

## An Unusual Cause of Fixed Dilated Pupils After Cardiac Surgery

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### Abstract

**Background** The presence of fixed, dilated pupils after cardiac surgery is an ominous sign, typically indicating severe diffuse hypoxic-ischemic brain injury. Rarely, however, this finding can be seen as a result of focal midbrain ischemia. It is important to differentiate between these syndromes, as the latter might be amenable to acute stroke treatments, and because they affect consciousness very differently.

**Case** A 46-year-old man with diffuse atherosclerosis underwent coronary artery bypass grafting and closure of an incidentally discovered patent foramen ovale. He underwent neurologic evaluation on post-operative day 6 because he was not speaking and appeared to have a new right hemiparesis. Eye movements, pupillary, and lid function were all normal at this time. MRI showed multiple posterior circulation infarcts, involving both cerebral peduncles. On post-operative day 12, he became unresponsive, quadriplegic, and had bilaterally fixed, dilated pupils. CT showed low attenuation in nearly the entirety of both cerebral peduncles.

**Discussion** Midbrain infarction is rare. Bilateral midbrain infarction is even rarer and typically presents as locked-in syndrome with preservation of pupillary function and at least vertical eye movements. In our review of the literature, we found only three other cases of midbrain infarction associated with bilateral mydriasis. As in our case, these characteristically involved the anteromedial midbrain bilaterally.

**Conclusions** Fixed, dilated pupils after cardiac surgery can rarely be caused by bilateral anteromedial midbrain infarctions. It is important to differentiate this from the much more common diffuse hypoxic-ischemic injury.

**Keywords** Midbrain · Infarction · DWI · Ocular motility · Pupils

### Introduction

The presence of fixed and dilated pupils after cardiac surgery is an ominous sign and typically indicates severe, diffuse hypoxic-ischemic brain injury [1]. While the former is invariably associated with severely impaired consciousness, patients with midbrain infarctions can have remarkably intact consciousness and therefore different outcomes [2]. As well, treatments differ widely for the two conditions. It is therefore crucial to recognize the difference between these problems when evaluating such patients. Here we report a patient with bilaterally fixed and dilated pupils, ophthalmoplegia, and flaccid quadriplegia associated with infarction of large portions of both sides of the anterior midbrain after cardiac surgery.

### Case Report

We evaluated a 46-year-old right-handed man in the cardiothoracic surgical ICU on post-operative day 6 for persistent somnolence and right hemiparesis. His past medical history was notable for a diffuse vasculopathy of unknown etiology, but presumed to be due to accelerated atherosclerosis. Vasculitis had previously been excluded after an extensive evaluation. Angiography showed that

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this process involved essentially all of the extra- and intracranial cerebral arteries in addition to the celiac, superior mesenteric, inferior mesenteric, and right renal arteries. One year prior to the present illness, he had a cerebral infarction involving splenium of the corpus callosum with persistent mild left hemi-inattention and hemiparesis and moderate cognitive deficits. He also had hypertension, type 2 diabetes mellitus, and a history of methamphetamine and tobacco abuse.

Coronary artery bypass grafting and closure of an incidentally discovered patent foramen ovale were performed 2 weeks after a non-ST elevation myocardial infarction. Cardiopulmonary bypass at a temperature of 32°C for 93 min was used, and the operation was uncomplicated. Fever and leukocytosis, which persisted throughout his post-operative course, were noted on post-operative day 1. Despite a thorough search, including multiple blood cultures, no source of infection was identified.

The patient was agitated during the first two post-operative days and was therefore sedated and maintained on a mechanical ventilator. CT of the head on post-operative day 1 showed only his known splenium infarct. On post-operative day 4, all sedative medications were discontinued. Over the subsequent 2 days, his level of arousal slightly improved such that he inconsistently followed simple commands. However, he was not speaking and, contrary to his pre-operative mild left hemiparesis, was noted to move his left side more than the right.

Neurologic evaluation took place on post-operative day 6. At that time, his eyes were most often closed, although he did open them and visually orient to the examiner after vigorous verbal stimulation. With continued vigorous verbal stimulation, he would track the examiner, albeit inconsistently, and better on the left than the right. He inconsistently followed commands to protrude his tongue, open and close his eyes, and move his left hand. He did not move his right upper extremity or either lower extremity to command. He did not speak spontaneously or upon request. The cranial nerve examination was normal except for failure to blink to threat from the right and right facial weakness that was apparent on grimace to pain. Specifically, eye movements, pupillary function, and lid function were all normal at this time. The right upper and lower extremities were flaccidly plegic, but he briskly withdrew the left limbs from pain. On plantar stimulation, the right toe was upgoing and the left was downgoing. The FOUR score was 14 (E3, M3, B4, R4).

MRI performed on post-operative day 7 revealed several areas of restricted diffusion in both cerebellar hemispheres, the left middle cerebellar peduncle and lateral pons, both cerebral peduncles, the left hippocampus, and the left parieto-occipital junction (Fig. 1). MR angiography showed the known diffuse intra- and extra-cranial atherosclerotic changes. While there were numerous areas of moderate to

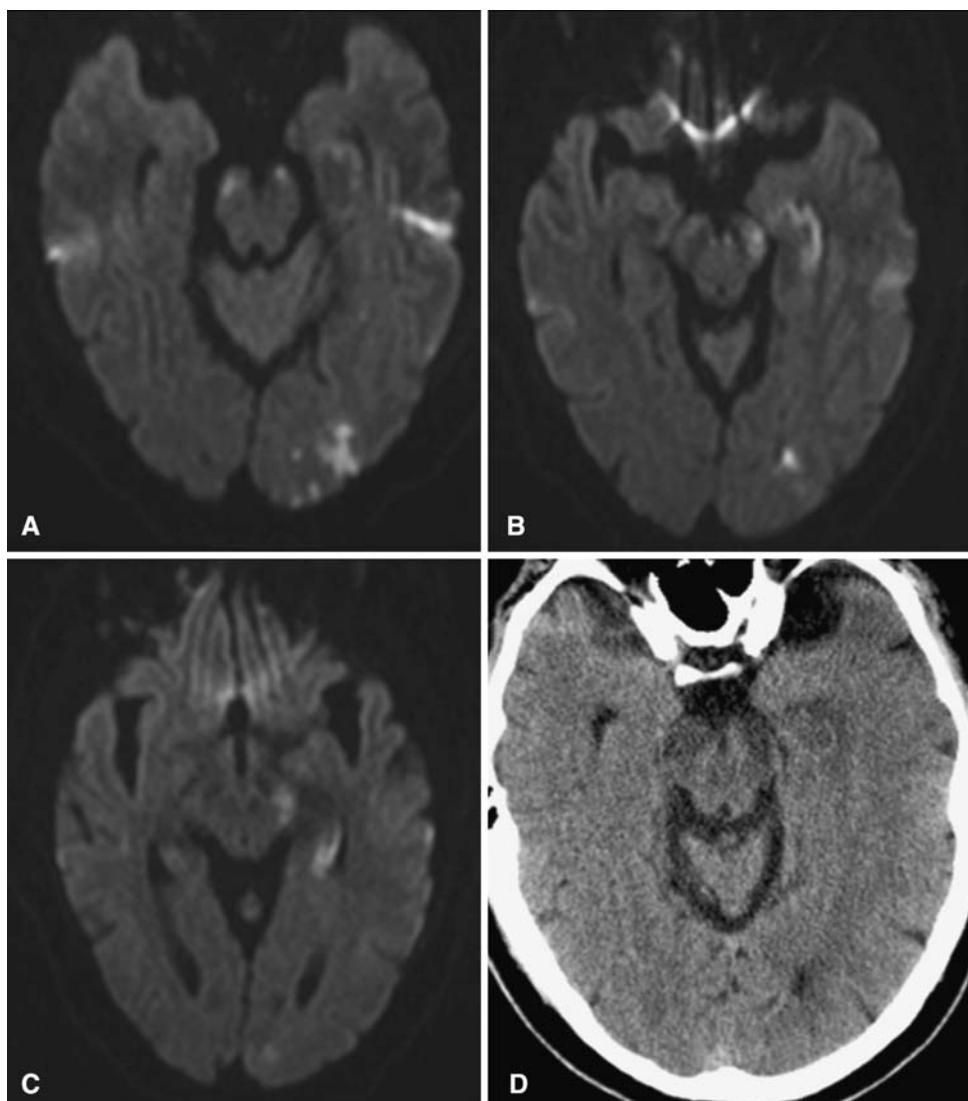
severe stenosis in the vertebral arteries, flow in the basilar artery appeared normal on time-of-flight images. Transesophageal echocardiography revealed no source of embolus in the heart or aortic arch. Continuous ECG monitoring did not reveal atrial fibrillation.

For the next 5 days, no change in the patient's neurologic status was noted in the medical record. He remained febrile but was hemodynamically stable and successfully extubated. On post-operative day 12, we were called by the primary service when he was noted to no longer follow commands and to have bilaterally fixed and dilated pupils. The time of onset of these changes was uncertain, having occurred some time in the preceding 24 h. The FOUR score was 3 (E0, M0, B0, R3). The eyes were closed and did not open to painful stimuli applied to any limb, the trunk, or the head. He did not follow commands to move his limbs or to move his eyes in any plane, nor were there any pursuit movements or optokinetic nystagmus. The right pupil was 8 mm and slightly irregular; the left pupil was 7 mm and round. Neither pupil reacted to light. The eyes were orthotopic, and horizontal and vertical oculocephalic reflexes were absent. Corneal reflexes were absent, and there was no cough or gag response to deep tracheal suctioning. He had a Cheyne-Stokes breathing pattern and was flaccidly quadriplegic. The plantar response was mute bilaterally. CT performed just before the neurologic examination showed low attenuation in the areas noted to have restricted diffusion 4 days earlier, most conspicuously involving nearly the entirety of both cerebral peduncles (Fig. 1). His resuscitation status was made do not resuscitate/do not intubate and he died the following day after becoming apneic during nasotracheal suctioning. Autopsy was not performed.

## Discussion

Our patient had bilaterally fixed and dilated pupils, ophthalmoplegia, and flaccid quadripareisis associated with infarction of large portions of both sides of the anterior midbrain after cardiac surgery. The absence of corneal, gag, and cough reflexes raise the possibility that more caudal portions of the brainstem were also involved. Because of essentially complete disruption of the connections between all descending tracts from the cortex and their effector nuclei, it was not possible to accurately determine his level of consciousness on the basis of physical examination. The case is remarkable in both the topography of the infarcts and the severity and peculiarity of the associated clinical deficits. It is one of only a very few cases to report bilaterally fixed and dilated pupils in association with infarction of the midbrain. It also illustrates well the difficulty in recognition of stroke in critically ill patients.

**Fig. 1 (a–c)** Axial diffusion-weighted MRI from postoperative day 7 showing areas of restricted diffusion in the cerebral peduncles, left inferomedial temporal lobe, and left parieto–occipital junction. **(d)** CT from postoperative day 12 demonstrating evolution of bilateral cerebral peduncle infarctions



Midbrain infarction is rare, accounting for only 3–9% of posterior circulation infarcts [3, 4]. Of these, only 2% are bilateral [3, 4]. Accordingly, knowledge about the clinical manifestations and etiology of bilateral midbrain infarction is limited to that provided by the analysis of only a few cases. Most of the reported cases describe a locked-in syndrome with preservation of pupillary function and at least vertical eye movements [5–9]. It is hypothesized that in these cases, limb and bulbar paralysis occur due to damage to the corticospinal and corticobulbar tracts that run through the lateral portions of the cerebral peduncles [5]. Voluntary eye movements are thought to be relatively spared because the infarcts typically do not involve the medial-most portions of the cerebral peduncles, in which are located the fibers connecting the cortex to pontine horizontal gaze centers, nor do they involve the fibers running to the vertical gaze centers in the rostral midbrain tectum and tegmentum [10].

In our review of the literature, we found only three other cases of midbrain infarction associated with bilateral mydriasis [4, 11]. Two of these patients had associated bilateral oculomotor nerve palsies; in one there is no mention of eye movement abnormalities. All three were quadriplegic. In the two of these cases in which the topography of the infarcts is described, as in our patient, the anteromedial midbrain was involved bilaterally [4]. A similar syndrome of enlarged, non-reactive pupils, near total ophthalmoplegia, and flaccid quadripareisis has been described in association with traumatic and spontaneous hemorrhage involving the medial midbrain and cerebral peduncles [12, 13]. As in our case, some of these patients did not exhibit exotropia in association with nonreactive, dilated pupils, as would be expected with isolated oculomotor nerve and/or nucleus lesions.

In a large case series that addresses both the topography and etiology of midbrain infarction, 8 of 11 cases of

bilateral infarction were caused by large artery disease [4]. Of the other three cases, one was cardioembolic, one was due to vertebral artery dissection, and one was cryptogenic. Because of the lack of an MRI or neuropathologic examination, the cause of our patient's infarctions cannot be determined with certainty. We hypothesize that his initial, scattered infarctions in the posterior circulation were the result of intraoperative emboli, probably related to cross-clamping of a diseased aorta [14]. As a result of these initial infarctions, which most prominently involved the lateral portions of the cerebral peduncles, the patient was left in a nearly locked-in state, with preservation of only some volitional control of eye movements, the tongue, and the left hand. The delayed development of bilateral fixed and dilated pupils was probably the result of damage to the anteromedial midbrain as seen on CT (Fig. 1), although we cannot exclude involvement of other areas of the midbrain. This delayed damage might have occurred as a result of a second embolic event originating in the heart or aorta, in situ vertebral or basilar artery atherothrombosis, or due to edema from evolution of the large, bilateral peduncular infarcts. One of the former two explanations seems more likely, as the absence of corneal, cough, and gag reflexes suggests ischemia involving areas of the brainstem caudal to the midbrain that were not involved on previous exams and imaging.

Delay in recognition of in-hospital stroke and subsequent neurologic assessment has been well described [15]. This issue may be especially pertinent for patients in ICUs, in whom the presence of injuries, other illnesses, and sedating medications may mask new focal neurologic dysfunction while simultaneously providing competing explanations for it [16]. Because such delays are conceivably preventable and limit the application of acute stroke therapies, this is an important clinical problem. The present case illustrates this well. Although the clinical syndrome was eventually identified as a probable new ischemic stroke, new neurologic signs and symptoms may have been present for as long as 24 h before this diagnosis was made. This uncertainty about the time of onset significantly diminished the potential utility of acute stroke therapies, which were not used for this patient.

## Conclusion

Infarction of the midbrain is rare and can uncommonly present with bilaterally fixed and dilated pupils and

quadriplegia. This presentation appears to be associated with bilateral anteromedial midbrain lesions. Awareness of this syndrome and rapid differentiation of it from other causes of bilaterally fixed and dilated pupils, such as severe diffuse hypoxic-ischemic cerebral injury, are important for the recognition of patients with focal midbrain ischemia. Such patients might benefit from acute stroke therapies and, despite their clinical picture, may have relatively preserved consciousness.

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