Prolonged Severe Bradycardia in the Artery of Percheron Infarct

Sir,

Thalamus is a paired forebrain structure, containing predominantly gray matter, and has dense neuronal connections with various other structures.[1,2] The arterial blood supply to thalami is divided into four territories: anterior, paramedian, posterior, and inferolateral.[3,4] It is from the branches of the posterior cerebral artery which includes the posterior communicating artery, paramedian thalamic artery, subthalamic artery, thalamo-geniculate artery, and posterior choroidal artery.[5,6] The artery of Percheron (AOP) represents a rare anatomical variant of thalamic blood supply wherein a single arterial trunk from the posterior cerebral artery supplies both sides of the thalamus and midbrain.[1,2]

The prevalence of AOP among the general population is around 7–11% and an average of 0.4–0.5% of ischemic strokes can be attributed to AOP infarcts.[7] AOP occlusion leads to infarcts in the bilateral paramedian thalamus and midbrain.[1-4] Such a diagnosis is often overlooked due to other common differentials, such as basilar artery syndrome, organophosphorus poisoning, toxic metabolic encephalopathies, and vein of Galen occlusion,[1-4] with overlapping symptoms. Also, an early plain computed tomography imaging of the head may not show any abnormalities. Severe bradycardia is a very rare manifestation in patients with AOP infarct and thus we present such a case before you.

We present a case of a 33-year-old male who was found unconscious and unresponsive at home, with saliva drooling from his mouth. Upon interrogation, no history of any involuntary movements was found. There were no tongue/lip bites, urine/stool incontinence, or any abnormal posturing (decorticate/decerebrate) seen. After 12 hours of being normal, he was presented at our hospital. He was afebrile with a blood pressure of 110/70 mmHg and a heart rate of 40 beats per minute, with a regular rhythm. His random blood glucose was 106 mg/dl. He was unconscious, not responding to verbal commands, no eye-opening to pain, and no verbal output, but localized a painful stimulus with both arms. Bilateral pinpoint pupils were reacting sluggishly to light. There was no neck rigidity or Kernig's sign. Because of low GCS, he was immediately intubated and put on ventilatory support. The serum acetylcholinesterase level was normal on serial monitoring throughout hospitalization. Magnetic resonance imaging (MRI) brain [Figure 1] revealed an acute infarct in the bilateral paramedian aspect of the thalamus and left crus cerebri, confirming the diagnosis of bilateral thalamic and midbrain infarct. His MR intracranial and neck vessel angiography and venography were normal. He was started on aspirin 150 mg/day, clopidogrel 75 mg/day, and atorvastatin 40 mg/day. He did not have hypertension, diabetes mellitus, or hyperlipidemia. But he had persistent sinus bradycardia with a heart rate between 38 and 44 beats per minute persistently on continuous electrocardiographic monitoring. He was not receiving any negative chronotropic drugs, and his thyroid function, electrolytes, coagulation profile, and renal and hepatic functions were normal. Serum homocysteine and APLA, and ANA profile revealed no abnormalities. Raised ICT was ruled out on MRI. His bradycardia did not respond to atropine and was treated with injectable isoprenaline intravenously as an initial bolus of 0.05 mg IV followed by an IV infusion of 5 mcg/min for 5 days. After 48 hours, there was an improvement in his sensorium and hence was extubated. He was found to have confusion and disoriented by time, place, and person. Hence, detailed higher mental function (HMF) evaluation was not possible then. However, after 1-week admission, an improvement of sensorium was noted and the patient was shifted to the general wards. At that time, HMF was re-evaluated, and he was found to have subcortical executive dysfunction and subcortical memory loss. Modafinil 100 mg twice a day was added for excessive sleepiness. He also had vertical gaze palsy with mild ataxia of limbs and gait. Sinus bradycardia persisted for 10 days. His 2D Echocardiography revealed a small patent foramen ovale (PFO) with a left-to-right shunt. This could have been

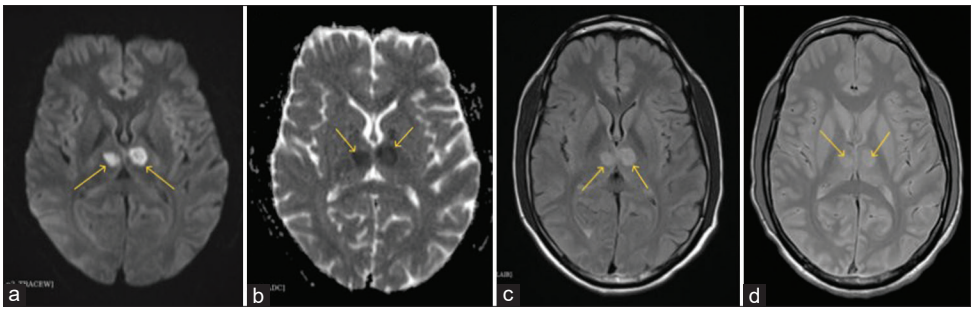

Figure 1: Magnetic resonance imaging (a and b) Lateral medial thalamic diffusion restriction (a) with ADC reversal (b-d) FLAIR and T2W image shows bilateral medial thalamic hyper-intensity

worked up with a Transesophageal Echocardiography but was not done due to the financial constraints of the patient. However, potential sources of paradoxical embolus such as deep vein thrombosis (DVT) were ruled out. The patient was discharged with stable hemodynamics and a pulse of 64/min. On follow-up, Donepezil 5 mg/day was added for persistent subcortical executive dysfunction and subcortical memory loss.[8]

Disorders of consciousness are the most common initial presentation of AOP infarct, with drowsiness and excessive sleepiness being the most common presentations. Thalamus along with its connections with the brainstem has reticular activating system (RAS) nuclei, whose dysfunction leads to hypersomnia, drowsiness, and coma.[1-3] Other manifestations seen with AOP infarct include subcortical executive dysfunction, short-term memory impairment, vertical gaze palsy, eyelid retraction, and convergence retraction nystagmus.[1-7] Cognitive memory impairment/loss is seen in such patients because of the higher cortical connections of the thalamus.[2,9] Lesions of the Rostral interstitial and Edinger–Westphal nucleus i.e. in the dorsal midbrain, are associated with supranuclear gaze palsy, and other abnormal ocular reflexes, such as conversion–retraction nystagmus and light near dissociation. Over-excitation of the 3rd cranial nerve leads to nystagmus.[10,11] Eyelid retraction, known as the Collier's sign, is also seen in such an infarct due to damage to the posterior commissure levator inhibitory fibers.[10,11] These features together constellate a relatively uncommon neuro-ophthalmologic syndrome called Parinaud syndrome, also known as dorsal midbrain syndrome.[10,11] Bilateral infarcts are rarely seen due to bilateral occlusions in the PCA or its perforating branches to the thalamus and midbrain.[2] The presence of an AOP occlusion is to be strongly suspected. As AOP arises as a solitary trunk from the P1 segment of PCA, its occlusion causes bilateral paramedian thalamic infarcts with or without the involvement of the midbrain.[1,2,6]

Our case had persistent bradycardia for more than a week after the AOP infarct. It is proposed that the anterior part of the insula has a direct sympathetic connection with the posterior hypothalamus,[2-4] the latter controlling the heart rates. These structures, via their connections with the rostral ventrolateral medulla and the zona increta, link the sensory inputs to the visceral, arousal, and attention responses. Thus, paramedian thalamic infarcts can disrupt the sympathetic efferent activity of the posterior hypothalamus causing unopposed bradycardia. The connections of the median thalamus with the descending sympathetic tract through the central tegmental tract can also mediate bradycardia in patients with AOP. As per the literature, the PFO in itself is not associated with bradyarrhythmias.[12] On the contrary, PFOs are more commonly associated with tachyarrhythmias, such as Supraventricular Tachycardias.[12] Though persistent bradycardia is rare [Table 1], it is important to watch out for it in all patients with AOP infarct. Fortunately, our patient did not have bradycardia lesser than 35 beats per minute and did not require cardiac pacing as the hemodynamic stability was maintained.

Table 1: Comparison of the current study with other published studies on AOP with bradycardia

Author	Year	Country	Manifestation	MRI
Asavaaree *et al*.[1]	2018	USA	Altered consciousness, and severe bradycardia.	Bilateral thalamic and midbrain infarction
Peruzzotti-Jametti *et al*.[2]	2011	Italy	Fluctuating sensorium, dysarthria, anisocoria, vertical gaze palsy, and severe bradycardia.	Symmetric bilateral thalamic, hypothalamic, and midbrain acute infarctions
Aaron Ravelo *et al*.[4]	2021	USA	Drowsiness, bradycardia	Bithalamic infarct
Current case	2022	India	Drowsiness, Irritability, excessive daytime sleepiness, and bradycardia.	A lesion in the bilateral paramedian aspect of the thalamus and left crus cerebri with hemorrhagic conversion in the left thalamus

Physicians should be aware of this rare presentation of AOP infarct. AOP infarction commonly presents with acute onset drowsiness and sleepiness in the initial few days. A gradual recovery in sleepiness is seen but a frontal subcortical cognitive dysfunction is observed, which may improve over the next few weeks.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Submitted: 27-Nov-2022 **Revised:** 03-Feb-2023 **Accepted:** 09-Feb-2023
Published: 07-Apr-2023

DOI: 10.4103/aian.aian_947_22