Cerebral Symptoms in Pulmonary Arteriovenous Fistula

A Result of Paradoxical Emboli (?)

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SUMMARY

Two cases of pulmonary arteriovenous fistulas with hemiparesis and other neurologic findings, possibly from paradoxical embolization, are described. Many theories have been put forward to explain the pathophysiology of the frequently present neurologic manifestations. We regard paradoxical embolization through the fistula as the most important factor in the pathogenesis of the neurologic deficit.

Due to the potential hazard of paradoxical cerebral embolization and possible subsequent brain abscess formation, surgical resection of all pulmonary arteriovenous fistulas wherever feasible is recommended.

Additional Indexing Words:
Pulmonary arteriovenous fistula Brain abscess Cerebral embolism

Over 350 cases of pulmonary arteriovenous fistula have been recognized since the initial autopsy diagnosis of this condition by Churton in 1897 and the first clinical diagnosis by Smith and Horton in 1939. Clinical manifestations of pulmonary arteriovenous fistulas include cyanosis, clubbing, extracardiac murmur, pulmonary hemorrhage, secondary polycythemia, and pulmonary mass. Hereditary hemorrhagic telangiectasia is frequently present.

Of particular interest is the approximately 33% incidence of neurologic abnormalities. Headache, dizziness, tinnitus, convulsions, and hemiplegia are occasionally present. Although neurologic symptoms are often transient, permanent damage has occurred. The neurologic manifestations have been attributed to anoxemia, polycythemia, thrombosis, and abscess. An alternative etiologic hypothesis mentioned briefly in the past, but receiving little attention, is paradoxical embolization. By this mechanism systemic venous emboli would bypass the lung filter and be diverted directly into the systemic arterial circulation via the arteriovenous shunt. We wish to report two cases in which paradoxical embolization possibly occurred through a pulmonary arteriovenous fistula.

Report of Cases

Case 1

W. C. M., a 26-year-old Caucasian man, was admitted to the neurologic service of Barnes Hospital April 5, 1958. Ten days before admission he developed a severe occipital headache, followed by a temporary paresthesia over the right side of his body. Subsequently the headache worsened, and he became drowsy. Progressive aphasia and confusion developed 4 days later. Significantly, he had experienced episodes of right hemiparesis, hemianesthesia, and transitory aphasia in 1951, 1952, and 1956. There was a family history of telangiectasia, and the patient had multiple telangiectases over his lips which had occasionally bled severely. He also had a history of frequent epistaxes until age 17.

On examination, the patient exhibited mixed aphasia, weakness in the right arm and hand and...
a positive right Babinski sign. Cardiovascular examination was negative. The admission hemoglobin value was 17.1 g/100 ml. Chest roentgenograms showed a left lower lobe coin lesion, 18 mm in diameter. Pneumoencephalography demonstrated a shift to the right of the third and left lateral cerebral ventricles, and a left carotid angiogram revealed downward displacement of the left middle cerebral artery. A diagnosis of brain abscess was made, and on April 14, 1958, left parietal craniotomy was performed with removal of a large brain abscess from which alpha streptococci were cultured. The postoperative course was satisfactory. Penicillin and streptomycin were administered intrathecally and Achromycin orally. He was discharged with residual motor aphasia, weakness in the right extremities, and a mild sensory deficit.

The patient was readmitted on July 29, 1958, because of grand mal seizures. No new neurologic signs were elicited. The hemoglobin value was 16.4 g. The left lower lobe coin lesion had decreased in size from 18 to 15 mm; it was interpreted as being due to an inactive granulomatous process. The patient was discharged with instructions to take diphenylhydantoin and phenobarbital.

On September 16, 1961, the patient was readmitted complaining of loss of vision for a 2-hour period 3 weeks prior to admission. Partial clearing occurred, but he continued to note an area of blurring in the inferior nasal visual field of the left eye. He also complained of memory defects. His seizure activity had been under good control. A systolic bruit was heard over the left posterolateral chest area. Decreased cortical sensation, hyperreflexia, and muscle spasticity were present on the right. Chest roentgenograms revealed that the coin lesion in the left lower lobe had doubled in size from 15 to 30 mm since 1958, and a linear density medial to the lesion was thought to represent "feeder" vessels. Pulmonary artery angiography (fig. 1) demonstrated a large arteriovenous fistula in the left lower lung field. Cerebral arteriograms were not done, but the neurologist felt that the cerebral problems were probably due to an embolus from the basilar artery lodging in a branch of the right posterior cerebral artery. On September 27, 1961, left lower lobectomy was performed. The arteriovenous fistula measured 1.3 cm by 2.0 cm. Microscopic sections (fig. 2) of the specimen revealed dilated vascular chambers with irregularly thickened walls.

The postoperative course was uneventful, and to date he has had no further neurologic symptoms.

Case 2

P. R., a 24-year-old Caucasian woman, was admitted to Barnes Hospital on March 29, 1967. She had previously enjoyed good health with the exception of a transient episode of aphasia and right facial weakness lasting 1 hour 4 months prior to admission. The patient also had had numerous mild epistaxes for many years. On the day of admission, she was discovered on the floor...
by her husband when he returned from work. She was unable to speak, and her husband immediately took her to the hospital. The patient had been taking an oral contraceptive.

On examination, she was afebrile and alert. The chest was clear, and results of cardiac examination were normal. The spleen and liver were not palpable. She had marked motor aphasia, a right central facial paralysis, and flaccid paralysis of the right upper and lower extremities. The deep tendon reflexes were brisk bilaterally, and a positive Babinski sign was elicited on the right. Sensory perception was normal.

The admission hemoglobin concentration was 12.1 g/100 ml, and hematocrit was 37%. Electroencephalogram demonstrated bifrontal and left-sided slow features consistent with organic disease. Spinal fluid showed opening pressure of 195 mm saline, closing pressure, 160 mm, saline, protein, 44 mg/100 ml, sugar, 48 mg/100 ml, and no cells or xanthochromia. A left carotid angiogram showed definite obstructive lesions in an otherwise normal left middle cerebral artery (fig. 3). These were considered to be cerebral emboli.

On March 31, 1967, heparin therapy was begun. Cardiac catheterization was performed on April 4. Pressures in the right ventricle and pulmonary artery were normal, and a pulmonary artery hydrogen curve was indicative of recirculation. The pulmonary artery angiogram (fig. 4) revealed a large pulmonary arteriovenous fistula in the inferior and anterior wall of the right lower lobe. Aortic arch and inferior vena caval angiograms were normal. On April 12, a right lower lobectomy was performed. A 2.5 by 3 cm

**Figure 3**

*Case 2. Carotid angiogram shows abrupt, large filling defect (proximal and distal margins marked by long arrows) and small filling defect (short arrow) in middle cerebral artery.*

**Figure 4**

*Case 2. Pulmonary artery angiogram with concentration of contrast material in pulmonary arteriovenous fistula.*

**Figure 5**

*Case 2. Photomicrograph of arteriovenous fistula showing saccular, dilated vascular structure with irregularly thickened walls.*
arteriovenous fistula was present on the inferior lobar surface, the microscopic section of which revealed a saccular vascular chamber with irregularly thickened walls (fig. 5). The postoperative course was uncomplicated and the patient was discharged on May 6, 1967. To date, she has had no further neurologic problems, and the residual effects of the aphasia and hemiparesis have greatly diminished.

Discussion

Symptoms and signs referable to the central nervous system in patients with pulmonary arteriovenous fistula are often reported. Yater and associates described neurologic findings in 20 of 45 patients, Sloan and Cooley in 22 of 79 patients, and Muri in 26 of 79 patients.

The etiology of these neurologic manifestations has been variously assessed. Polycythemia, with its known tendency to facilitate thrombus formation, and cerebral anoxemia are the factors generally considered most significant. Cases of brain abscesses associated with pulmonary arteriovenous fistula have been reported. The abscesses are usually ascribed to the polycythemia and hypoxia. Runstrom and Sigroth suggested that cerebral angiomatos malformations may be responsible for the cerebral signs and symptoms. Steinberg and McClanahan described a case of meningoencephalitis and pulmonary arteriovenous fistula. Sloan and Cooley and Bergquist and associates discussed the possibility of air emboli, with the air gaining entrance into the circulation through a defect in the wall of the fistula. Hunter recently described the sudden development of aphasia and hemiplegia in an 18-year-old patient with pulmonary arteriovenous fistula. A carotid angiogram demonstrated a defect in the middle cerebral artery suggestive of an embolus. Hunter hypothesized that the embolus originated within the arteriovenous fistula although there was no evidence for this in the surgically resected specimen.

Paradoxical embolization occurring across the pulmonary arteriovenous shunt has attracted only brief mention as the possible etiology of the frequent neurologic findings. This cause of brain abscess and cerebral embolism is well recognized in other situations. Ingham reported six cases of paradoxical embolism preceded by pulmonary artery embolism, and in each case at autopsy a thrombus was seen in transit through a patent foramen ovale. Congenital heart disease with right-to-left shunts is associated with paradoxical embolization and possible subsequent formation of brain abscess. The mechanism of paradoxical embolism would be similar in patients with pulmonary arteriovenous fistulas, in whom systemic venous emboli would be transmitted across the communicating vessels of the fistula into the pulmonary vein and systemic arterial circulation. This passage may be facilitated by the preferential shunting of large amounts of blood through the low resistance communication. The exceedingly important filtering function of the pulmonary microcirculation would thereby be bypassed. The emboli, when transmitted to the intracerebral circulation, could be the source of the multiple reported neurologic difficulties from mild sensory and motor deficiencies to severe hemiplegia and brain abscesses. In Hunter's case, it is possible that the hemiplegia was caused by a paradoxical embolus originating in a systemic vein, rather than in the arteriovenous fistula, as he hypothesized.

In both cases discussed in this report, there was evidence of prior transient episodes of acute neurologic disease. These transient episodes, not uncommon in the life history of patients with pulmonary arteriovenous fistulas, suggest the possibility of paradoxical embolization of small systemic venous thromboemboli. It is interesting that the second patient used oral contraceptives and her blood group is type A, both of which are factors considered by some investigators to increase the incidence of thromboembolic disease. In case 1, the neurologic findings immediately before pulmonary surgery strongly suggested embolization to the posterior cerebral artery. In case 2, carotid angiography precisely delineated an embolic obstruction in an otherwise normal left middle cerebral artery to account for the hemiplegia and aphasia.
Auscultation, the levophase of the pulmonary angiogram, and the aortic arch angiography ruled out cardiac or aortic arch anatomic defects which might predispose to embolism from the heart or aorta. In addition, in case 2, neither secondary polycythemia nor hypoxemia was present to account for the cerebral findings. In both of these patients, paradoxical embolization across the pulmonary shunt to the intracerebral circulation is a plausible explanation for the sudden development of neurologic findings.

Is the anatomic configuration of pulmonary arteriovenous fistulas compatible with the occurrence of paradoxical embolism? In previous reports there are descriptions of direct communications between the arterial and venous systems, and there are illustrations of pathologic specimens showing large cavernous thin-walled sacs with distended afferent artery and efferent veins clearly large enough to permit the passage of particulate emboli. Goldman’s photograph of a hardened liquid latex cast of the vascular passageways shows large communications between the artery and the vein. A recently published illustration shows the cast of a vascular malformation of adequate diameter (2 to 5 mm) to allow easy passage of an embolus. In all probability, some of these lesions may not have communicating channels large enough to allow passage of significantly large embolic material. However, over a period of time, degenerative changes in the vessel wall probably occur due to the large flow across the shunt. These changes probably aid in increasing the size of the communicating channels as well as increasing the overall radiologic size of the lesion as exemplified by case 1. We have not encountered reports of systemic emboli other than to the brain in cases of pulmonary arteriovenous fistula. The explanation may be that the size of embolus permitted passage by the fistula may be small enough that it does not cause significant or recognizable symptoms except in the brain.

In the treatment of pulmonary arteriovenous fistulas, we advise surgical resection, if technically feasible. The neurologic sequelae resulting from intracerebral arterial emboli and the possibility of brain abscess formation constitute a powerful argument for the surgical removal of the arteriovenous malformation.

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25 Years Ago
Immunologic Tolerance
Scientific Beginnings

... If, therefore, the frequent identity of blood types in twin pairs can be explained neither as the result of monozygotic twinning nor as chance identity between fraternal twins, nor as the sum of these two factors, it is evident that some mechanism is operating to produce frequent phenotypic identity of blood types in genetically dissimilar twins. The vascular anastomosis between bovine twins, known to be a common occurrence, provides an explanation.

... Since many of the twins in this study were adults when they were tested, and since the interchange of formed erythrocytes alone between embryos could be expected to result in only a transient modification of the variety of circulating cells, it is further indicated that the critical interchange is of embryonal cells ancestral to the erythrocytes of the adult animal. These cells are apparently capable of becoming established in the hematopoietic tissues of their co-twin hosts and continuing to provide a source of blood cells distinct from those of the host, presumably throughout his life.—R. D. OWEN: Immunogenetic consequences of vascular anastomoses between bovine twins. Science 102: 400, 1945.
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