Surgery or not, that is the question in Hughes-Stovin syndrome

Sirs,

A male Afghan patient of 23-year-old was evaluated because of acute haemoptysis.

His previous history included cerebral venous sinus thromboses. He also reported recurrent fever, weight loss and orogenital ulcers. A computed tomography (CT) scan showed bilateral pulmonary artery aneurysms (PAA) (Fig. 1A). A diagnosis of Hughes-Stovin syndrome (HSS) according to the 2021 HSS International Study Group criteria (1) and reference atlas (2) was made. Additionally, the patient fulfilled the 2014 International Criteria for Behçet's Disease (3).

A CT scan on admission showed pulmonary haemorrhage, PAA-associated bronchus erosion and pulmonary artery thrombosis of the right lower lobe. Surgical management was not performed due to highly active disease and PAA size was not suitable for endovascular intervention. Rescue therapy with intravenous (IV) methylprednisolone (1 g) and IV cyclophosphamide (1.2 g) was started and haemoptysis resolved. However, the patient developed a rapidly progressive deep vein thrombosis (DVT) with near-total occlusion of the inferior vena cava despite immunosuppressive treatment and anticoagulation (enoxaparin 1 mg/kg). Therefore, treatment was switched to IV infliximab 275 mg every 4 weeks (5 mg/kg) and oral methotrexate (15 mg/week) after six pulses of cyclophosphamide (cumulative 7.2 g). No further events occurred with this treatment and anticoagulation was stopped. A follow-up CT scan after 6 months showed significant PAA regression (Fig. 1B).

One year after initial presentation, spontaneous PAA rupture occurred in the absence of anticoagulation. Immediate bronchoscopy demonstrated massive bleeding within the right lower lobe. Interventional bronchus occlusion (Fig. 1C) and subsequent lobectomy were performed, which stopped the bleeding. Histopathology demonstrated extensive residual changes of pulmonary vasculitis prone to rupture of pulmonary arteries and veins (Fig. 1D). Of note, histopathological signs of active inflammation were absent and inflammatory markers were normal.

HSS is a rare inflammatory systemic condition that is considered to be part of the Behçet's syndrome (BS) spectrum (4). Recurrent vasculo-occlusive disease and pulmonary vasculitis with PAA formation constitute the hallmark of HSS (1).

For BS, inflammatory thrombus formation in pulmonary arteries with subsequent recanalization has been implicated in the pathogenesis of PAA and perivascular cuffing of inflammatory cells might contribute to PAA fragility (5).

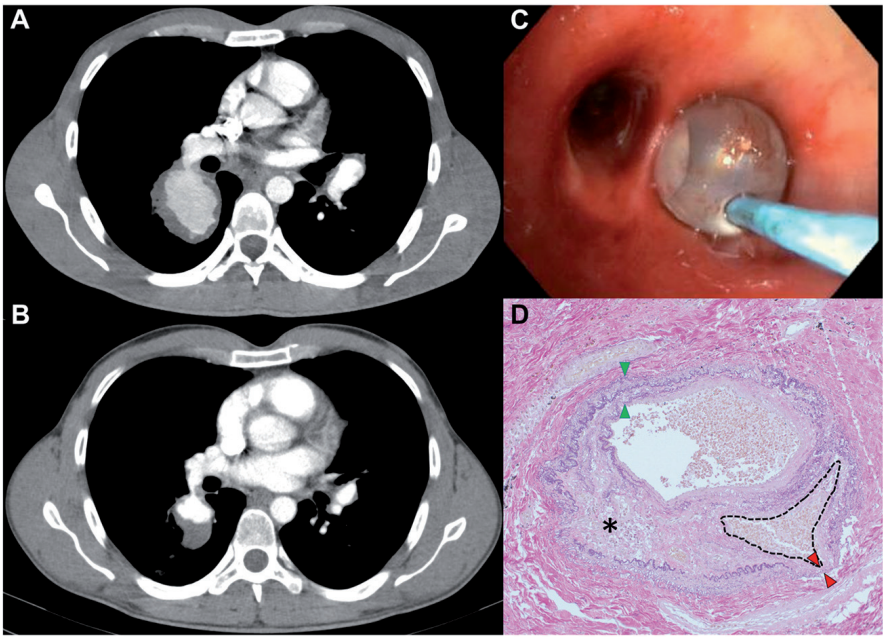

Fig. 1. A: Computed tomography (CT) scan of the chest (axial, contrast enhanced): bilateral pulmonary artery aneurysm (right PAA: 53 x 43 mm, left PAA: 36 x 19 mm) with intra-luminal thrombosis prior to immunosuppressive therapy.
B: Follow-up CT scan of the chest (axial, contrast enhanced) after intravenous cyclophosphamide (6 x 1.2 g, cumulative 7.2 g) and infliximab (2 x 275 mg, 5 mg/kg) therapy demonstrated marked bilateral PAA regression (right PAA: 23 x 17 mm, left PAA: 23 x 11 mm).
C: Emergency bronchoscopy: interventional bronchus occlusions (tamponade) of the right lower lobe.
D: Surgical specimen (lobectomy): Large pulmonary artery with residual thrombus and disrupted wall architecture (*), false aneurysm (dotted line) with highly thinned vessel wall (red arrowheads as opposed to normal wide vessel wall marked with green arrowheads). These findings are consistent with residual changes of pulmonary vasculitis without active inflammation (Elastica-van-Gieson, original magnification x100).

In general, it has been proposed that PAA diameter ≥5.5 cm, rapid progression, thrombus formation or signs of rupture represent indications for surgery (6). However, PAA formation due to pulmonary vasculitis may constitute a special entity where optimal treatment seems less clear. Surgical treatment of pulmonary involvement in BS exhibited unfavourable outcomes in the past since the inflammatory and relapsing nature of this condition has been less recognized by surgeons (7). Recurrent anastomotic aneurysms (suture dehiscence) and contralateral PAA rupture represent major problems, especially, when surgery is performed in active disease (7-9). While intensive immunosuppression may lead to PAA regression and disease remission, it does not necessarily prevent fatal haemorrhage. Residual damage may predispose to spontaneous PAA rupture even in the absence of active disease as demonstrated by our case. We recommend an interdisciplinary assessment of the lesions and evaluation of interventional and surgical approaches, which should preferably be performed when disease remission is achieved.

Endovascular interventions have been applied in BS and may also be considered in cases of high-risk or unstable PAA with suitable size (1, 8).

The role of anticoagulants in HSS is unclear and great caution is required. Interestingly, the majority of HSS patients described by Emad *et al*. (1) received anticoagulation therapy, while the 2018 EULAR recommendations for BS (10) do not advise anticoagulation when PAA are present.

To conclude, clinicians should consider the risk of fatal PAA rupture in cases of disease remission and/or significant PAA regression due to fragile vascular architecture. We recommend an interdisciplinary evaluation of interventional and surgical approaches.

N. Ruffer[1,2], *MD*
M. Krusche[1], *MD*
K. Holl-Ulrich[3], *MD*
I. Kötter[1,2], *MD*

[1]III Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany;
[2]Department of Rheumatology and Immunology, Klinikum Bad Bramstedt, Germany;
[3]Pathology Hamburg, Labor Lademannbogen MVZ GmbH, Hamburg, Germany.

Please address corresponding to:
Nikolas Ruffer
III Department of Medicine,
University Medical Center Hamburg-Eppendorf,
Martinistraße 52,
20246 Hamburg, Germany.
E-mail: n.ruffer@uke.de
ORCID iD: 0000-0001-8394-969X

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