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Satoshi Kataoka, MD
Department of Neurology, Chugoku Rosai Hospital
1-5-1, Hirotagaya, Kure
Hiroshima 737-0193 (Japan)
Tel. +81 823 72 7171, Fax +81 823 74 0371
E-Mail satoshi@chugokuh.rofuku.go.jp

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Long-Distance Air Travel: A Potential New Risk Factor for Cerebral Sinus Thrombosis?

Levent Güngör, Musa Kazım Onar

Department of Neurology, Faculty of Medicine,
Ondokuz Mayıs University, Kurupelit-Samsun, Turkey

Background

Over the past 10 years cerebral vein and sinus thrombosis has been diagnosed more frequently because of the development of sophisticated magnetic resonance imaging (MRI) techniques. For the occlusion of dural sinuses with a spontaneous thrombus, a precipitating factor such as pregnancy, trauma, malignancy, in-

fection or thrombophilia is necessary. Several thromboembolic events such as deep-vein thrombosis and pulmonary embolism are known to be related to air travel. Here we report 2 male patients with hereditary thrombophilia who developed cerebral sinus thrombosis after long-distance flights.

Case 1

A 46-year-old male patient was admitted to our clinic with a complaint of vision loss for 5 days. Ten days before his complaint started, he had had two 18-hour flights in economy class between Samsun and Havana within a 4-day period. He also suffered moderate neck pain and headaches that began just after landing. During the flight, he had drunk 3 glasses of wine, had no regular exercise, and did not leave his seat except to go to the toilet. He slept for much of the time during both flights.

He had been diagnosed as having portal-vein thrombosis and protein S deficiency two years earlier, and was using warfarin. Before his journey to Cuba, his international normalization ratio (INR) was 2.2, but during the flight he missed 2 dosages. His physical examination showed no pathology, and the only pathological finding on neurological examination was concentric visual field narrowing.

Cranial MRI and MR venography revealed total occlusion of the left jugular vein and recanalized thrombus in the left transverse and sigmoid sinuses (fig. 1). Protein S level was 23% before using warfarin. The INR was 2.1 on admission. The other laboratory investigations, including complete blood count, renal, hepatic and thyroid functions, erythrocyte sedimentation rate, homocysteine, fibrinogen, D-dimer, protein C, antithrombin III, factor V Leiden, and methylenetetrahydrofolate reductase (MTHFR) and prothrombin gene mutations, were normal.

His warfarin dose was increased and the INR was regulated to 3.0–3.5. Two weeks later, the patient was symptom free, and his neurological examination was normal.

Case 2

A 23-year-old male patient was admitted to our clinic with a complaint of headache and sensorial loss. Twenty days earlier he had had a 4-hour flight between Istanbul and London in economy class. After this flight, he had nausea, vomiting and mild ataxia that lasted 3 days. Six days before admission, he had begun to experience severe headaches and loss of sensation in his tongue, the right side of his face and the right arm. He had remained seated during the flight except for short walks to the toilet, and had slept for about 2 h. He was hydrated regularly and drank 2 cups of coffee.

He had been rachitic and had undergone surgery for Meckel diverticulitis as a child. He had no known systemic illness. His physical examination was normal, and the only pathological finding on neurological examination was right-sided papilledema. MRI and MR venography showed acute thrombus in the superior sagittal sinus and both transverse sinuses (fig. 2). Blood count, renal, liver and thyroid functions, and erythrocyte sedimentation rate were normal. There was no evidence of infection. Laboratory tests for coagulation revealed homozygous MTHFR mutation. The same mutation was also found in his mother and sister.

He was treated successfully with anticoagulant therapy. Two weeks later, he was symptom free, and his neurological examination was normal.

These two cases were reported as a poster presentation at the 3rd Turkish National Congress of Cerebrovascular Disease in Antalya, Turkey, June 2006.

Fig. 1. Patient 1. **a** Absence of flow in the left transverse and sigmoid sinuses (arrows) on MR venography. **b** Irregular isointense thrombi in the superior sagittal and left transverse sinuses (arrows) on T₁-weighted MRI after gadolinium injection.

Fig. 2. Patient 2. Hyperintense acute thrombus in the superior sagittal sinus (arrows) on T₁-weighted MRI axial (**a**) and coronary (**b**) sections.

Discussion

The first case of deep-vein thrombosis related to air travel was described in 1954 [1]. The number of travelers who make long-distance flights has increased during the last few years, and there has been a corresponding increase in several other thromboembolic and neurological complications of air travel. Until recently, air travel has not been considered a novel risk factor for cerebral vein and sinus thrombosis. Only Pfausler described 5 cases of cerebral sinus thrombosis related with long-distance flights [2].

Air travel creates a tendency toward thromboembolic events. The exact underlying mechanisms are unclear. Immobilization plays an important role in thrombosis, especially of the venous system of the lower extremities. During the flight, the body takes up less oxygen owing to the lower air pressure [3]. Low cabin humidity, reduced fluid intake and the diuretic effects of alcohol and coffee lead to dehydration [4, 5]. Lengthy immobilization, together with changes in oxygen concentration, air pressure and humidity in the cabin, can lead to hemoconcentration and increased blood viscosity. Healthy subjects can tolerate these changes well. The effects on coagulation of factors such as temperature changes, vibration, noise, acceleration and electro-

magnetic radiation during flights are unclear [6, 7]. Several reports demonstrate a tendency toward thrombosis during air travel. Hypoxia inactivates the fibrinolytic pathways of the endothelial cells. After transatlantic flights, tissue plasminogen activator activity decreases, the level of plasminogen activator inhibitor-1 increases, and activated partial thromboplastin time decreases [5]. D-dimer, factor VII and factor VIII levels also increase during flight [8]. Individuals with factor V Leiden mutation who undergo hormone therapy experience increased thrombin formation during air travel. Prothrombin fragments and the thrombin-antithrombin complex are activated in hypobaric and hypoxic conditions [6].

In the cases of Pfausler [2], several other factors such as dehydration, diarrhea, taking oral contraceptives, and donating plasma activate coagulation during air travel. Our patients also had predisposing genetic abnormalities; one had protein S deficiency, and the other a homozygous MTHFR gene mutation. The common properties of the patients were headaches, mild localizing signs, drinking alcohol and coffee, and flying for longer than 4 h. In addition, the initial symptoms were nonspecific. The patients improved considerably with effective anticoagulant therapy.

Conclusion

On the basis of the cases presented here, we can conclude that medium- and long-distance air travel may be a risk factor for cerebral vein and sinus thrombosis, especially in patients with hereditary thrombophilia. A single dose of low-molecular-weight heparin injected subcutaneously just before a long-distance flight might prevent a thromboembolic event in a patient with thrombophilia.

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Levent Güngör, Ass. Prof.
Ondokuz Mayıs University, Faculty of Medicine
Department of Neurology
TR-55139 Kurupelit-Samsun (Turkey)
Tel. +90 362 312 1919-3715, Fax +90 362 457 6041
E-Mail ligunor@omu.edu.tr

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Painless Aortic Dissection with Unusual Extension into Intracranial Internal Carotid Arteries

Iyadurai Stanley^a, Vijay K. Sharma^{b,c}, Georgios Tsvigoulis^b,
Annabelle Y. Lao^b, Andrei V. Alexandrov^b

^aDepartment of Neurology and ^bNeurosonology and Stroke Research Program, Barrow Neurological Institute, Phoenix, Ariz., USA; ^cDivision of Neurology, National University Hospital, Singapore, Singapore

A 68-year-old Caucasian woman fell at home and 2 h later she was seen for sudden inability to move her left side. She admitted mild suffocating sensation and light-headedness prior to the fall. She denied loss of consciousness and chest pain. She was taking blood-pressure-lowering medications and had no other identifiable vascular risk factors.

While in the emergency room, she became lethargic and slow in verbal communication. The blood pressure was 100/50 mm Hg in the left arm with a regular left radial pulse at 101 beats per minute. All right upper extremity pulses were barely palpable. Both lower extremity arterial pulses were palpable and equal. She was afebrile and had a respiratory rate of 18 per minute. Abnormal neurological findings included left facial droop, visual neglect and left hemiparesis (power MRC grade 0 and 3 in the upper and lower extremities, respectively; NIHSS 10 points). No history or signs of collagen or connective tissue disorders were found.

Chest roentgenography revealed a widened mediastinum, while electrocardiogram and cardiac enzymes were within normal limits. Brain CT revealed multiple and bilateral cortical watershed hypodensities with angiography showing the type A ascending aortic dissection with extension into both carotids, including the distal internal carotid artery (ICA) (fig. 1).

Her condition deteriorated rapidly with decreasing level of consciousness, hypotension and respiratory distress requiring intubation and ventilation. No surgical interventions were performed owing to the wide extent of arterial dissections and evolving brain damage. She died at 5 h from the stroke symptom onset.

Our patient presented with a severe aortic dissection that extended widely with a complete occlusion of the right carotid system and extension into the intracranial left ICA. To our knowledge, such a wide extension has not been described previously.

An aortic dissection may extend into major branches for variable distances. It carries a high mortality rate and is accompanied by cerebral infarction in approximately 6% of cases [1, 2]. Right common carotid artery occlusion is most frequently seen in 85% of stroke cases. The reported cases had identifiable risk factors with the dissection process stopping at the ICA bulb [2]. In contrast, our patient did not have any of these predisposing conditions and the dissection extended well beyond proximal ICAs.

Our patient presented with painless aortic dissection in contrast to the typical sudden and severe chest, back or abdominal pain with a sharp, ripping or tearing character [2]. Painless aortic dissection seen in 5–15% of cases carries higher mortality [3]. Hypertension at the time of presentation is common [2]. Our patient presented with a low blood pressure after a syncopal episode, reported at presentation in 12% of cases [3].

The diagnosis of aortic dissection depends largely on a high index of clinical suspicion. Widened mediastinum on chest X-ray as noted in our patient lacks specificity and is seen only in about 50% of cases. Conventional, CT or MR angiography and transesophageal echocardiography are useful in the diagnosis of aortic dissection, depending on their availability [2].

Patients presenting with acute ischemic stroke within 3 h of symptom onset are considered for systemic thrombolysis and can be inadvertently treated with intravenous tissue plasminogen activator [4]. Because aortic rupture with dissection is the principal mechanism for early death, the use of thrombolysis is clearly contraindicated. CT angiography and ultrasound screening can aid timely diagnosis of aortic dissection and further management [5]. Stroke at presentation is not considered a contraindication for surgical intervention [1] for type A aortic dissection, irrespective of the extension of the dissecting process into the branches. However, an evolving brain hypodensity on CT scan has not been clearly addressed in this setting.