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CASE REPORT

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Ischaemic stroke, factor V Leiden heterozygosity and left atrial thrombosis in sinus rhythm: a case report

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Abstract We describe a 63-year-old man in sinus rhythm (SR) with an ischaemic stroke involving basal ganglia region on the right side. The patient was known to be heterozygous for factor V Leiden (FVL) mutation. On diagnostic work-up, no arterial sources of embolism were found. Transoesophageal echocardiography evidenced a left atrial (LA) thrombosis without relevant cardiopathies. LA thrombosis is generally associated to atrial fibrillation, atrial enlargement, mitral valve stenosis and left ventricular dysfunction, whereas mitral regurgitation is considered protective. To our knowledge, this is the first report of cardioembolic stroke related to a LA thrombosis in a patient in SR without risk factors for thrombus formation except for FVL heterozygosity.

Key words Cardioembolic stroke • Factor V Leiden • Left atrial thrombosis

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Introduction

Left atrial (LA) thrombosis is uncommon in patients with sinus rhythm (SR) and is associated to other cardiopathies [1]. Mitral stenosis and left ventricular dysfunction are risk factors for LA thrombosis [1], while mitral regurgitation is considered protective [2].

Here we describe a stroke patient in SR with a LA thrombus and factor V Leiden (FVL) mutation heterozygosity.

Case report

A 63-year-old patient was referred to our emergency department in January 2004 due to a sudden motor deficit involving his left limbs. The patient reported a history of rare complex partial seizures from adolescent age well controlled by carbamazepine 400 mg t.i.d. and levetiracetam 500 mg t.i.d. A previous brain MR, performed because of his epilepsy in 2002, had highlighted multiple chronic lacunar infarctions. Given the lack of major vascular risk factors (namely diabetes and hypertension), the patient had been advised to undergo a second-level coagulation work-up (assessment of protein C, protein S and antithrombin III plasma levels, detection of lupus anticoagulant, anticardiolipin antibodies and thrombophilic gene polymorphisms) and was found to be heterozygous for FVL mutation. No case of arterial or vein thrombosis was reported in his family. At admission to our ward a moderate facio-brachio-crural left hemiparesis was evident on neurologic examination. Concerning vascular risk profile, only moderate hypercholesterolaemia was present (total cholesterol 245 mg/dl). A brain MR performed after 24 h highlighted an ischaemic area involving the posterior region of basal ganglia on the right side (Fig. 1). Intracranial MR angiography and extracranial duplex ultrasonography were unremarkable, as well as routine laboratory investigations, ECG and

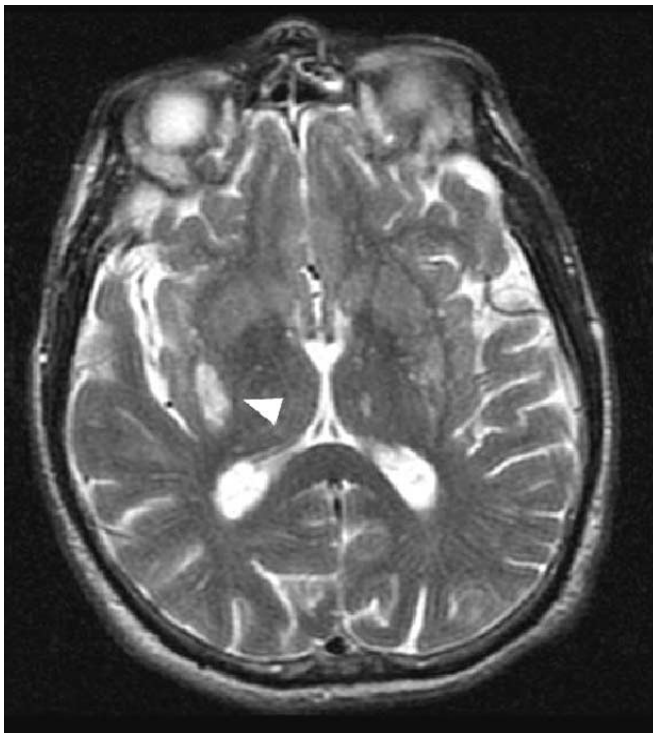

Fig. 1 Magnetic resonance T2-weighted axial image showing an ischaemic area in the posterior region of right basal ganglia (*white arrowhead*)

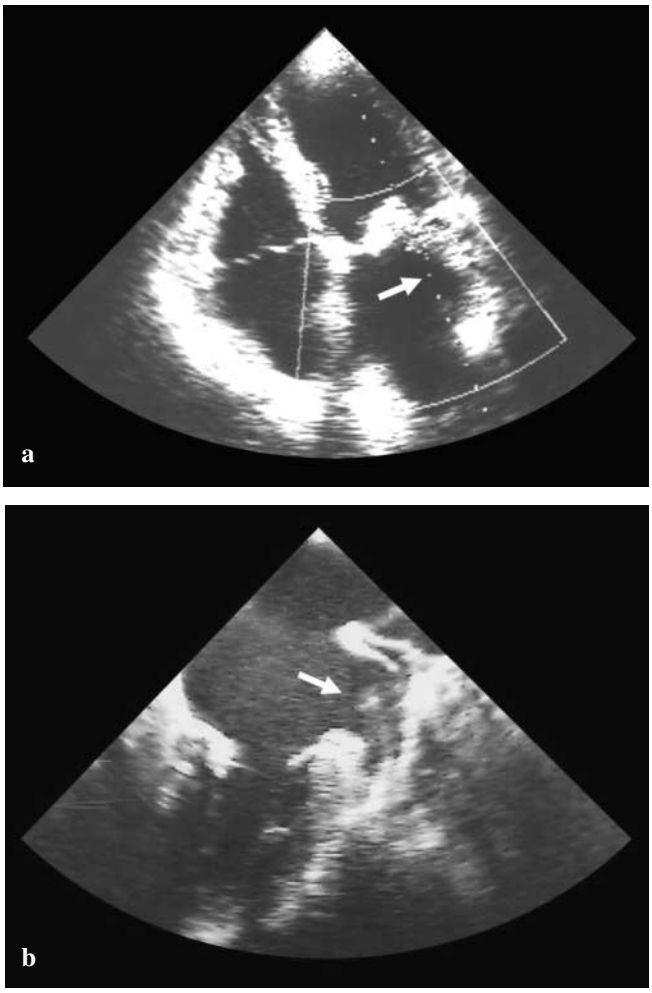

Fig. 2a Transthoracic echocardiography view evidencing a moderate regurgitation in left atrium (*white arrow*). **b** Transoesophageal echocardiography view highlighting a thrombus in the left atrium (*white arrow*)

chest radiography. Serum homocyst(e)ine levels were normal, too. Lupus anticoagulant, anti-phospholipid, antinuclear, anti-ENA and anti-dsDNA antibodies were absent. To rule out paroxysmal atrial fibrillation (AF), three Holter ECG recordings were performed without evidence of anomalies. Transthoracic echocardiography (TTE) evidenced a mild mitral valve stenosis (2D area 2.0 cm^2) on rheumatic basis associated to moderate regurgitation (2+/4) (Fig. 2a). The E/A ratio was normal and the ejection fraction was 72%. Transoesophageal echocardiography (TEE) showed a slight left atrium enlargement (diameter 50 mm). LA appendage was also enlarged (2D area 7.97 cm^2) with a mural thrombus but without spontaneous echo contrast (Fig. 2b). Peak outflow and inflow velocities were normal (respectively 59 and 42 cm/s). Anticoagulant therapy with sodium warfarin was started. At discharge from our ward two weeks later the patient was almost asymptomatic. On a second TEE performed after three months atrial thrombus was no longer evident. At the last follow-up visit in January 2005, the patient was still in SR and did not report any new neurologic episodes.

Discussion

LA thrombosis is infrequent in patients in SR and is usually concomitant with other pathologic conditions – namely moderate mitral stenosis, previous mitral valve surgery, severe aortic regurgitation, left ventricular dysfunction, moderate or severe LA enlargement, and previous history of AF [1]. LA thrombi have been reported in 1% of SR patients with a recent neurologic deficit [3]. Mitral valve regurgitation has been found to be protective against LA thrombus formation also in the presence of moderate mitral valve stenosis [2], presumably because it determines a jet effect in the left atrium [4, 5]. In the present report we described a patient in SR suffering from an ischaemic stroke at the level of posterior putamen. Because of its location and size (>15 mm in diameter), an embolic pathogenic mechanism was probable [6]. Whereas cervical and precerebral arteries were unremarkable on MR and ultrasonographic studies, TEE highlighted a LA thrombosis. Interestingly, the patient – heterozygous for FVL mutation – did not have any of the "high-risk" features for LA thrombosis. In fact, the patient was persistently in SR, LA was modestly enlarged and mitral valve stenosis was only of mild degree. On the contrary, a presumably "protective" moderate mitral valve regurgitation was detected on

echocardiography. Moreover, the local blood stasis related to the LA appendage area was largely counteracted by the normal outflow and inflow velocities. In this view, in the present case FVL may be very relevant to LA thrombus formation in spite of the protective actions of valve regurgitation and appendage blood flow. Definitive data on the presumptive role of inherited thrombophilic conditions and arterial thrombosis are still lacking but a link with ischaemic strokes in patients with atrial septal abnormalities has been hypothesised [7, 8]. As atrial pressures are more similar to the deep venous than the arterial circulation and thrombus formation is usually observed in low shear tracts (in particular the semilunar valve in deep veins and the LA appendage), there seems to be a likely role for FVL in promoting LA thrombosis. Indeed, a relationship between LA thrombosis and a circulating prothrombotic molecule – homocysteine – has been recently reported in a stroke population with nonvalvular AF [9] and in an anecdotal case with SR [10]. An alternative explanation for LA thrombosis in our low-risk patient could be the occurrence of brief asymptomatic episodes of AF. Nevertheless, at last follow-up visit the patient was still in SR and did not complain of subjective symptoms possibly related to dysrhythmias. Therefore, LA thrombosis (and subsequent cerebral embolisation) may be promoted by high-risk features for deep vein thrombosis (such as FVL heterozygosity) also in patients in SR without relevant cardiopathies or with only slight functional abnormalities.

As regards our patient's earlier asymptomatic lacunar infarctions, no precise cause was identified. Diabetes, hypertension and cigarette smoking were not reported in his previous history and a putative role for FVL heterozygosity in favouring silent ischaemic strokes is only hypothetical.

In conclusion, the present case points out the importance of TEE in stroke evaluation of elderly patients when certain embolic sources are not evident. Moreover, the concomitance of FVL heterozygosity and LA thrombosis may suggest a promoting role for deep venous thrombosis risk factors in LA thrombosis both in SR and in AF stroke patients.

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