

“Economy Class” stroke syndrome?

Abstract—The authors report three cases of ischemic stroke in young adults that occurred during or after an airplane flight. Workup was negative for any cause of stroke other than the presence of a patent foramen ovale (PFO). There is an increasing awareness of deep vein thrombosis and pulmonary embolism occurring in relation to long flights. Individuals with a PFO under these circumstances may be vulnerable to stroke from paradoxical embolism. “Economy class” stroke syndrome may be underdiagnosed and is an eminently preventable cause of stroke.

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Y. Isayev, MD; R.K.T. Chan, MBBS, MRCP(UK); and P.M. Pullicino, MD, PhD

An association between air travel and thromboembolism was first recognized in 1988 and was named the “economy class syndrome.”¹ Multiple subsequent reports have confirmed the link between long flights and deep vein thrombosis (DVT) and pulmonary embolism (PE). We are aware of only one report of embolic stroke related to an air flight in a patient with a patent foramen ovale (PFO).² In the last 2 years, we have seen 3 patients younger than 50 years of age in whom ischemic stroke occurred in relation to air travel and all had a PFO.

Case report. *Case 1.* Four hours into a 12-hour flight from Tokyo, a healthy 46-year-old right-handed man developed sudden right visual loss while straining in the bathroom. Neurologic examination showed a right homonymous hemianopia. An MR scan of the brain showed infarction in the territory of the left posterior cerebral artery. An MR angiogram was normal. A transesophageal echocardiogram revealed a PFO with a right-to-left shunt detected on Valsalva maneuver. The results of lower limb venous Doppler performed 7 days after the event were negative. The patient was administered warfarin sodium. Twelve months after the stroke the patient still has a right homonymous hemianopia.

Case 2. An athletic 46-year-old man developed sudden shortness of breath and left-sided weakness as he reached for his luggage in the overhead compartment at the end of a 14-hour flight. He had not gotten up from his seat during the flight. On examination he had a right gaze preference, left visual hemineglect, and a left hemiplegia. He received IV tissue plasminogen activator. A brain MR scan revealed a large infarct involving the territory of the inferior division of the middle cerebral artery. The results of MR angiogram and a conventional cerebral angiogram were normal. A transesophageal echocardiogram revealed a small PFO

with a right-to-left shunt detected during the Valsalva maneuver. A venous Doppler of the low extremities performed 7 days after the stroke was normal. The patient improved greatly with almost complete resolution of his deficits. He continues to be treated with long-term anticoagulation.

Case 3. A healthy 41-year-old white woman developed sudden left-sided hearing loss, transient vertigo, and left-sided facial numbness 12 hours after a flight. She was a passenger on 2 flights of approximately 90 minutes each separated by 6 hours of sitting in a transit lounge. The second flight was in a cramped and poorly pressurized propeller aircraft. On examination she had complete left-sided hearing loss confirmed by an audiogram. She had slight sensory loss to pinprick around her mouth on the left. The rest of the neurologic examination was normal. Cerebral MRI revealed a small acute infarct in the left caudolateral pons in the region of the vestibulocochlear nucleus. Magnetic resonance angiography showed a relevant vascular occlusion. TEE revealed a large PFO. She was administered warfarin but had persisting deafness on the left side.

All patients were healthy, nonsmoking, nonobese individuals with no vascular risk factors and no significant medical history. Results of laboratory workup including protein C, protein S, factor V mutation, anti-thrombin III, lupus anticoagulant, anti-cardiolipin antibody, homocysteine level, antinuclear antibodies, and sedimentation rate were normal in all three patients. The third patient also had normal factors VIII, IX, and XI.

The first two patients were optimally anticoagulated with IV heparin at the time of lower limb venous Doppler study.

Discussion. Paradoxical embolism through a PFO appears the most plausible cause of stroke in our patients. The history and MRI findings were highly suggestive of cerebral embolism, and investigation did not detect any other potential cause for stroke, other than PFO. Two of the three patients performed physical activity likely to produce a Valsalva maneuver just before the onset of stroke symptoms. The failure to demonstrate a DVT does not necessarily diminish the likelihood of paradoxical embolism.³ It

From the Department of Neurology (Drs. Isayev and Chan), State University of New York at Buffalo; and Department of Neurosciences (Dr. Pullicino), New Jersey Medical School, Newark.

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Address correspondence and reprint requests to Dr. Patrick M. Pullicino, Department of Neurology, New Jersey Medical School, Medical Center,

sufficient to implicate paradoxical embolism as the cause of stroke among young patients with cryptogenic stroke because of the high frequency of PFO in this group of patients.⁴ This is particularly true if the intra-atrial defect is large⁵ or if a Valsalva maneuver occurred before or at the onset of the symptoms. Optimal long-term management of patients with PFO-associated stroke is unclear. Antiplatelet therapy, anticoagulation, or repair of septal defect are considered acceptable treatment options.^{4,5} We chose anticoagulation rather than the other options because all our patients are professionals who might be at increased risk for DVT because their frequent business-related air travel, and two of the three patients declined surgical intervention.

Cases of PE and DVT occurring during or after long flights have been reported with increasing frequency.^{1,2,6-9} In 1986, a report observed that over a 3-year period, PE was the second most common cause of sudden death among long-distance air travelers.¹⁰ Two recent prospective studies found that 4.5% and 10% of passengers developed DVT after prolonged flights.^{6,7} In the case of pulmonary embolism, a traveling distance of 5000 km or more was a significant contributing factor.⁹

Individuals who have a PFO and develop DVT are theoretically at risk for stroke due to paradoxical embolism. PFO characteristics such as size and the occurrence of Valsalva maneuver at the time a clot is in the right atrium also are important determinants for stroke. The prevalence of PFO in the general population ranges between 17% and 35%, but is greater among young adults with unexplained (cryptogenic) stroke (54–56%).⁴ Given this high prevalence of PFO and the occurrence of DVT and PE in air travelers, a proportion of air travelers is likely to be at risk for paradoxical embolism. Prolonged sitting in a small, confined space during a flight is probably the most important cause of venous stasis, which predisposes to DVT and PE. Additional cabin-related risk factors for hypercoagulability include dehydration, low humidity, relative hypoxia/low air pressure, and in-flight alcohol consumption. We have called this syndrome “economy class stroke syndrome” to emphasize that cramped seating condition is an important risk factor. However, DVT/PE also has been described in passengers flying in the business or first class cabin.

Little is known about the frequency and risk factors for stroke during or after air travel. The only

prior report mentioned three patients with ischemic stroke that occurred in relation to air travel. Only one of these patients had a PFO and DVT; the other two patients had other potential stroke risk factors.² As air travel increases worldwide, physicians should be aware of the potential association between stroke during or after prolonged air travel and PFO. It may be possible to prevent stroke from paradoxical embolism in passengers with PFO by preventing the development of DVT. The simplest ways are adequate hydration, alcohol avoidance, and frequent, regular exercise of lower extremities, although the effectiveness has yet to be proven.^{1,6-9} Using compression stockings has been effective in preventing asymptomatic DVT.^{6,7} Passengers who are at high risk for developing DVT may require additional measures including aspirin or preventive subcutaneous heparin.⁸ Screening for PFO may be considered among frequent flyers who had prior DVT or have a high risk for DVT. Further research is needed to determine the frequency and risk factor for stroke related to air travel.

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