

lung biopsy in HP classically shows lymphocytic infiltration and granulomas, histologic pattern of nonspecific interstitial pneumonia has been described in recognized HP.<sup>5</sup> Ultimately, the sensitization of the musician against the molds found in his saxophone is important evidence for HP.

The additional study on saxophonists showed that saxophones are frequently colonized by fungal species and constitute a source of potentially inhalable and pathogenic molds. Indeed, cases of HP due to *Fusarium* sp, *Penicillium* sp, and *Cladosporium* sp have been reported. The lack of sensitization of the musicians may be explained by too poor a level of exposure or too short a contact with the molds, since it is known that a long exposure is necessary to stimulate an immune response.<sup>6</sup>

## CONCLUSION

We present a case of HP in a saxophonist due to the inhalation of molds from his instrument and an additional investigation that emphasizes the fact that musicians may be a population at risk for immunologically induced lung disease. Physicians should be aware of this potential disease in subjects who play a wind instrument.

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## REFERENCES

1. Girard M, Lacasse Y, Cormier Y. Hypersensitivity pneumonitis. *Allergy*. 2009;64(3):322-334.
2. Lodha S, Sharma OP. Hypersensitivity pneumonitis in a saxophone player. *Chest*. 1988;93(6):1322.
3. Reboux G, Piarroux R, Roussel S, Millon L, Bardoumet K, Dalphin JC. Assessment of four serological techniques in the immunological diagnosis of farmers' lung disease. *J Med Microbiol*. 2007;56(pt 10):1317-1321.
4. Richerson HB, Bernstein IL, Fink JN, et al; Report of the Subcommittee on Hypersensitivity Pneumonitis. Guidelines for the clinical evaluation of hypersensitivity pneumonitis. *J Allergy Clin Immunol*. 1989;84(5 pt 2):839-844.
5. Lima MS, Coletta EN, Ferreira RG, et al. Subacute and chronic hypersensitivity pneumonitis: histopathological patterns and survival. *Respir Med*. 2009;103(4):508-515.
6. Cormier Y, Bélanger J, Durand P. Factors influencing the development of serum precipitins to farmer's lung antigen in Quebec dairy farmers. *Thorax*. 1985;40(2):138-142.

# Azygos Vein to Pulmonary Vein Fistula Is a Pathway for Cerebral Embolism

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**A 43-year-old man was admitted for right upper and lower limb weakness and aphasia. He had suffered dizziness and transient blindness 6 months ago**

**and had also been found lying in the bathroom on another occasion. Multiple cerebral infarctions were confirmed by brain CT scan and MRI. Diffuse nodes in the mediastinum and postperitoneum had been found in pulmonary CT scans and MRI scans since 1999. Pulmonary CT scan revealed multiple bilateral pneumatoceles in the lungs. Contrast CT scan showed an enlarged azygos vein on the right side of the spinal column and an enlarged azygos arch. CT scan-guided biopsy revealed a few fibers, fat, and vascular tissues in the mass. Transcranial Doppler bubble test showed gas microembolic signals in both middle cerebral arteries. Pulmonary digital subtraction angiogram confirmed an enlarged azygos vein. A fistula was found between the pulmonary and azygos veins with turbulent flow from pulmonary to azygos at rest. Cavography revealed that the pulmonary vein appeared simultaneously with the superior cava vein during Valsalva maneuver. In summary, the pathway of cerebral embolism was based on three pathologic mechanisms: (1) increased inferior vena cava pressure, (2) enlarged right azygos aneurysm, and (3) the presence of a fistula between the azygos and pulmonary veins. *CHEST* 2010; 138(3):726-729**

**Abbreviations:** TCD = transcranial Doppler

**T**he main causes of cerebral embolisms include cardiac embolism, extracranial arterial embolism, paradoxical embolism (DVT with atrial septal defect), trauma (fat or air emboli), and iatrogenic embolism (cardiac catheterization or cerebral angiography). In some cases, other atypical causes should be considered. We report a case of cerebral embolism caused by an unusual pathway from an azygos vein to the pulmonary vein.

## CASE REPORT

In June 2008, a 43-year-old man was admitted to our hospital with weakness of his right limbs and aphasia. He reported suffering from dizziness and a transient blindness lasting 30 min 6 months prior. Two months before admission, he was found lying in his bathroom in the morning and was taken immediately to a local hospital. He was lethargic with mixed aphasia and right hemiplegia. The brain MRI showed multiple infarctions in the pons, basal ganglia, temporal lobe, occipital lobe, and the splenium of the corpus callosum. After treatment with antiplatelet therapy for 3 weeks, his muscle power improved, but the

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aphasia got worse. There was no prior history of hypertension, diabetes, or coronary heart disease. An enlarged mediastinum was found during a regular health check 8 years ago. Pulmonary CT scan and MRI revealed diffuse nodes. Pathology by mediastinum biopsy at the local hospital revealed normal fatty tissue.

On admission, his pulmonary, heart, and abdominal physical examination was normal except for varicose veins of the lower extremities and mild scoliosis in thoracic segments. He had normal BMI. Neurologic examination revealed that he had motor aphasia, memory deficiency, dysesthesia, and weakness of the right face and extremities. The biochemistry tests of liver and kidney, lipid profile, and blood gas test were within the normal range. Plasma angiotensin-converting enzyme was 14 U/L (normal range: 18-55 U/L). EEG was normal. Brain MRI was repeated, and diffusion weight imaging showed multiple recent infarctions in the frontal lobe, occipital lobe, insular lobe, and head of the caudate nucleus, as well as multiple old infarctions in the right thalamus and bilateral cerebella.

Transcranial Doppler (TCD) and carotid color flow sonography showed normal flow velocity and morphology except for an undeveloped vertebral artery on the right side. Neck and brain CT scan angiogram revealed normal cerebral arteries above the level of the aorta, including bilateral carotid arteries, middle cerebral artery, anterior cerebral artery, posterior cerebral artery, and basilar artery.

Embolus detection of the bilateral middle cerebral arteries with TCD (Viasys\_EME; CareFusion Corporation; San Diego, CA) found no spontaneous embolism signal during 1 h of monitoring. However, frequent embolism signals were found during Valsalva maneuver after injection of agitated saline solution (bubble study) with a silent period of 23 s and lasting 1 min 20 s. This finding was reproducible.

Both transthoracic echocardiography and transesophageal echocardiography revealed normal cardiac structures. Abdominal ultrasound revealed a segmental expansive portal vein with maximum diameter 2.1 cm but normal liver and biliary tract. Chest MRI showed enlarged mediastinum, rich with fat, extending from the postperitoneal cavity to the middle thoraces, without significant change compared with the investigation 9 years previous (Fig 1).

The plain and contrast pulmonary CT scans were repeated and revealed nonenhanced diffuse soft tissue-like masses in the mediastinum and postperitoneum rich with fatty tissue and with spots of calcification (Fig 2). The wall of the middle and inferior segments of the esophagus appeared thickened. An expansion of the arch of azygos vein was found (Fig 3). A biopsy of the left thoracic mass was undertaken with real-time guiding of CT scanning. The pathology reported a sample with a few fibers, fat, and vascular tissue.

A pulmonary digital subtraction angiogram was performed and was normal in the arterial and capillary phases. An enlarged azygos vein was confirmed on the right side of the vertebral column. A fistula was found between the pulmonary vein and azygos vein on the right side with tur-

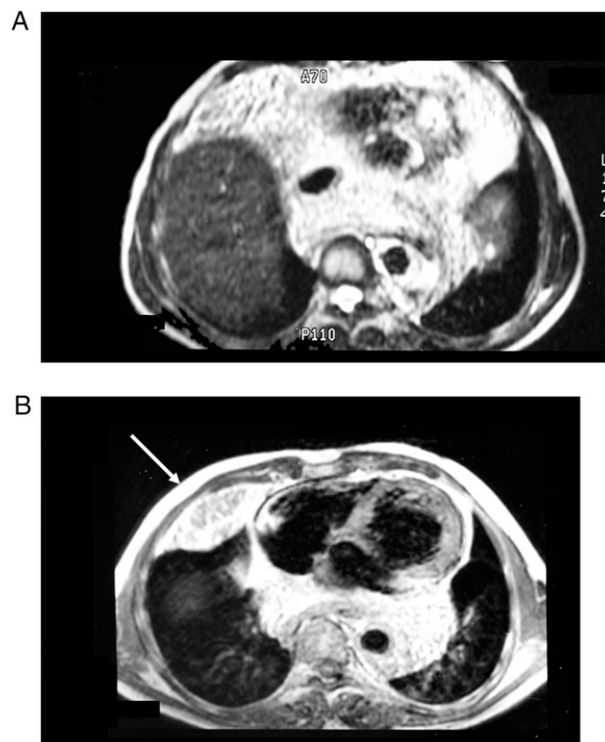


FIGURE 1. T1-weighted MRI revealed fat-rich mass in mediastinum and abdominal cavity, which is suppressed in T2 FLAIR (not shown). A CT scan-guided biopsy was performed in the mass (B, arrow).

bulent flow from the pulmonary to azygos in resting state (Fig 4), and the vena cava appeared simultaneously with the pulmonary vein. Cavography revealed a normal vena cava during rest but showed a reversal of flow into the expansive right azygos vein with eagle mouth morphology at the level of the pulmonary artery. Then, a pulmonary vein appeared (Fig 4) with reversal flow from the azygos vein to the pulmonary vein during Valsalva movement. The patient was started on warfarin therapy and has remained symptom free until now.

## DISCUSSION

This patient had the clinical features of multiple infarction involving bilateral hemispheres and either the anterior or posterior circulation. We considered an embolism mechanism. The embolus, which may have formed inside the azygos aneurysm<sup>1</sup> or varicose veins of the lower extremities, flows from the superior cava reversing to the azygos and then through the fistula between the azygos vein and the pulmonary vein; the embolus flows to the left atria. To the best of our knowledge, this embolic pathway from a systemic vein to the pulmonary vein then to the brain's arterial circulation has never been reported. The establishment of this pathway is based on the pathologic mechanisms in this case: (1) Increased inferior vena cava pressure induced by long-term compression of mediastinum lipomatosis, (2) enlarged azygos aneurysm, and (3) fistula between the azygos and pulmonary veins.

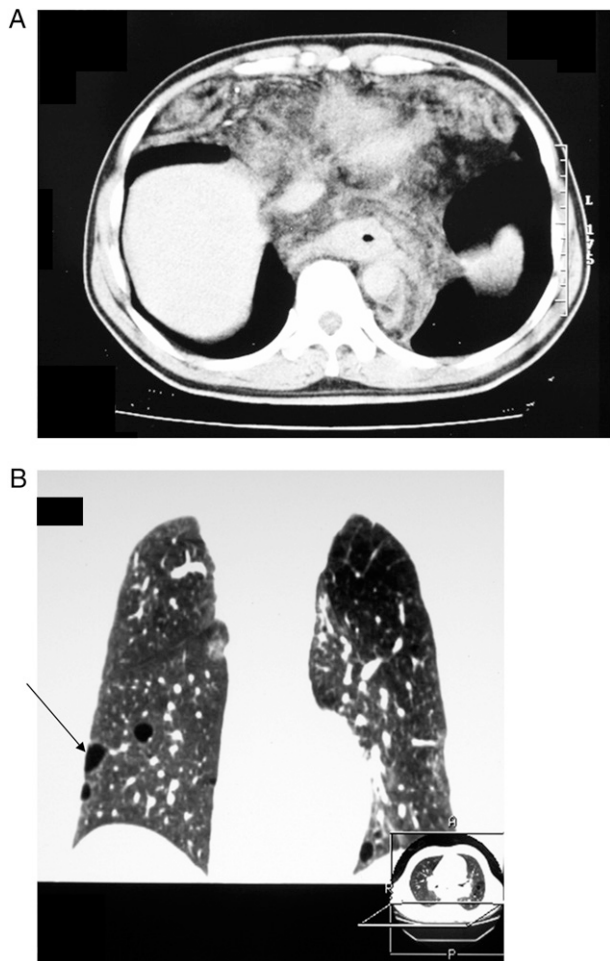


FIGURE 2. Pulmonary CT scanning revealed fat-rich mass with spots of calcification in the mediastinum (A) and multiple pneumatoceles in bilateral lungs (B, arrow).

Mediastinum lipomatosis is a rare and benign condition characterized by deposition of adipose tissue in the mediastinum.<sup>2</sup> Several MRI scans, CT scans, and two pathology examinations confirmed the diagnosis in this patient. The condition causes little compression to the neighboring airway or the larynx, but compression of the inferior vena cava system was indicated by an enlarged portal vein and varicose veins of the lower extremities and the morphology of the lower portion of the azygos vein in this case.

Azygos aneurysm is uncommon. The causes of azygos vein enlargement are heart failure, obstruction of the inferior vena cava, portal hypertension, and malformation of inferior vena cava.<sup>3</sup> It also results from compression of vena cava and liver cirrhosis<sup>4</sup> and can be induced by an arteriovenous fistula between the descending aorta and azygos vein after catheterization.<sup>5</sup> In this case, a constant reversal flow from the pulmonary vein to the azygos vein may play a role in the azygos vein enlargement.

The azygos vein is formed by the confluence of the ascending lumbar veins, subcostal veins, and lumbar azygos. It ascends in the posterior mediastinum up to the level of the fourth vertebra, where it arches anteriorly above the

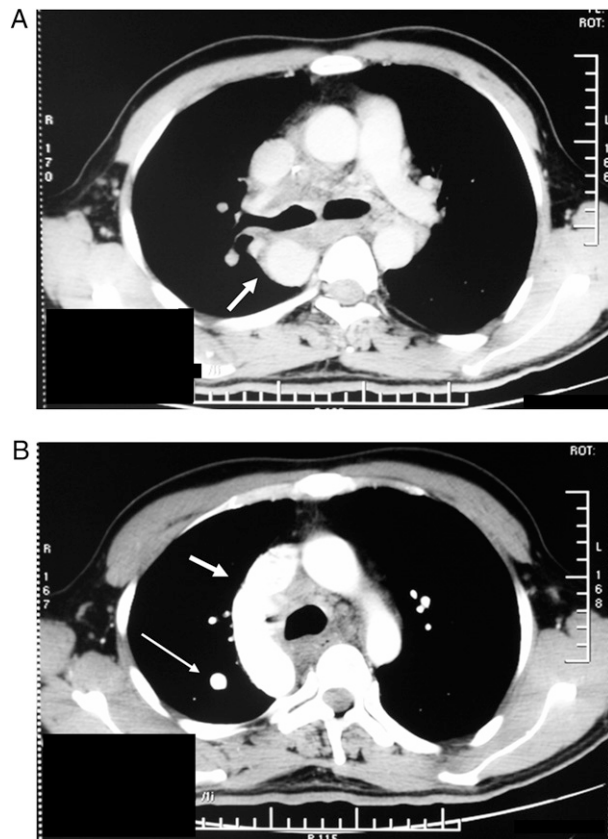


FIGURE 3. CT scan with contrast shows an enlarged azygos vein on the right side of spinal column (A, arrow), enlarged azygos arch (B, short arrow), and expand pulmonary vein (B, long arrow).

right pulmonary hilum, ending in the superior vena cava. An anatomic-embryological correlation of the anomalous venous pulmonary connection is presented to gain insight into its pathogenesis. The embryonic development of the pulmonary veins is in two stages: the primary connection of these veins (collectors) with the embryonic systemic veins from which the definitive veins then arise. These channels normally disappear once the pulmonary vein sinus is connected with the roof of the left atrium (secondary definitive connection); when the latter does not exist, any of the primitive channels will persist to originate the anatomic sites of the anomalous venous pulmonary connection.<sup>6</sup> Partial anomalous pulmonary venous connection is a congenital anomaly present in 0.4% to 0.7% of postmortem examinations. This rare congenital condition in which one (or more), but not all, of the pulmonary veins fail to connect to the left atrium usually occurs in the right lung. Partial anomalous connection of the right pulmonary vein is 10 times more frequent than that of the left pulmonary vein.<sup>7</sup> There are reports of rare partial anomalous pulmonary venous connection to the left subclavian vein, brachiocephalic vein, azygos vein, portal vein, and coronary sinus.<sup>8</sup> Yabek et al<sup>9</sup> reported a 5-year-old girl with partial anomalous pulmonary venous connection to the azygos vein with intact atria septum, and Jennings and Serwer<sup>10</sup> reported a 13-year-old girl with anomalous connection of the right pulmonary veins to the azygos vein and an intact atria septum. Toyoshima et al<sup>11</sup>



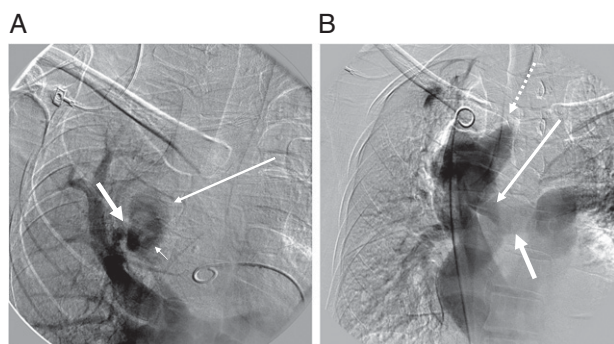


FIGURE 4. Right pulmonary angiography revealed a fistula (A, large arrow) between pulmonary vein and enlarged azygos vein (A, long arrow), with turbulent flow at rest (A, tiny arrow). The pulmonary vein (B, large arrow) in cavography appeared coincidentally with superior cava vein (B, dashed arrow) during Valsalva maneuver. The lower segment of azygos vein was compressed in a shape of an olecranon (B, long arrow) and the upper portion enlarged.

reported one case of partial anomalous pulmonary venous return showing an anomalous right total pulmonary venous returning to the azygos vein.

The pressure in the pulmonary vein is normally higher than in the vena cava. However, in chronic compression of a diffuse mediastinum mass, the pressure difference in the vena cava may increase because of hypertension of the inferior vena cava system, reversible during a Valsalva maneuver, which allows the flow from azygos vein to pulmonary vein through the fistula. It will cause a positive TCD bubble test, as in this case.

Normally, the blood flow from the large antecubital vein to the cerebral arterial circulation is reported to be around 10 to 25 s.<sup>12</sup> Embolism monitoring of TCD cannot reveal embolic signals in normal subjects before this period, which implies that the bubble of agitated saline cannot cross through the pulmonary circulation. The fact that the bubble signal appeared around 23 s after injection of the agitated saline and lasted much longer in this case indicated an abnormal pathway rather than an intracardiac right-to-left pathway. A more common situation, not applicable in this case, is patent oval foramen, causing transport of the bubble solution from the large antecubital vein to cerebral arterial circulation to take < 20 s (around 7-16 s). Another uncommon pathway of venous embolism to the brain is through the fistula between the pulmonary artery and pulmonary vein.<sup>13</sup> Maher et al<sup>14</sup> reported that stroke or transient ischemic attacks occurred in 30% of such patients with pulmonary arteriovenous fistula.

Recently, pulmonary arteriovenous malformations < 2 cm in diameter with afferent arteries > 3 mm in diameter have been documented to cause transient ischemic attacks, strokes, and brain abscesses. Treatment is recommended for all pulmonary arteriovenous malformations with single feeding vessels  $\geq$  3 mm in order to reduce the risk of paradoxical embolization.<sup>15</sup> Embolization therapy had been suggested for this patient with the fistula between azygos vein and pulmonary vein. However, he refused transcatheter embolization or thoracoscopic surgery. Oral anticoag-

ulant drug was administered to prevent the recurrence of stroke.

The lack of pressure measurements between the superior and inferior vena cava, as well as between the vena cava and pulmonary vein, is a limitation in this case. This case thus provides indirect rather than direct evidence to support the pressure reversal between azygos vein and pulmonary vein during the Valsalva maneuver.

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#### REFERENCES

- Gomez M-A, Delhommais A, Presicci PF, Besson M, Roger R, Alison D. Partial thrombosis of an idiopathic azygos vein aneurysm. *Br J Radiol.* 2004;77(916):342-343.
- Puttarajappa C, Dhoble A. Mediastinal lipomatosis as a cause of low voltage complexes on electrocardiogram and widened mediastinum: A case report. *Cases J.* 2008;1(1):171.
- Léna H, Desrues B, Heresbach D, et al. Azygos vein aneurysm: contribution of transesophageal echography. *Ann Thorac Surg.* 1996;61(4):1253-1255.
- Lee SY, Kuo HT, Peng MJ, et al. Azygos vein varix mimicking mediastinal mass in a patient with liver cirrhosis: a case report. *Chest.* 2005;127(2):661-664.
- Saito N, Horigome H, Shiono J, Saida Y. Regression of arteriovenous fistula between the descending aorta and azygos vein after catheterization. *Am J Roentgenol.* 2001;176(2):550-551.
- Muñoz Castellanos L, Kuri Nivón M, Sánchez Vargas CA, Espínola Zavaleta N. Anomalous pulmonary venous connection. *Arch Cardiol Mex.* 2008;78(3):247-254.
- El Bardissi AW, Dearani JA, Suri RM, Danielson GK. Left-sided partial anomalous pulmonary venous connections. *Ann Thorac Surg.* 2008;85(3):1007-1014.
- Ammash NM, Seward JB, Warnes CA, Connolly HM, O'Leary PW, Danielson GK. Partial anomalous pulmonary venous connection: diagnosis by transesophageal echocardiography. *J Am Coll Cardiol.* 1997;29(6):1351-1358.
- Yabek SM, Akl BF, Berman W Jr. Partial anomalous pulmonary venous connection to the azygos vein with intact atrial septum. *Chest.* 1979;76(4):486-487.
- Jennings JG, Serwer GA. Partial anomalous pulmonary venous connection to the azygos vein with intact atrial septum. *Pediatr Cardiol.* 1986;7(2):115-117.
- Toyoshima M, Sato A, Fukumoto Y, et al. Partial anomalous pulmonary venous return showing anomalous venous return to the azygos vein. *Intern Med.* 1992;31(9):1112-1116.
- Droste DW, Reisener M, Kemény V, et al. Contrast transcranial Doppler ultrasound in the detection of right-to-left shunts: reproducibility, comparison of 2 agents, and distribution of microemboli. *Stroke.* 1999;30(5):1014-1018.
- Moussouttas M, Fayad P, Rosenblatt M, et al. Pulmonary arteriovenous malformations: cerebral ischemia and neurologic manifestations. *Neurology.* 2000;55(7):959-964.
- Maher CO, Piepgras DG, Brown RD Jr, Friedman JA, Pollock BE. Cerebrovascular manifestations in 321 cases of hereditary hemorrhagic telangiectasia. *Stroke.* 2001;32(4):877-882.
- Faughnan ME, Palda VA, Garcia-Tsao G, et al. International guidelines for the diagnosis and management of hereditary hemorrhagic telangiectasia. *J Med Genet.* 2009. In press. [DOI:10.1136/jmg.2009.069013].