A 36-year-old woman with chronic rheumatic heart disease (RHD) with moderate mitral regurgitation, on oral penicillin prophylaxis for 6 years, developed progressive effort intolerance and severe chest discomfort over 1 week. Initial evaluation on hospitalisation revealed moderate respiratory distress at respiratory rate of 35/minute, sinus tachycardia at 120/minute with blood pressure of 118/70 mm Hg. Jugular venous pressure was elevated to 8 cm with normal waveforms. Systolic heart murmur suggestive of mitral regurgitation and 3rd heart sound were present with extensive bilateral crepitations. ECG showed non-specific repolarisation abnormality. Chest X-ray on admission confirmed cardiomegaly with left atrial and left ventricular enlargement, straightening of the left heart border and alveolar oedema (Figure 1).

Initial blood chemistry, haemogram and RHD reactivation tests, including C reactive protein, ASO titre and ESR were unrevealing. Heart failure responded to therapy but chest pain persisted. Chest X-ray repeated on the fourth hospital day (Figure 2) showed clearing of venous congestion and new development of multiple wedge-shaped opacities with the base towards the pleura.

What is the differential diagnosis at this stage? What could have caused the pulmonary oedema in this RHD patient?

1. Congestive heart failure (CHF) due to rheumatic reactivation—myocarditis
2. CHF due to worsening mitral regurgitation—valvulitis
3. CHF due to associated anaemia, fever, respiratory infection
4. Primary pneumonitis or Adult Respiratory Distress Syndrome (ARDS) – atypical presentations
5. Pulmonary embolism, a rare phenomenon

Congestive cardiac failure in chronic RHD is still very common in developing countries. A rigorous search for infective endocarditis, tachyarrhythmias, rheumatic reactivity, progressive valvular disease and other precipitants like anaemia, infections, sepsis, renal dysfunction, and thyrotoxicosis must be routinely undertaken. The importance of excluding coronary heart disease, metabolic or hypertensive cardiac dysfunction cannot be overemphasised.

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Based on the radiological suspicion of pulmonary embolism, evidence for deep vein thrombosis [DVT] was looked for with Doppler studies of the lower limbs, repeated twice, 4 days apart. DVT was not detected. Blood D-dimer assay was elevated at 35μg/ml. Figure 3 shows the lung perfusion scan. The study is with technetium 99 MAA lung perfusion study. Multiple perfusion defects, wedge-shaped cold areas, are seen in the different views provided. This is diagnostic of PTE.

Subsequently, prolonged APTT (63s control 26s), Kaolin clotting time (146s control 95s), diluted Russel’s Viper venom time, lupus anticoagulants (LA), LA1- 92s (reference range < 45s) and LA2- 43s (reference range < 38s), LA1: LA2 ratio 2.1, elevated antiphospholipid antibody, IgG 15.4 U/ml (reference range < 10), IgM 11.3 (normal < 10), and anticardiolipin antibody IgG 11.4 U/ml (reference range <10) were noted. Titres pointed towards underlying antiphospholipid antibody syndrome (APLAS). Connective tissue disorder and coagulopathy testing were otherwise negative. Similar results were obtained on repeat testing after 2 months.

**What is the coagulopathy in this case?**

Echocardiography confirmed rheumatic mitral involvement by posterior mitral leaflet thickening, restricted mobility and moderate mitral regurgitation. Moderate left ventricular (LV) dysfunction with ejection fraction of 40% and moderate pulmonary hypertension were present. Cardiac catheterisation revealed normal coronary artery anatomy and tissue perfusion.

**Why should pulmonary embolism develop in RHD?**

1. LV dysfunction secondary to chronic mitral regurgitation or carditis of rheumatic reactivity
2. Heart failure-related reduced blood flow
3. CHF-related sluggish blood flow and pulmonary venous congestion
4. Right atrial stasis due to atrial fibrillation and
5. Prolonged immobilisations and subsequent DVT are some of the factors operating in RHD that can possibly lead to pulmonary embolism.

The diagnosis of pulmonary embolism was confirmed and therapy started immediately with intravenous Heparin. Warfarin was started subsequently and antifailure medications reduced.

**What initiated the clinical deterioration?**

Our patient demonstrated simultaneous onset of effort intolerance and chest discomfort. Dyspnoea and chest pain are present in only 59% and 17% cases of PTE respectively. In our case, overt heart failure at presentation appears to have effectively ‘masked’ the clinical and radiographic evidence of PTE. Typical echocardiography findings of PTE were absent due to pre-existing pulmonary hypertension and right ventricular hypertrophy of chronic RHD.

Also, we found no laboratory evidence to suggest rheumatic
fever reactivation. Thus, retrospectively we strongly suspect that underlying APLAS is the reason for the sudden clinical deterioration.

Based on the available evidence we feel that this is how the illness progressed:
1. Underlying RHD and moderate mitral regurgitation were stable (patient on oral penicillin prophylaxis) and probably coincidental.
2. Primary APLAS is the culprit pathology.
3. Pulmonary oedema resulted due to APLAS-related global LV dysfunction and
4. PTE due to APLAS and pulmonary congestion.

Intravenous heparin infusion was started and anti-failure medications and analgesics continued. Clinical improvement was rapid with complete resolution of chest pain and dyspnoea. Warfarin was started and International Normalised Ratio (INR) maintained between 2.5 and 3.5.

When to suspect and how to manage APLAS?

The absence of typical risk factors for PTE in women, like obesity, cigarette smoking, oral contraceptive pills, hypertension and prolonged travel, leaves only coagulation abnormalities as the possible cause for pulmonary embolism. About half the time APLAS is primary and in the remaining cases secondary to SLE. APLAS is known to produce both arterial and venous thrombosis and recurrent miscarriages. Appropriate laboratory testing in this setting confirms the diagnosis. Maintenance of high therapeutic anticoagulation (International Normalized Ratio, INR, of over 3.0) appears to prevent recurrence of vascular thrombosis although the exact duration of this anticoagulation is still debated.

Repeat echocardiography after 6 months showed improvement of left ventricular function and the patient is well at 1 year follow-up.

How does cardiac dysfunction occur in APLAS?

Myocardial ischaemia, infarction and dysfunction can occur in APLAS due to
1. Intracardiac thrombi with subsequent embolisation
2. Coronary and pulmonary in situ thrombosis
3. Severe acute cor pulmonale related to thromboembolism, which could affect left ventricular function due to interven-

4. Tissue level microvascular dysfunction or
5. Direct myocardial depressant effect.

Normal coronary angiogram, in this instance, eliminates atherosclerotic occlusions and embolisation. Reversibility of global LV dysfunction cannot be expected in the first 3 mechanisms. We have recently reported SLE and APLAS in a patient with pancarditis and reversible LV dysfunction. Thus, we suspect the role of microvascular dysfunction and direct myocardial depressant effect in our case, which would explain the reversible global LV dysfunction without regional wall motion abnormality, and normal coronary angiography.

References