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# Paradoxical Cerebral Emboli Associated with Pulmonary Arteriovenous Shunts: Report of Three Cases

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Paradoxical embolism to the cerebral circulation is rarely diagnosed in life; however, three such cases have recently been observed: two with multiple congenital pulmonary arteriovenous malformations and one with an acquired arteriovenous fistula. In each case the pulmonary lesion(s) were treated by percutaneous balloon embolizations.

Paradoxical embolism should be included in the differential diagnosis of cerebral arterial embolism for which there is no obvious source, especially when there is also evidence of concurrent peripheral venous thrombosis and/or pulmonary embolism.

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Paradoxical embolism, defined as the transmission into the arterial system of material from the venous circulation through a right-to-left shunt, was first described by Cohnheim in 1876 [1]. In 1884, Rostan [1] referred to "l'embolie croissée," and in 1889, Zahn [2] suggested the term "paradoxical embolism." Multiple reports concerning the postmortem diagnosis of paradoxical embolism subsequently appeared in the medical literature. In 1930, two reports appeared simultaneously, which included the first cases that had been recognized during life [3, 4]. Thus far, few cases have been diagnosed antemortem; however, with greater awareness and the use of advanced diagnostic techniques, the possibility of this pathologic condition should be entertained with increasing frequency. This article details three cases of paradoxical cerebral arterial embolism mediated by pulmonic arteriovenous shunts that were diagnosed and treated by transvascular pulmonary balloon embolization.

## Case Reports

### Case 1

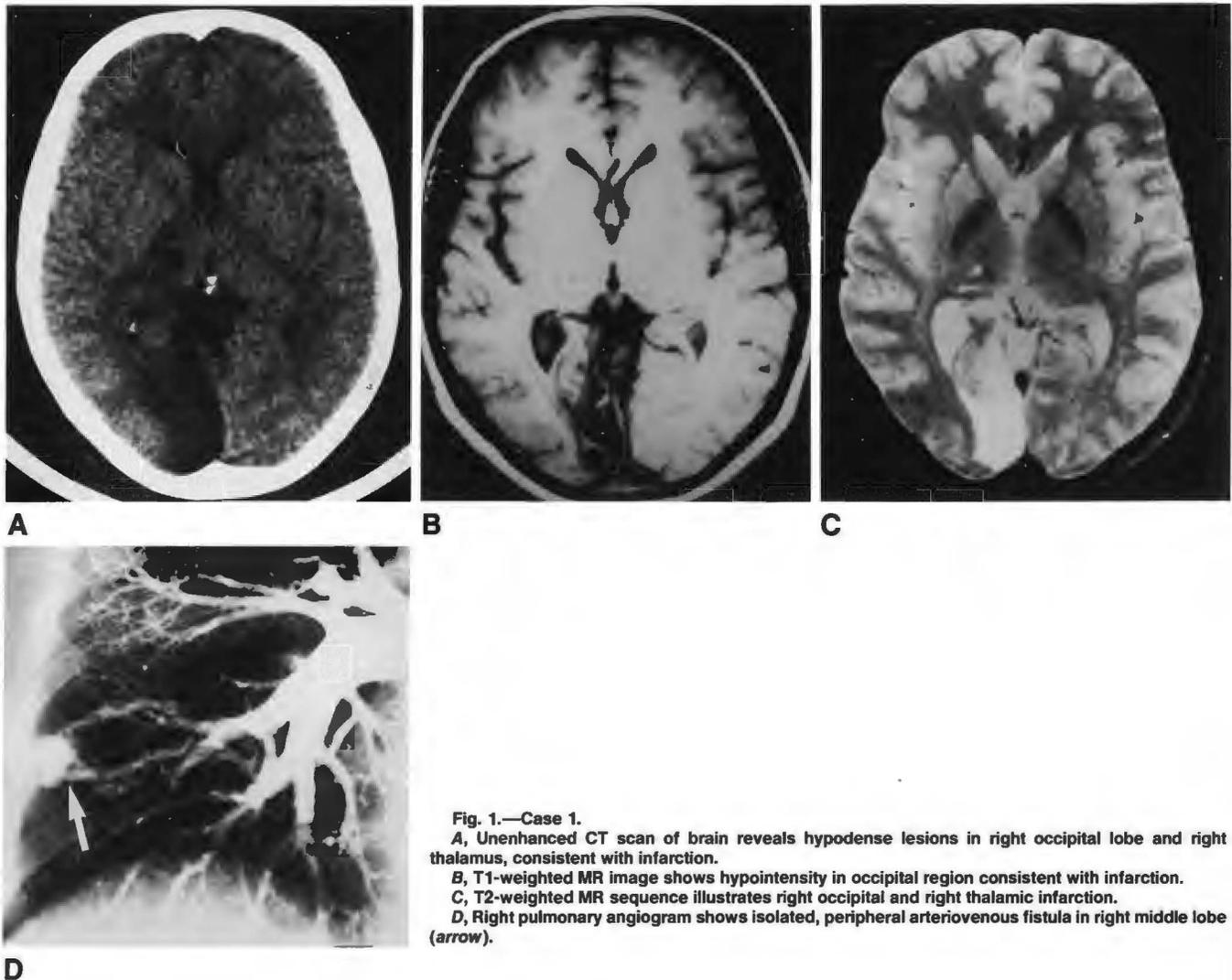
A 19-year-old woman with a history of IV heroin abuse presented with multiple head injuries but no evidence of neurologic deficit. She was noted to be febrile, with a temperature of 40°C, and complained of chest pain and shortness of breath. She had a history of subacute bacterial endocarditis involving the right side of the heart, which had been treated with IV antibiotics. She had also been treated for a right gluteal abscess, which was incised and drained.

Blood cultures were positive on admission for  $\beta$ -hemolytic streptococci and *Staphylococcus aureus*, and the patient was treated with appropriate IV antibiotics for 10 days. On examination, she was noted to have left hemiparesis and left homonymous hemianopsia. A CT scan of the head revealed right occipital and right thalamic infarction (Fig. 1A). T1- and T2-weighted MR images of the brain showed a right occipital lesion consistent with infarction (Figs. 1B and 1C). Chest X-ray demonstrated multiple small, ill-defined, left upper, right lower, and middle lobe infiltrates consistent with multiple pulmonary emboli. On cardiac catheterization, no cardiac vegetations were seen, but a possible right midlung arteriovenous fistula (AVF) was noted. A subsequent pulmonary angiogram revealed an AVF in the right midlung (Fig. 1D). The patient was treated successfully by embolization with two detachable balloons

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**Fig. 1.—Case 1.**  
**A,** Unenhanced CT scan of brain reveals hypodense lesions in right occipital lobe and right thalamus, consistent with infarction.  
**B,** T1-weighted MR image shows hypointensity in occipital region consistent with infarction.  
**C,** T2-weighted MR sequence illustrates right occipital and right thalamic infarction.  
**D,** Right pulmonary angiogram shows isolated, peripheral arteriovenous fistula in right middle lobe (arrow).

(Becton Dickinson & Co., Lincoln Park, NJ). A postembolization angiogram confirmed complete occlusion of the AVF and absence of balloon migration.

#### Case 2

A 57-year-old woman with a history of Osler-Weber-Rendu syndrome associated with multiple pulmonary arteriovenous malformations (AVM) was admitted with a 3-day history of diarrhea and stiff neck, increasing fever and chills, and mental status deterioration. She had undergone 14 prior pulmonary balloon embolizations in an effort to treat the multiple pulmonary AVMs.

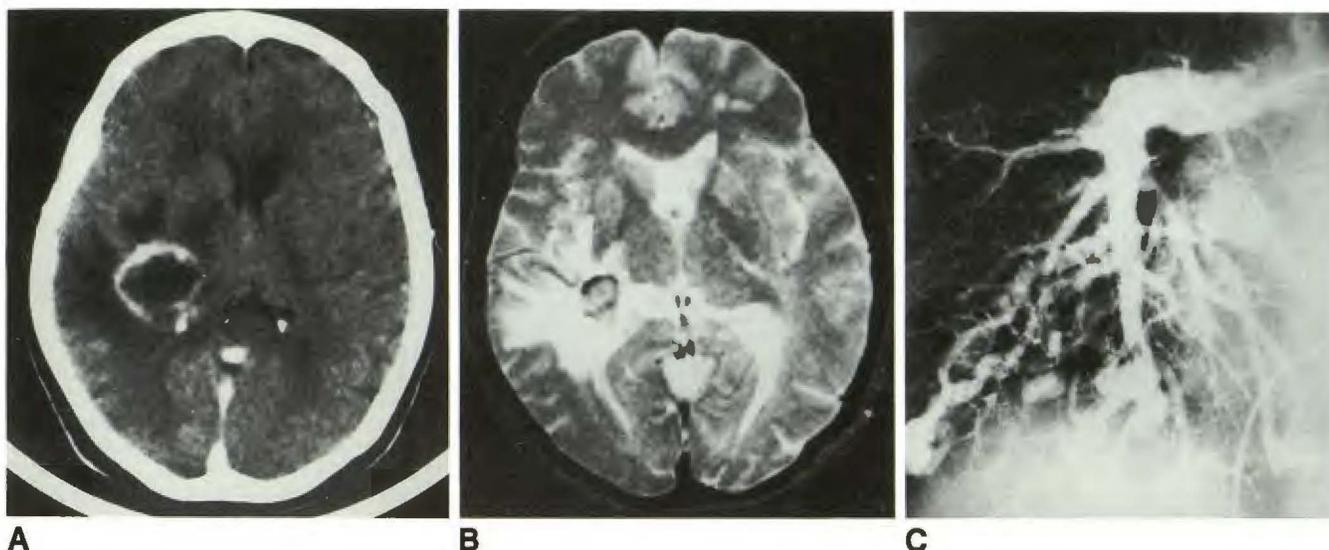
The patient had an oral temperature of 37.7°C. Fundoscopic, conjunctival, and oral mucosa examinations were normal. Her neck was stiff, and she had positive Kernig and Brudzinski signs. The cardiovascular system examination was normal, and the chest was clear to auscultation. A CT scan of the head with and without IV contrast administration revealed a ring-enhancing right parietal lesion measuring approximately 2.0 × 2.0 cm surrounded by edema, consistent with abscess formation (Fig. 2A). Owing to its location adjacent to the ventricle, biopsy was not performed and the patient was managed conservatively. All CSF and blood cultures were negative.

The patient's abscess was thought to be due to multiple infected teeth, which could be treated with coverage for oral anaerobes. An MR examination of the brain without contrast medium demonstrated the right parietal lesion, which was also compatible with abscess (Fig. 2B). The pulmonary angiogram revealed multiple residual AVMs (Fig. 2C).

Following treatment, the patient's symptoms of dizziness and slow speech gradually improved over the subsequent days of her hospitalization. Further embolization of the remaining pulmonary AVMs was planned for the purpose of prophylaxis against future, recurrent emboli.

#### Case 3

A 57-year-old diabetic woman who was non-insulin-dependent was admitted following a motor vehicle accident. The patient was found to have a room-air arterial blood gas of pH 7.4, PCO<sub>2</sub> of 30, and PO<sub>2</sub> of 62 (normal values, pH = 7.4, PCO<sub>2</sub> = 40, and PO<sub>2</sub> = 95). A chest X-ray revealed a right lung lesion that was consistent with an AVM of uncertain origin. A ventilation perfusion lung scan demonstrated a large defect in the patient's left lung field. Initially, this was thought to be a pulmonary embolus and the patient was placed



**Fig. 2.—Case 2.**  
**A,** Axial enhanced CT scan of brain reveals ring-enhancing lesion with surrounding edema in right parietal lobe, consistent with cerebral abscess.  
**B,** T2-weighted MR image of brain shows hyperintense edematous zone in right parietal lobe surrounding hyperintense mass with hypointense peripheral ring.  
**C,** Right pulmonary angiogram shows multiple pulmonary arteriovenous malformations.

on heparin. She subsequently underwent a pulmonary arteriogram, which showed five pulmonary AVMs. Two of these were in the left lung and three were in the right (Fig. 3A). An initial attempt to embolize the AVMs was unsuccessful. The patient was readmitted for transvascular treatment to improve her oxygenation and prevent any possible embolic complications. On presentation, the lungs were clear, and the cardiac and neurologic examinations were normal.

T1-weighted MR images of the brain demonstrated a focal area of decreased intensity seen in the right posterior cerebellar hemisphere at the gray-white matter junction (Fig. 3B). On T2-weighted MR images, this lesion was of high signal intensity, consistent with chronic infarction. Similar but more subtle areas of infarction were identified in the right temporal and right occipital lobes.

The largest AVM in the right middle lobe was subsequently occluded with a detachable balloon without complications. A second AVM in the left lower lobe was embolized at a later date. Further prophylactic therapeutic embolization of the remaining AVMs was planned.

## Discussion

The clinical triad of criteria for paradoxical emboli includes (1) venous thrombosis and/or associated pulmonary embolism (excluding thrombosis of pulmonary veins); (2) an arteriovenous communication that will permit a right-to-left shunt (usually through a patent foramen ovale, atrial septal defect, ventricular septal defect, or patent ductus arteriosus); and (3) arterial embolism without evidence of a source of these emboli in the left side of the heart [5]. A diagnosis of proved paradoxical cerebral emboli, according to the literature, rests upon the unlikely finding of an embolus at the site of the anatomic channel connecting the venous with the arterial systems [6].

Most reported cases of paradoxical embolism have not been associated with overt congenital heart disease. Rather,

they have occurred in association with a silent patent foramen ovale, which is a relatively common finding. It is known that even mild degrees of right-to-left shunting may in fact occur in normal individuals under certain circumstances [7].

An extracardiac source of paradoxical cerebral emboli is a pulmonary AVM. A majority of pulmonary AVMs are congenital, and about 60% have been seen in association with Osler-Weber-Rendu syndrome or hereditary hemorrhagic telangiectasia (HHT). Secondary or acquired pulmonary AVFs occur with trauma, chronic pulmonary inflammatory disease, longstanding hepatic cirrhosis, and metastatic disease to the lung.

Patients with pulmonary AVMs may manifest cerebral symptoms [5]. A recent review of HHT suggests that a high percentage (49%) of acquired cerebral lesions seen in affected patients are secondary to paradoxical cerebral emboli mediated through the pulmonary AVMs [7]. It is most common for pulmonary AVMs to be associated with the hereditary syndromes. Furthermore, multiple pulmonary AVMs are also usually associated with HHT [8]. In one family of 231 members, pulmonary AVMs were present in 147 of the individuals with HHT [9]. However, occasionally they may occur sporadically without a demonstrable genetic basis.

Neurologic complaints are common in HHT with associated pulmonary AVM(s). The symptoms range from generalized headache, confusion, and seizures to transient ischemic attacks, paraesthesias, stroke, and abscess formation. In one review, documented neurologic complications totaled 41% of patients with pulmonary AVM and HHT, but only 18% in subjects with pulmonary AVM without HHT [7].

The mechanisms of such neurologic symptoms in HHT are many. Associated hypoxemia and polycythemia are thought to produce transient symptoms. Presence of concomitant cerebral AVMs may cause intermittent bleeding with attend-

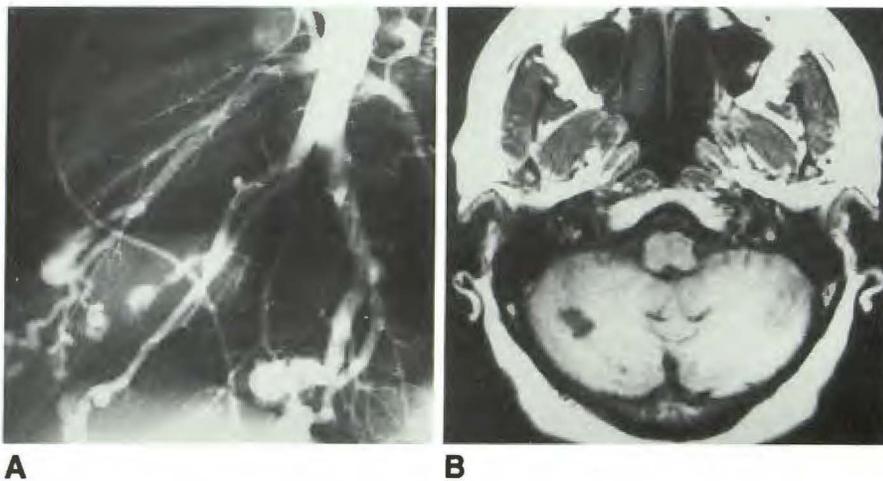


Fig. 3.—Case 3.

A, Pulmonary angiogram reveals multiple pulmonary arteriovenous malformations in right lower lobe.

B, T1-weighted MR image of brain shows focal area of decreased intensity in right posterior cerebellar hemisphere, consistent with chronic infarction.

ant symptomatology [7, 10–12]. However, the frequency of paradoxical cerebral emboli transmitted through pulmonary AVMs resulting in stroke or abscess is often underestimated. Because both the pulmonary and mucocutaneous lesions may not be prominent, one should routinely search for a pulmonary AVM on chest radiographs and examine the skin for telangiectasias in any patient with a cerebral embolus in whom no left-sided cardiovascular source of stroke can be found.

It is still not clear whether the primary source of such paradoxical cerebral emboli is in the peripheral venous system, only to pass through a lung that has lost its filtering function, or whether the emboli arise in the aneurysmal portion of the AVM. However, early venous opacification at the time of pulmonary angiography suggests that flow through pulmonary AVMs is rapid and not conducive to in situ formation of thrombus, thus favoring the former theory.

Because HHT is an autosomal dominant trait with increasing penetrance and expressivity with age [10], the families of any patient with HHT or isolated pulmonary AVM(s) should be evaluated for the physical manifestations of HHT and screened for the presence of pulmonary AVM. These relatives may have clinically silent pulmonary AVMs and would therefore be susceptible to paradoxical embolization, with resulting stroke or abscess formation. Screening of family members involves study by chest radiography and an arterial blood gas determination. Evaluation by pulmonary arteriography will confirm a suspected diagnosis and provide important details about feeding arteries and draining veins. Additional radiologic investigations to supplement these studies may include a CT or MR scan of the brain to rule out occult cerebral lesion(s). Such screening is important, since an acquired cerebral insult or even an associated vascular malformation of the brain may occur in relatively asymptomatic patients with family histories of HHT.

Cardiac and vascular complications seen in drug abusers are directly related to the vascular effects of drug contaminants and to unsterile injection techniques. Skin abscesses, cellulitis, and thrombophlebitis are the most frequent complications of IV drug abuse [13]. Infected emboli to the lungs may be the result of induced septic peripheral thrombophle-

bitis, thrombus in the right heart (tricuspid endocarditis), or direct IV injection of contaminated embolic material. A postulated breakdown in the normal capillary/tissue barriers between artery and vein subsequently occurs in some cases of pulmonic septic embolization, with direct arteriovenous communication and AVF formation.

In regard to therapy, relatively speaking, any patient with a demonstrable pulmonary AVM or AVF in the lower half on the lung should be treated. The reason for this is that the preferential pulmonary blood flow is to the lower lobes in the upright position, which increases the statistical likelihood of paradoxical embolization through a lower lung pulmonary vascular shunt. Treatment traditionally has been open surgical intervention, with either a lobectomy or ligation of the feeding artery and vein. This often entails little parenchymal loss because of the subpleural location of most pulmonary AVMs [14].

Balloon occlusion has provided an alternative, less invasive treatment, especially in patients with multiple pulmonary AVMs [15–18]. This technique is performed angiographically with a detachable balloon that is flow-directed into the feeding artery in order to occlude the AVM. Balloon occlusion may be repeated for enlarging or newly developed pulmonary AVMs. Patients typically return to normal activities within 2 or 3 days of the transvascular AVM occlusion.

In summary, paradoxical cerebral emboli in subjects with pulmonary AVMs or AVFs are not uncommon. A review of the literature indicates that the acquired pulmonary AVF is rare, with sporadic AVMs or pulmonary AVMs associated with HHT being more frequent. The significance of recognizing paradoxical cerebral emboli lies in the subsequent clarification of the underlying primary disease process, which then allows initiation of specific appropriate treatment oriented toward ablating the pulmonic arteriovenous shunt, thereby averting further potential embolic complications.

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