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Pulmonary arteriovenous malformations: a radiological and clinical investigation of 136 patients with long-term follow-up

P.E. Andersen [a,b,*], P.M. Tørring [c], S. Duvnjak [a,b], O. Gerke [d,e], H. Nissen [f], A.D. Kjeldsen [b,g]

[a] Department of Radiology, Odense University Hospital, Denmark
[b] Department of Clinical Research, University of Southern, Denmark
[c] Department of Clinical Genetics, Odense University Hospital, Denmark
[d] Department of Nuclear Medicine, Odense University Hospital, Denmark
[e] Department of Biostatistics, University of Southern, Denmark
[f] Department of Cardiology, Odense University Hospital, Denmark
[g] Department of Otorhinolaryngology Head and Neck Surgery, Odense University Hospital, Denmark

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AIM: To assess the clinical outcome of patients with and without hereditary haemorrhagic telangiectasia (HHT) after embolisation of pulmonary arteriovenous malformations (PAVM) from a single national centre.

MATERIALS AND METHODS: The present register-based observational study including all patients with PAVM treated with embolisation at a reference centre for HHT and PAVM was undertaken over a 20-year period. Demographic data, HHT genotyping, clinical presentation, and outcome were registered. Patients with HHT were compared to the patients without HHT. Clinical examination, contrast-enhanced echocardiography, and computed tomography (CT) were used to assess the clinical outcome at follow-up.

RESULTS: One hundred and thirty-six patients with 339 PAVM underwent embolisation during the study period: 22 did not have HHT; 62% had HHT1, 10% had HHT2, 4% had JP-HHT, 8% had clinical HHT without identified genetic mutations. Solitary PAVM were more common among patients without HHT than with HHT. Mean follow-up after the first embolisation was 58 months. Mean age at first embolisation was 46.5 years, and at last follow-up 51.8 years. The clinical success without shunt at follow-up was 87%. The 30-day mortality related to the embolisation was 0%. Twenty patients died during follow-up (mean age 69 years). Most patients could be treated during one session, but many will need a long follow-up with repeated clinical examinations and embolisation.

CONCLUSION: The majority of patients referred for embolisation of PAVM had HHT. Multiple PAVM is associated with HHT. Patients with PAVM should be screened for HHT and patients with HHT for PAVM. Embolisation is a safe procedure with high clinical success.

* Guarantor and correspondent: P. E. Andersen, Department of Radiology, Odense University Hospital/University of Southern Denmark, J.B. Winsløwsvej 4, DK-5000 Odense C, Denmark. Tel. +45 65412188; mob.: +45 21207031; fax +45 65907244.
E-mail address: p.e.andersen@rsyd.dk (P.E. Andersen).

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Introduction

Pulmonary arteriovenous malformations (PAVM) are anastomotic shunts between the pulmonary arteries and veins causing right-to-left shunts. Thus, PAVM may cause paradoxical systemic embolisation to the brain (inducing thrombosis or brain abscess), decreased oxygenation of the blood, or may rarely rupture. Generally, there is an indication to treat these malformations with embolisation to prevent complications.[1–10] PAVM are classified as simple, complex, or rarely, diffuse.[11,12] Simple PAVM have one supplying artery, whereas complex PAVM have more supplying arteries. PAVM may occur sporadically or in association with hereditary haemorrhagic telangiectasia (HHT).[1,13–16] About 90% of patients with PAVM have underlying HHT[13,17]: however, PAVM can occur in a variety of acquired medical conditions, such as hepatic cirrhosis, chest trauma, actinomycosis or following cardiopulmonary surgery in children. The remainder of PAVM are believed to be idiopathic and tend to be solitary.[18]

HHT is an autosomal dominant inherited vascular disease with a prevalence of about 15.5/100,000.[19] HHT patients may develop mucocutaneous telangiectatic lesions and visceral arteriovenous malformation. Three disease-causing genes have been identified: *ENG* (MIM 131195) causing HHT1, *ACVRL-1* (MIM 601284) causing HHT2, and *SMAD-4* (MIM 600993), which causes the rare JP-HHT syndrome (juvenile polyposis syndrome in combination with HHT).[29] Approximately 30% of adult patients with HHT will have PAVM that needs treatment, and some will have AVM in the brain, in the liver, or in the bowel.[5,21–23]

The aim of the present study was to investigate the clinical outcome after embolisation of PAVM with long-term follow-up of an unselected consecutive patient cohort from a single national centre. Further aims were to provide demographical, epidemiological, clinical, and radiological characterisation of patients with PAVM; to describe the phenotypic differences between PAVM patients with and without HHT; and to disclose the clinical outcome at long-term follow-up with comparison of HHT genotypes and non-HHT patients.

Materials and methods

Study design

The present study was a single centre retrospective register-based observational study,[24] which included all consecutive patients with the intention to treat PAVM with embolisation during the period 22 October 1996 to 31 December 2016. Patients were enrolled prospectively in the study, and a cohort study identifying these patients was extracted from medical and radiological records. There were no exclusion criteria. Patients' age and gender were recorded. Type, location and number of PAVM, treatment sessions, HHT genotyping, clinical data, contrast-enhanced echocardiography (CE), and radiological examinations (chest radiography, computed tomography [CT] and pulmonary angiography) have been recorded.

Odense University Hospital is the Danish reference centre for HHT diagnostics and PAVM treatments, and almost all Danish patients with diagnosed HHT and/or PAVM are referred to this centre for clinical diagnosis, genetic examination, and management of associated vascular malformations.

Clinical evaluation

The clinical examination included evaluation of telangiectatic lesions, family history, medical history regarding epistaxis, gastrointestinal bleeding, and neurological symptoms. The diagnosis of HHT was based on the clinical Curacao criteria, and/or by the presence of a pathogenic variant in one of the known HHT genes.[25] HHT genotyping was performed in HHT-suspected patients, as described previously.[20,26]

CE was performed as described earlier.[17,27–30] In an apical four-chamber view, the appearance of microbubbles after 6–8 heart cycles into the left atrium was recorded and graded on an arbitrary scale from 1–4, with grade 1 being few bubbles <10, grade 2 moderate amounts of bubbles, grade 3 large amounts of bubbles but less than on the right side, and grade 4 similar opacification of right and left ventricle.

Interventional procedures

Embolisation was performed by two radiologists (PEA and SD) both with >15 years of experience in interventional radiology and both with the European Qualification in Interventional Radiology (EBIR). Embolisation was performed as described previously.[6,8,15,31] Antibiotics were given only in selected cases in high-risk patients and heparin only in prolonged procedures. Pulmonary pressure measurements were recorded only in selected cases and not performed routinely.

When a PAVM with feeding artery ≥ 3 mm or in some cases even smaller[31] was detected, embolisation was performed with use of detachable silicone balloons,[32] standard, detachable or hydro-coils, or vascular plugs.[33–35] Exchange of guidewires and catheters was performed submerged to avoid air embolism to the systemic arteries, especially the coronary arteries. Usually only one lung was treated during one session in cases with multiple bilateral PAVM. There were no absolute contraindications to embolisation. Relative contraindications were high pulmonary arterial pressure, significant hepatic arteriovenous shunt and cardiac failure, pregnancy, renal insufficiency, and previous allergic reactions to contrast media.

The study was approved by the Danish Data Protection Agency (file no. 15/10194) according to the Danish Act on Processing of Personal Data (Act no. 429 of 31 May 2000), and Danish Health and Medicines Authority (file no. 3-3013-974/1).

Outcomes

The follow-up plan was established at multidisciplinary team (MDT) meetings. Follow-up was terminated when the

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