Pulmonary artery thrombosis in a patient with severe acute respiratory syndrome

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CASE REPORT

Pulmonary artery thrombosis in a patient with severe acute respiratory syndrome

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Severe acute respiratory syndrome (SARS) is an emerging infectious disease with both pulmonary and extra-pulmonary manifestations. Although coagulation abnormalities are common in these patients, clinically overt thromboembolic events are rarely reported. This report describes the first case of pulmonary artery thrombosis in a patient with laboratory confirmed SARS.

A 43 year old woman, working as a health care assistant in a medical ward designated for the care of severe acute respiratory syndrome (SARS) patients during the outbreak in 2003, was admitted because of fever, dry cough, diarrhoea, chills, and rigor for two days. On admission, she had a temperature of 38.5°C. Physical examination showed bilateral basal crepitations. Preliminary investigations showed a normal white cell count (5700 cells/µl, normal range 4000–11000 cells/µl), but her lymphocyte count was depressed (1000 cells/µl, normal range 1500–4000 cells/µl). The platelet count was normal on admission (294×10^9/l, normal range 150–400×10^9/l), and the coagulation profile was unremarkable at that time. Liver and renal function tests were also normal. The chest radiograph showed bilateral lower zone consolidations (fig 1). High resolution computed tomography of the thorax showed ground glass opacities at lingular segment, left upper, and right lower lobes (fig 2). In view of the possible occupational exposure, a clinical diagnosis of SARS was made. She was given intravenous ribavirin 400 mg every eight hours and oral prednisolone 25 mg twice daily. One week after admission, the patient complained of increasing severity of dyspnoea and oxygen desaturation. Repeated chest radiography showed deteriora-
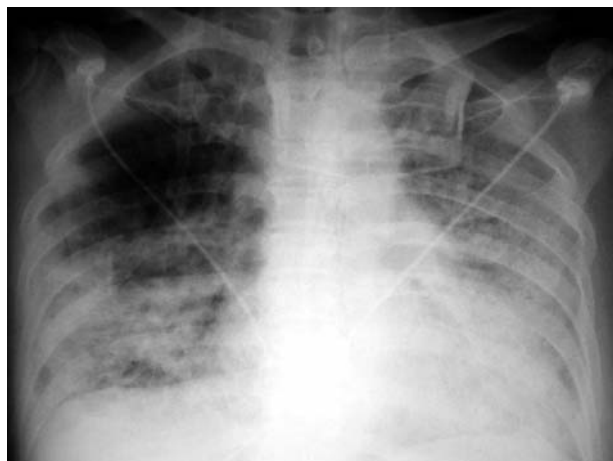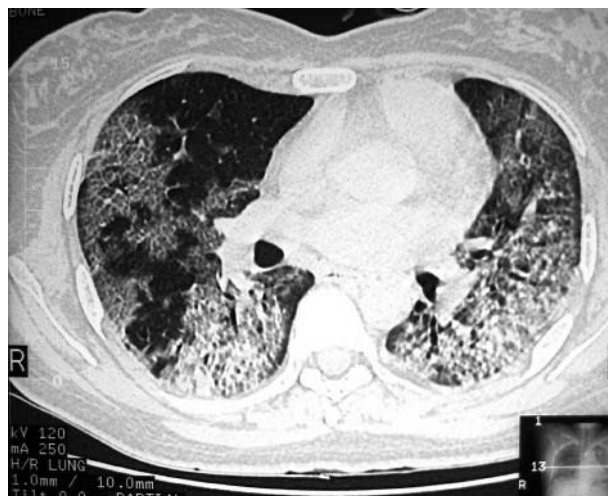

Figure 2 High resolution computed tomography of the thorax.

tion with worsening of right mid-zone shadow. Lopinavir (400 mg)/ritonavir (100 mg) (Kaletra) twice daily was added, and intravenous pulse methylprednisolone 500 mg daily was started for three consecutive days (from day 7 to 10), followed by tailing dose of corticosteroids. Despite resolution of fever, her symptoms continued to deteriorate and required intensive care on day 13. Chest radiography showed florid ground glass appearances in both lung fields. Intravenous immunoglobulin (IVIg) 21 gm daily and subsequently intravenous pentaglobulin 300 mg daily were given between day 13 and day 16. Her clinical course remained stable thereafter although the chest radiograph findings were static in the next 10 days. On day 27, she had recurrence of low grade fever and dyspnoea. ECG showed sinus tachycardia at about 120 beats per minute. Blood picture showed progressive thrombocytopenia (to a nadir of 35×10^9/l), associated with prolonged prothrombin (17.6 seconds, normal range 10.4 to 12.6 seconds) and activated partial thromboplastin time (39.2 seconds, normal range 24.5 to 37.6 seconds). The level of D-dimer was also raised (>1, normal range <0.5 µg/ml), suggesting the presence of disseminated intravascular coagulation. Septic investigation for nosocomial infection was negative. Doppler ultrasound of lower limbs did not show any deep vein thrombosis. However, the CT angiogram of the thorax detected the presence of a blood clot in the right main pulmonary artery with extension into the segmental artery of the right lower lobe, suggestive of thromboembolism (figs 3 and 4). Anticoagulation therapy in terms of nadroparin calcium

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Figure 1 Chest radiograph.

Abbreviations: SARS, severe acute respiratory syndrome; IVIg, intravenous immuonoglobulin; PAT, pulmonary artery thrombosis

Figure 3 Computed tomography pulmonary angiogram.

Figure 4 Computed tomography pulmonary angiogram.

(Fraxiparine, Sanofi-Winthrop, Gentilly, France) was started. Her symptoms gradually improved and subsided. After prolonged period of convalescence, the patient was finally discharged from hospital. Subsequent examination for underlying thrombophilia, including protein C and S assays, and lupus anticoagulant all turned out to be negative. The patient was not taking any contraceptive pills or other drugs before admission. The microbiological diagnosis of SARS was retrospectively confirmed by a fourfold rise of antibody titre against SARS associated coronavirus (SARS-CoV) by indirect immunofluorescence test (from a titre of <25 taken on day 10 to a value of 800 on day 27), and positive reverse transcription polymerase chain reaction (RT-PCR) results in sputum and saliva on day 14 after onset of symptoms.

DISCUSSION
SARS, a newly described infectious disease caused by a novel coronavirus,[1] has been responsible for infecting more than 8000 people and killing in excess of 700 worldwide since its emergence last year.[2] The clinical manifestations and laboratory abnormalities of SARS have been well summarised elsewhere.[3][4] Various coagulation abnormalities such as prolonged activated partial thromboplastin time and raised D-dimers have been reported previously in up to 65% and 45% of adult SARS patients respectively,[5][6] and multiple necropsy series of SARS patients showed that vascular thromboses

Learning points
- Patients with SARS may be prone to pulmonary thromboembolic events attrributable to an underlying thrombophilic state.
- Pulmonary embolism may present with clinical deterioration such as unexplained haemodymaic instability or hypoxemia, or both, in a patient with SARS.
- Clinicians caring for SARS patients must maintain a high index of suspicion for the occurrence of pulmonary thromboembolism in their patients.

were not uncommonly seen in lung specimens,[7][8] suggesting the possibility of an underlying thrombophilic state with predisposition to thrombus formation in the lungs. Of note, in a recently published necropsy series comprising a total of eight SARS patients,[9] it was found that four patients had pulmonary thromboemboluses within the pulmonary arteries, three had deep venous thrombosis, and one patient had marantic valvular vegetations associated with infarctions of the heart, kidneys, spleen, and occipital lobe. In addition, based on the experience at a SARS hospital intensive care unit in Singapore,[9] it was found that 20.5% of patients had deep vein thrombosis, and 11.4% showed clinical evidence of pulmonary embolism. In our case, the radiological appearance of the lesion, together with absence of thromboemboluses in the contralateral side of the lung and the lack of evidence of deep vein thrombosis, favour the diagnosis of pulmonary artery thrombosis (PAT).[10][11] PAT has been reported to be associated with drug induced, systemic, or intrinsic causes of thrombophilia, as well as with pulmonary artery occlusion by tumours.[12][13] Although PAT can run a chronic course resulting in cor pulmonale, acute massive PAT can also occur. Such a presentation can occur in our patient, given that PAT has been reported in the setting of severe pulmonary parenchymal disorders such as tuberculous or mycotic pneumonia.[12][13] Moreover, the use of IVIg in our patient might have contributed to the development of a hypercoagulable state, as there have been reports of strokes occurring during or shortly after infusions of the drug in patients with antoimmune haematological and neuromuscular disorders;[14–16] interestingly, there has been a recent report of five SARS patients developing large artery ischaemic strokes, three of which had received IVIg for treatment of SARS.[17] These factors, together with the presence of disseminated intravascular coagulation in our patient,[18][19] might have contributed to the development of pulmonary thromboembolism. We believe the suggestion that a subset of SARS patients with raised D-dimer levels might benefit from anticoagulation therapy should be re-examined in the light of our experience.[20] Pulmonary embolism may present with clinical deterioration such as unexplained haemodynamic instability or hypoxemia, or both, as occurred in our patient. In our opinion, as well as the experience reported elsewhere,[9][17] we believe that this phenomenon may be more common than is generally appreciated. Clinicians should be more alert to this uncommonly reported complication and have low thresholds for starting appropriate investigations and treatments in this particular group of patients.

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