs, Turkey) Fluctuations in the level of consciousness (coma to somnolence) Retrograde amnesia Depressive mood	Brain MRI Brain MRA	• This patient is the first case with a 10-year history of anterograde amnesia due to AOP stroke • More cases with long-term follow-up may provide a better understanding of the clinical persistence of the symptoms and the thalamic structures primarily responsible for the amnesic syndrome • This case highlights the difficulty in the prediction of the prognosis in the AOP stroke presenting with an isolated memory disorder

(continued)

Table 1. (continued)

Authors	Number of cases (age/country)/ main complaints	Medical imagery	Conclusion
Bailey and Khadjooi (2016)	$n = 1$ (47 Yrs, United States) Low level of alertness (deep coma to mild somnolence) Memory problems	Brain CT scan Brain MRI	• AOP stroke is an uncommon cause of coma presenting in elderly and middle-aged individuals • The patient may have a source of cardioembolism or classical cardiovascular risk factors • Reduced consciousness can range from a deep coma to hypersomnolence • Ophthalmological signs and neuropsychological deficits may also be evident • Despite an investigation, the cause remains undetermined in the majority of cases • Overall the prognosis is good with low mortality and often rapid reversal of the coma, necessitating early diagnosis and optimal supportive care • Reaching the correct diagnosis in patients presenting with nontraumatic coma can be challenging, but incorrect diagnosis can result in delays in appropriate management and potential for harm due to employment of unnecessary treatments and ongoing symptoms • This case highlights the difficulty in recognizing a stroke syndrome presenting as isolated reduced consciousness and the importance of revisiting a diagnosis when a patient fails to respond to initial treatment
Aryan et al. (2016)	$n = 1$ (40 Yrs, India) Complication following re-exploratory trans-sphenoidal surgery for a pituitary adenoma	Brain MRI	• A case of an AOP stroke occurring in a patient following endoscopic trans-sphenoidal surgery • This rare complication should be thought about in the setting of re-exploratory pituitary surgery
Vasconcellos et al. (2016)	$n = 1$ (59 Yrs, Brazil) Abrupt drowsiness Decreased level of consciousness Coma Cervical dystonia (spasmodic torticollis-anterocollis) Ataxic gait Vertical gaze palsy (upward and downward) Convergence insufficiency Mydriatic nonreactive pupils and light intolerance	Brain MRI	• Great degree of awareness of stroke syndromes can improve patient outcome with early recognition and suitable treatment option like thrombolysis or vascular interventions

(continued)

Table 1. (continued)

Authors	Number of cases (age/country)/ main complaints	Medical imagery	Conclusion
Zhou et al. (2015)	*n* = 1 (68 Yrs, United States) Coma Behavior changes (agitation and aggression) Cognitive and communication impairment Fluctuating arousal and orientation Impaired learning and memory (impaired anterograde and retrograde memory) Paraphasia Monotonous speech with hypophonia Auditory and visual hallucinations Vertical gaze paralysis	Brain CT scan Brain MRI Brain MRA	• A case of a patient with acute AOP stroke resulting in bilateral mirror-like median thalamic infarctions involving the dorsomedial and intralaminar nuclei bilaterally • There was an initial difficulty in diagnosis due to the presence of altered mental state only • A unique feature of this presentation included the evolution of symptoms into the Korsakoff syndrome, characterized by memory deficits and confabulation • Involvement of the mammillothalamic pathways bilaterally has been implicated in its causation • The proximity of the lesions caused by infarction in the territory of the AOP to the mammillothalamic pathways is probably the cause of the syndrome in this patient • A literature review did report a few cases with Korsakoff syndrome in bilateral thalamic infarctions • The better outcome in relation to management in an intensive care setting • The importance of neuroimaging in the presence of unexplained altered mental state and cognitive difficulty to diagnose the underlying problem is important, particularly because of available therapeutic intervention in acute stroke syndromes
Kamasak et al. (2015)	*n* = 2 (5 Yrs, Turkey) Case 1: Mutism and ataxia after chickenpox infection Case 2: Headache, somnolence, agitation, speech dysfunction following an upper respiratory tract infection	Brain MRI	• Bilateral strokes of the paramedian thalamus may result in severe illness and impairment • Common clinical manifestations include disorientation, confusion, hypersomnolence, deep coma and "coma vigil," or akinetic mutism (awake unresponsiveness), as well as severe memory impairment
Zelante et al. (2015)	*n* = 1 (65 Yrs, Italy) Drowsiness Gait instability Dysarthria Right ptosis, vertical gaze palsy Hypoesthesia and hemiparesis	Brain MRI Brain MRA	• Some evidence suggests that posterior communicating artery (PCoA) hypoplasia per se predisposes to thalamic lacunar stroke because of the critical role of PCoA in the collateral supply of proximal posterior cerebral artery territory • We suggest that the occurrence of the two anatomic variants might have led to a hemodynamic infarction due to a poor regional collateral flow

Note. CT = computed tomography; CTA = CT angiography; DWI = diffusion-weighted imaging; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; n = number; Yrs = years.

The complexity and polymorphism of AOP stroke semiology explain why bithalamic infarction is often misdiagnosed, lately detected, or even not detected. It is a real diagnostic challenge for clinicians to detect this condition in a timely fashion. Its diagnosis and treatment may be delayed because of the wide spectrum of its clinical features. Moreover, the initial CT scan can be normal (Khanni et al., 2018; Xu et al., 2017). Diagnosis of AOP stroke is often made retrospectively beyond the thrombolysis or endovascular treatment window. MRI is the neuroimaging of choice to be conducted when AOP stroke is highly suspected (Lamboley et al., 2011). MRI typically shows a hyperintense signal in the region supplied by AOP (Song et al., 2017).

In the three case series, the patients recovered completely. This is in line with previous studies which reported good prognosis of patients with AOP stroke (Arauz et al., 2014; Kichloo et al., 2019; Song et al., 2017).

In conclusion, these case series highlighted the difficulties of recognizing the AOP stroke in a timely fashion. These observations also illustrated the importance of considering this stroke syndrome as one of the differential diagnoses of hypersomnolence.

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Authors' Contributions

I.B.S., H.B.S., M.Z., and M.B. substantially contributed to the conception and design, acquisition of data, or analysis and interpretation of data. I.B.S., H.B.S., M.Z., E.E., R.T., and M.B. drafted the article or revised it critically for intellectual content. I.B.S., H.B.S., M.Z., E.E., R.T., and M.B. gave final approval of the version to be published.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: H.B.S. reports personal fees from AstraZeneca, Saiph, Teriak, Hikma, and Chiesi. The remaining authors declare that they have no conflicts of interest concerning this article.

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