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REVIEW

Economy Class Stroke Syndrome: Case Report and Review of the Literature

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Objectives. *Venous thromboembolism associated with travelling, or economy class syndrome, is increasingly recognised as a sequence of long haul flights and so paradoxical cerebral embolism through a patent foramen ovale.*
Materials and methods. *We present a new case of economy class stroke syndrome and review of the literature using MEDLINE search.*
Results. *Literature review identified 12 additional cases. In most of them, stroke occurred in close approximation with landing of the aircraft following a long-haul flight. Venous thromboembolism was present in 58%, while a patent foramen ovale was diagnosed with contrast echocardiography in all but one case. Our case presented with severe left hemispheric stroke, and significant delay, two days after a long-haul flight.*
Conclusions. *The small number of reported cases indicates either the rarity of this entity or unawareness of its existence. The true incidence of this condition remains unknown. However, because of treatment implications such as the need to treat venous thromboembolism or close the patent foramen ovale, clinicians should be aware of this entity.*

Key Words: Cerebrovascular accident; Foramen ovale; Patent; Deep vein thrombosis; Travel.

Introduction

The widespread use of contrast echocardiography during the last decade has resulted into an increased frequency of a patent foramen ovale (PFO) being diagnosed in both 'normal' subjects and patients with cryptogenic ischaemic stroke, considering therefore paradoxical embolism as the cause of the latter.

Venous thromboembolism (VTE, defined as deep vein thrombosis (DVT)—and/or pulmonary embolism (PE)) associated with travelling is reported with increasing frequency.[1–4] Scurr *et al.* reported a 10% incidence of asymptomatic DVT after long-haul flights using ultrasound,[1] however, it has been shown by other studies that symptomatic DVT occurs less frequently, with passengers being at a four-fold risk during the 4-week period following the air travel.

By contrast, there are only a handful of reports of paradoxical cerebral embolism through a PFO, during a long haul flight, the first case being described by Beighton in 1968.[5] We describe here a new case of economy class stroke syndrome and review the relevant literature.

Materials and Methods

Case report

A fit 49-year-old man was found collapsed on his bedroom floor with dense hemiplegia and aphasia due to a massive left hemispheric stroke. Before the stroke, he was capable of vigorous exercise including swimming and jogging. Two days earlier, he had travelled by airplane for a total duration of 19 h, from Anchorage (state of Alaska), USA to London, UK, including one stopover to Vancouver, Canada. His trip from Anchorage to Vancouver was economy class while the final arm of his travel was business class. His recent medical history included an arthroscopic repair of his left lateral meniscus three weeks earlier. CT brain scan performed on admission revealed considerable left

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middle cerebral artery territory hypodensity. MRI/MRA of the brain and neck vessels showed an extensive infarct involving the left striatum and extending through the internal and external capsules to the frontal, anterior parietal and temporal cortex (Fig. 1) and ruled out the presence of dissection of the left internal carotid artery, which was also confirmed with a carotid Duplex.

Resting ECG was normal. Duplex ultrasound scan of his leg veins was performed 4 days following the event and did not show evidence of deep venous thrombosis. Transoesophageal contrast echocardiogram showed an 18 mm PFO with right to left shunt. A thrombophilia screen, which included protein C, protein S, factor V Leiden, prothrombin G20210A mutation and antiphospholipid antibodies was negative. The patient was treated conservatively and made some symptomatic improvement. Fourteen months following the stroke, he underwent surgical closure of the PFO.

A MEDLINE/PUBMED search was performed in September 2003 (keyword: economy class stroke) to identify all similar cases in the medical literature, followed by manual search of the references of the relevant articles.

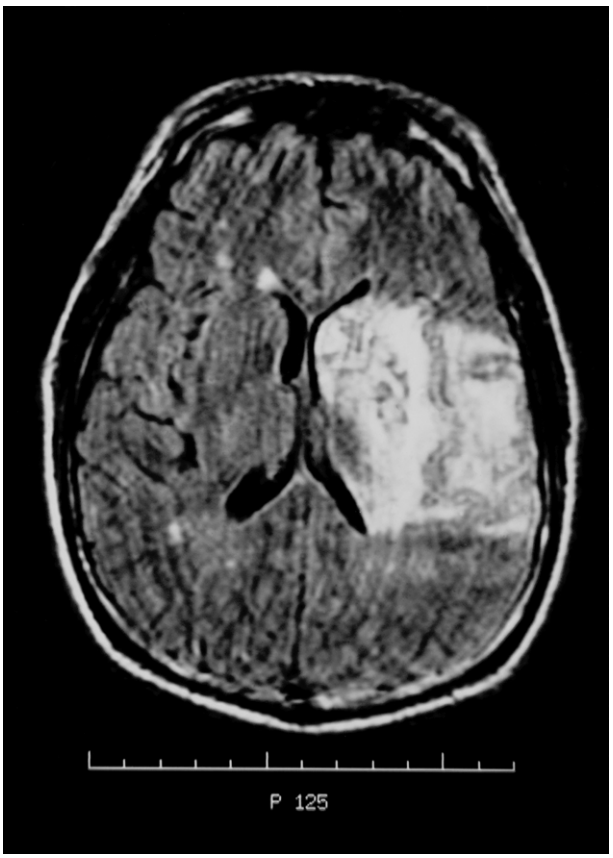

Fig. 1. MRI/MRA brain scan demonstrated an extensive infarct, in the distribution of the left middle cerebral artery.

Results

Twelve cases of flight-associated paradoxical brain embolism were identified from the literature review.[5–9] Table 1 summarises patient's clinical characteristics and travel patterns. Most patients were middle-aged (40–65 years old, mean age 50.8 years) and the female to male ratio was 2:1. Data regarding flight duration and/or distance was available in 10 of the 12 cases. With the exception of case 5, which followed two flights of short duration (approximately 90 min each) separated by 6 h of sitting in a transit lounge, in all remaining cases flight was more than 10 h in duration or 9,000 Km in distance.

Case 1 was reported in an Australian passenger in the 1960s, flying to London Airport, probably from Australia. Most strokes occurred immediately, prior to or within 12 h of arrival. Valsalva manoeuvre was reported in three cases. Although this condition has been described as 'economy class stroke syndrome', information on the class the patient was travelling on, was available only in one publication.[6]

Evaluation, management and prognosis review is shown in Table 2. There was evidence of VTE in seven (58%) cases; this was mostly pulmonary embolism. The possibility of thrombophilia was only examined in seven cases, one of which was positive. Brain imaging revealed middle cerebral artery infarction in seven cases (64%). Posterior circulation infarcts were less frequent, while multiple infarctions were seen only in one case. PFO was reportedly diagnosed using transoesophageal contrast echocardiography in all but one case. This was the case in the 1960s and it is possible that PFO was an autopsy finding.

Treatment was medical (anticoagulation) in all eight cases this information was available; in one patient a vena cava filter was inserted, while no patient had surgical or interventional closure of the PFO. Prognosis was variable, being good in four cases and fatal in three cases, while some five patients had persistent neurological deficits.

Discussion

The terms economy class syndrome and economy class stroke that are now established in the world literature to denote the association of thromboembolism and travel in the cramped conditions of the economy class. However, this condition may affect the

Table 1. Clinical characteristics and travel patterns in 12 reported cases of economy class stroke syndrome

Case no.	Author	Age	Gender	Flight duration or distance	Valsalva manoeuvre reported	Period of occurrence
1	Beighton *et al.*[5]	48	F	Probably long-haul flight	No	Just after landing
2	Masson *et al.*[6]	62	F	10 h	No	Just after landing
3	Isayev *et al.*[7]	46	M	12 h	Yes	4 h into a 12 h flight
4	Isayev *et al.*[7]	46	M	14 h	Yes	End of flight
5	Isayev *et al.*[7]	41	F	Two flights of approximately 90 min each, 6 h stopover	No	12 h after flight
6	Foerch *et al.*[8]	21	NR	>9,000 Km	Yes	Towards the end of flight
7	Foerch *et al.*[8]	63	NR	>9,000 Km	No	Towards the end of flight
8	Foerch *et al.*[8]	64	NR	>9,000 Km	No	Towards the end of flight
9	Lapostolle *et al.*[9]	53	F	9,080 Km, 10.5 h	No	On landing
10	Lapostolle *et al.*[9]	67	F	9,170 Km, 11 hrs	No	Before landing
11	Lapostolle *et al.*[9]	51	F	9,450 Km, 11.25 h	No	Before landing
12	Lapostolle *et al.*[9]	56	M	5,840 Km, 8 h	No	3 h before landing

NR, not reported.

crew and business class travellers alike.[10] Thus, the term economy class is a misnomer and it may be more accurate to call this condition thromboembolism/stroke associated with prolonged travel.

Paradoxical embolism through a PFO accounts for some 54% of cases of cryptogenic stroke in adults younger than 55 years of age.[11] A right to left atrial shunt is a prerequisite of paradoxical embolism. This could happen as a potential consequence of pulmonary embolism (which was documented on four of the literature review cases) or in cor pulmonare. However, it is as likely that brief physiological changes such as the Valsalva manoeuvre, commonly used by passengers to compensate for the pressure changes associated with aircraft descent might have a role to play.[12] It could had increased the right atrium pressure and resulted in a reversal of the atrial pressure gradient in three out of 12 patients of this review. Although less effective, coughing, deep inspiration and expiration pressures of 20, 40 and 60 mmHg are also known to reverse this gradient.[13] Nevertheless, even transient increase in venous pressure, could not only reverse the atrial pressure gradient, but also dislodge a proximal free-floating thrombus.

Most strokes identified by this review occurred in close proximity to landing after long-haul flights; obviously, the chance of having DVT is increased during long haul flights and this could explain this coexistence, but other reasons might also exist. It is also possible, that cases with delayed presentation have been overlooked, although a careful history could reveal a recent long-haul flight; therefore, the true incidence of this apparently rare clinical event might be underestimated.

The absence of DVT on ultrasound in cases of PE is not unusual. In review of the relevant literature between 1983 and 1997, it was shown that DVT was present only in 36–45% of patients with proven pulmonary embolism.[14] In the 13 reported cases, including ours, venous thrombosis was present only in four cases (31%). It is possible that in the presence of a PFO, small emboli, not sufficiently large to produce symptomatic PE, could instead result to a stroke. This is supported by the finding that in patients with PE, the mean pulmonary vascular obstruction is significantly lower in patients with normal venography than in patients with detectable DVT (38% vs. 48%, $p = 0.007$).[15]

Brain imaging demonstrated features of middle cerebral artery territory infarction in seven out of 11 cases of this review. This is a rather typical pattern of embolic infarcts, while in the three cases of posterior circulation infarction this was probably the result of the embolus passing through a posterior cerebral artery originating directly from the internal carotid artery (foetal type).

In view of the very low incidence of stroke during and immediately following intercontinental flights, it is hard to establish a 'cause and effect' association between air travelling and paradoxical cerebral embolism, which could justify the liberal use of the term economy class stroke syndrome. However, since VTE often becomes apparent several days following the flight, the 13 cases reported so far may be an underestimate of the true incidence of this condition. Epidemiological studies, which could establish the true magnitude of this problem, should be performed preferably focusing in young and middle aged previously healthy patients who sustained a stroke with no obvious predisposing factors.

Certainly, a considerable proportion of patients at high risk of DVT should be at risk of developing

Table 2. Evaluation, management and prognosis of the 12 reported cases of economy class stroke syndrome

Case no.	Author	DVT	PE	Thrombophilia abnormality	CT/MRI brain scan	Thromboembolism management	Prognosis
1	Beighton *et al.*[5]	Yes	No	Unknown	N/A	NR	Fatal
2	Masson *et al.*[6]	Yes	No	No	Multiple cerebral cortical/subcortical infarct	Anticoagulation	Good
3	Isayev *et al.*[7]	No	No	No	Posterior cerebral artery territory infarct	Warfarin	Persistent homonymous hemianopia
4	Isayev *et al.*[7]	No	No	No	Middle cerebral artery territory infarct	Anticoagulants	Good
5	Isayev *et al.*[7]	Unknown	No	No	Caudolateral pons	Anticoagulation	Persistent deafness (left side)
6	Foerch *et al.*[8]	No	No	No	Middle cerebral artery territory infarct	NR	No or minimal residual deficits
7	Foerch *et al.*[8]	No	No	No	Posterior thalamus infarct	NR	No or minimal residual deficits
8	Foerch *et al.*[8]	No	Yes	Yes	Multiple cerebral infarctions	NR	Fatal
9	Lapostolle *et al.*[9]	Yes	Yes	Unknown	Sylvian fissure infarct	Heparin/cava filter	Persistent hemiparesis
10	Lapostolle *et al.*[9]	Unknown	Yes	Unknown	Sylvian fissure infarct	Heparin	Persistent aphasia
11	Lapostolle *et al.*[9]	Unknown	Yes	Unknown	Sylvian fissure infarct	LMWH	Fatal
12	Lapostolle *et al.*[9]	Unknown	Yes	Unknown	Sylvian fissure infarct	LMWH	Persistent hemiplegia and aphasia

DVT, deep vein thrombosis; PE, pulmonary embolism; NR, not reported.

paradoxical cerebral embolism, given the high prevalence of PFO in the general population (~20–30%); the presence of a right to left intra-cardiac shunt, a known prerequisite of paradox embolism,[16] or the size of the PFO could be such risk factors.[17] Therefore, clinicians should be aware of this entity, while prevention should be according to established guidelines and passenger groups at risk of DVT should be targeted.[18] Adequate hydration, alcohol avoidance, exercise of lower extremities and use of compression stockings, aspirin or low-molecular weight heparin has been suggested.[8]

The appropriate treatment modality (surgical or percutaneous device closure, medical therapy with anticoagulants or antiplatelet agents) remains a matter of debate.[19] PFO is very common in the general population and stroke recurrence rate using aspirin is low; this is the reason why an appropriately powered study would include thousands of patients. The duration of anticoagulation required is itself a problem. There is no data to guide us, but we suggest since long-haul flight is a temporary risk factor, patients should be anticoagulated for at least 3–6 months to prevent recurrent VTE.[20,21]

Experts do not believe that it is necessary to close a PFO unless the patient has a contraindication to medical therapy or has a recurrent event on medical therapy.[22,23]

In conclusion, PFO is very common in the general population and so temporary right to left shunts, therefore it is really the frequency of flight induced DVT which determines the likelihood of the economy class stroke syndrome. The overall incidence of flight induced DVT is very small, but some[1] have reported a significantly higher incidence than others.[24] There is still need for more prospective epidemiological studies that will increase our understanding of this unusual and probably underdiagnosed condition.

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