**Ischaemic stroke with intact atrial septum – exclude arteriovenous malformations**

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Abstract A 44-year-old woman was referred to our centre for interventional cardiac catheterisation. The diagnostic work-up after a preceding ischaemic stroke led to the assumption of a patent foramen ovale due to a positive bubble study. Before the planned percutaneous closure of the patent foramen ovale, we performed a second bubble study, which showed an intact atrial septum. However, after two to three heart cycles bubbles could be detected in the left atrium, assuming a right-to-left shunt of an extracardiac origin most likely in the lung. We therefore performed cardiac catheterisation, yielding a pulmonary arteriovenous malformation in the lower lobe of the right lung. This was successfully closed interventionally by placing a Cook coil, as well as several plugs into the malformation and feeding vessels.

Discussion This case report shows that in a patient with ischaemic stroke, intact interatrial septum and positive bubble test for a right-to-left shunt, the underlying disease could be a pulmonary arteriovenous malformation. Retrospectively, the pulmonary arteriovenous malformation is the most probable cause for the ischaemic cerebral incidents in our patient.
The combination of epistaxis, iron deficiency, anaemia, and pulmonary arteriovenous malformation led to the diagnosis of hereditary haemorrhagic telangiectasia, validated by the mutation in the endoglin gene – hereditary haemorrhagic telangiectasia type 1.

Catheter-interventional treatment of pulmonary arteriovenous malformations has proven to be safe and effective\(^2\)–\(^5\) and is recommended for all adults with pulmonary arteriovenous malformations and children with symptomatic pulmonary arteriovenous malformations.\(^6\)

Hereditary haemorrhagic telangiectasia is a vascular disorder due to gene mutations with autosomal-dominant inheritance. So far, mutations in the endoglin gene and activin receptor-like kinase gene have been discovered, resulting in hereditary haemorrhagic telangiectasia type 1 and 2 with slightly differing phenotypes.\(^7\) Moreover, hereditary haemorrhagic telangiectasia in association with juvenile polyposis is linked to the mutation of Smad4. Further genes are under investigation, probably resulting in more subtypes.\(^7\) Hereditary haemorrhagic telangiectasia is being diagnosed clinically via the Curacao Criteria where four criteria – epistaxis, telangiectasia, visceral lesions, and positive family history for hereditary haemorrhagic telangiectasia – are being taken into consideration; three criteria make the diagnosis definite, two possible, and one unlikely.\(^8\) If the clinical diagnosis of hereditary haemorrhagic telangiectasia is confirmed, then genetic testing is recommended to identify the causative mutation and help establish the diagnosis in other – especially asymptomatic – family members.\(^6\)

Owing to the fact that there is a strong association between pulmonary arteriovenous malformations and
hereditary haemorrhagic telangiectasia, the detection of the former should always lead to a search for the diagnosis of the latter.9

Through molecular analysis, a mutation in the endoglin gene was detected in our patient, thus placing her in the subtype hereditary haemorrhagic telangiectasia type 1. Studies have shown that endoglin mutation is highly associated with pulmonary arteriovenous malformations, as well as with cerebral arteriovenous malformations.7 Current international guidelines for hereditary haemorrhagic telangiectasia recommend routine screening for pulmonary arteriovenous malformations in all patients with suspected hereditary haemorrhagic telangiectasia,6 as they bear the risk of causing severe neurological problems such as ischaemic stroke or brain abscess.2 Therefore, contrast echocardiography should be performed to unveil these vascular abnormalities and refer the patient to the recommended management, which is embolotherapy.9 It has been shown that even small pulmonary arteriovenous malformations can be the cause for ischaemic stroke.10 This makes screening for pulmonary arteriovenous malformations and closure even more important. In addition, a considerable number of patients with hereditary haemorrhagic telangiectasia and pulmonary arteriovenous malformations are undiagnosed at the time of the ischaemic stroke as was the case in our patient. This emphasises that the event of an ischaemic attack/stroke in a young adult should give rise to a diagnostic work-up covering congenital malformations of the heart, for example patent foramen ovale, acquired cardiac lesions, haematologic abnormalities, as well as vascular lesions such as pulmonary arteriovenous malformations – highly suspicious for hereditary haemorrhagic telangiectasia.

References