Balloon pulmonary angioplasty in sarcoid-related pulmonary hypertension

To the Editor:

A 43-year-old, never-smoking, African-American female was referred to our outpatient clinic for progressive dyspnoea. She had a medical history of sarcoidosis with lymph-node, pulmonary, skin and ocular involvement. Diagnosis was based on a previously conducted chest high-resolution computed tomography (CT) that showed bilateral hilar and mediastinal lymphadenopathy containing calcifications and multiple small lung nodules with peri-lymphatic distribution along the pleura and fissures A histological analysis of biopsy specimens from a lymph node located in the left side of the neck revealed large granulomas with multinucleated foreign body giant cells without necrosis. Microbiological cultures were negative. Extrapulmonary manifestations consisted of anterior uveitis and several cutaneous lesions and the reason for initiating corticosteroid therapy, which ameliorated the sarcoidosis. After discontinuation of corticosteroid therapy, the patient's condition deteriorated and she developed progressive dyspnoea (New York Heart Association (NYHA) functional class 3). Thoracic CT showed bilateral pleural and pericardial effusion. There were no signs of pulmonary fibrosis or cardial signs of pulmonary hypertension (PH). Analysis of the pleural fluid showed exudation with lymphocytosis. An infectious cause was excluded.

Transthoracic echocardiogram revealed signs of PH with an estimated systolic pulmonary artery pressure of 80 mmHg and no signs of left heart disease. Corticosteroid therapy was restarted, and the patient was referred to our centre.

Computed tomography pulmonary angiography (CTPA) showed no pulmonary embolism but a stenosis of the origin of the pulmonary artery from the right middle lobe based on compression from outside due to the lymphadenopathy. CTPA findings are shown in figure 1 a, b and c.

There was also an acute stop of blood flow in the right lower lobe and left inferior lobe laterobasal, posterobasal and anteromedial visible. No webbing or bands were visible in the pulmonary arteries. A right heart catheterisation (RHC) was performed that confirmed pre-capillary PH with an elevated mean pulmonary artery pressure (mPAP) of 44 mmHg, pulmonary artery wedge pressure (PAWP) of 15 mmHg, a moderately elevated pulmonary vascular resistance (PVR) of 4.8 Wood Units (WU) and a cardiac index of 3.5 $L \cdot min^{-1} \cdot m^{-2}$. Cardiac magnetic resonance imaging was performed which showed no diastolic dysfunction and no signs of myocardial involvement of the sarcoidosis. Positron emission tomography (PET) with fludeoxyglucose (^{18}FD-glucose) showed mild ^{18}FD-glucose uptake in the hilar and mediastinal lymph nodes and diffuse ^{18}FD-glucose uptake in the skin, lungs, bones and muscles, compatible with sarcoid disease activity [1]. Diuretics were initiated and immunosuppressive treatment was intensified including high dose corticosteroids and a second-line immunosuppressant. Clinically, there was no improvement and evaluation with a RHC after 3 months showed no improvement of haemodynamics with a mPAP of 48 mmHg, PAWP of 15 mmHg, PVR of 6.1 WU and cardiac index of 3.2 $L \cdot min^{-1} \cdot m^{-2}$. In a multidisciplinary meeting, we decided to perform balloon pulmonary angioplasty (BPA) to dilate the stenotic the right middle lobe pulmonary artery. The procedure involved placing a 6 French (Fr) sheath in the right common femoral vein and inserting a 6-Fr gauge wedge-pressure catheter into the right pulmonary artery. Contrast angiography of the right pulmonary artery showed stenosis of the common trunk of the middle lobe artery and a complete obstruction of the lower lobe arteries. After passing the lesion from the right middle lobe with a wire, a 4 × 20-mm balloon was inflated with minimal result. After this a 6 × 20-mm balloon was inflated (first 1 min, then 3 min and finally, 5 min). The stenosis was

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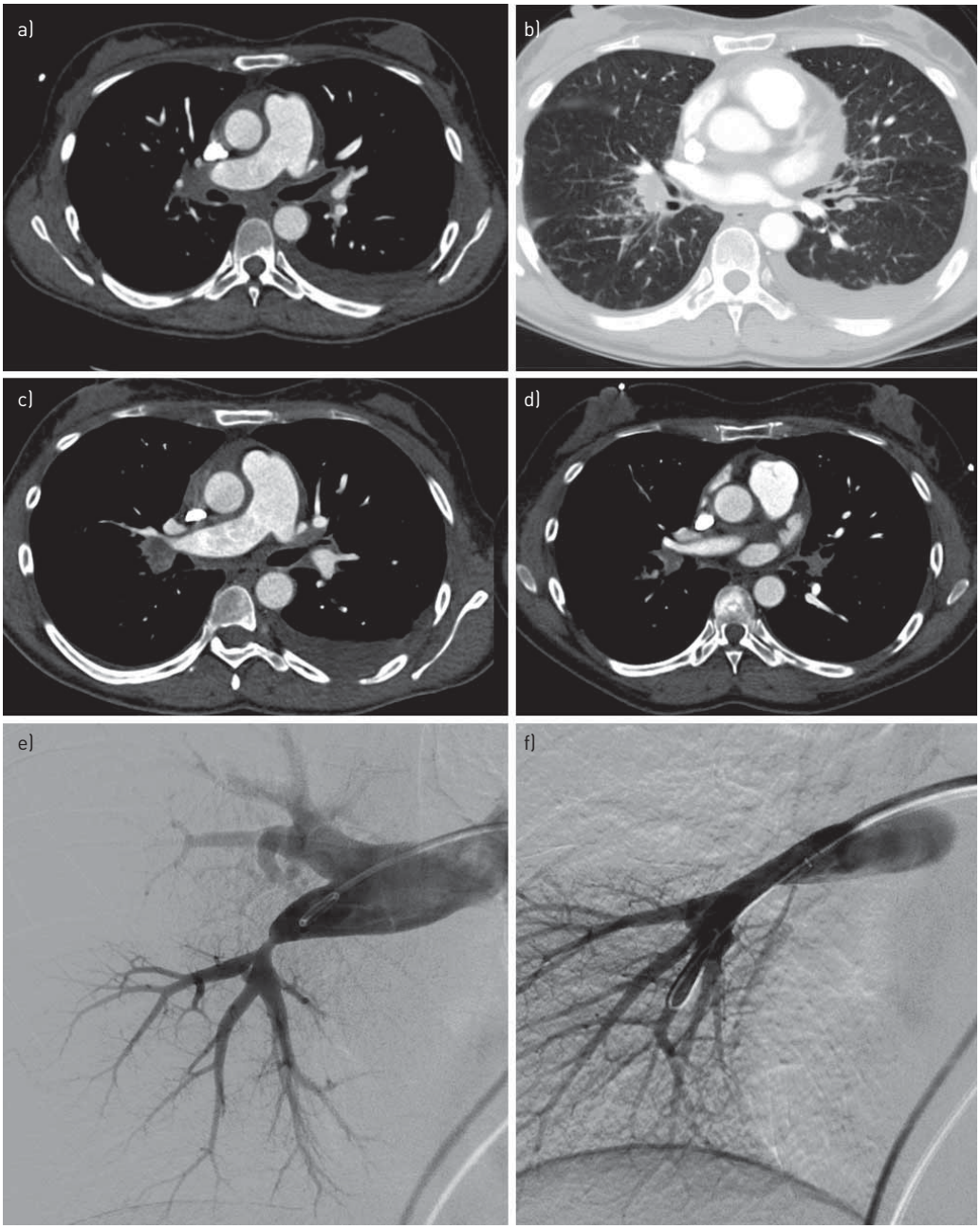

FIGURE 1 Overview of the computed tomography pulmonary angiography (CTPA) and pulmonary angiography before and after balloon pulmonary angioplasty (BPA). CTPA pre-BPA: a) Mediastinal setting shows bilateral hilar and mediastinal lymphadenopathy. b) Lung setting shows multiple small bilateral nodules with perilymphatic distribution and pleural fluid on the left. c) Severe narrowing of the lumen of the origin of the middle lobe artery with more than 50% loss of the lumen owing to external compression. CTPA post-BPA: d) Increase in the diameter of the lumen of the origin of the middle lobe artery. e) Pulmonary angiography pre-BPA with an 18-grade left anterior oblique view shows stenosis of the origin of the middle lobe artery. f) Pulmonary angiography after BPA with an 18-grade left anterior oblique view shows that the narrowed lumen of the origin of the right middle lobe artery was completely resolved with good filling of the peripheral branches.

difficult to bypass. Slight angio-disruption was evident on the last angiogram, but was self-limiting. A month later, we repeated this procedure. We dilated the already less stenotic lesion with an 8 × 20-mm balloon twice during 5 min. Hereafter, there was no longer a pressure gradient over the stenosis. Figure 1e and f shows contrast-enhanced pulmonary angiography images before and after BPA of the right middle lobe artery. After the procedure, the mPAP normalised to 22 mmHg. 6months after the procedure, the

patient showed clinical improvement, NYHA functional class 2 and a significant improvement of the 6-min walking test (422 to 475 m).

Although granulomatous inflammation in sarcoidosis is often the cause of symptoms, several non-inflammatory complications of pulmonary sarcoidosis have been identified. Recognition of these complications is important, as they are unlikely to respond to anti-inflammatory therapy [2]. PH is a well-known complication of sarcoidosis with a prevalence of up to 5% of all sarcoidosis cases [3–5]. Even though some cases are due to left heart disease, most cases have pre-capillary PH [2]. PH is most often seen in advanced fibrotic disease and thought to be attributed to the destruction of the distal capillary bed by fibrotic processes and/or hypoxaemia [6]. However, the severity of PH does not correlate well with the degree of pulmonary fibrosis and blood gas tensions; further, PH is described in sarcoidosis without fibrotic lung involvement suggesting other mechanisms contributing to the development of PH in patients with sarcoidosis. These proposed mechanisms include extrinsic compression of the large pulmonary arteries by mediastinal or hilar lymphadenopathy and/or fibrosis or specific granulomatous vascular involvement. Therapy can be divided into sarcoidosis-targeted treatment and PH-targeted therapy. Treatment of pre-capillary PH in sarcoidosis has only been studied in small groups, and there is no solid proof for the use of PH-specific vasodilator therapy [7]. Patients with active granulomatous inflammation and/or compression of the pulmonary artery due to enlarged lymph nodes might benefit from immunosuppressive treatment [7].

In this case, the development of PH was thought to be due to extrinsic compression of the large pulmonary arteries, although an inflammatory granulomatous vasculopathy could not be excluded. Our patient did not show any functional improvement. In addition, the CT images and echocardiography did not show any improvement. Therefore, we decided to perform a BPA.

BPA is a known treatment option in selected patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH) [8, 9]. To our best knowledge, there are no published data on BPA in patients with PH in sarcoidosis. After BPA, the stenosis of the right pulmonary artery from the right middle lobe was no longer present, and the patient's haemodynamics normalised along with clinical improvement. This case report shows that BPA might be successful in selected patients with PH associated with sarcoidosis and that recent advances in BPA are promising even for indications other than CTEPH.

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