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Case report

Acute chest pain and breathlessness in a haemodialysis patient

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We describe a 64-year-old end-stage renal failure patient who had exhausted autogenous arteriovenous fistulas after 4 years of regular haemodialysis. He had no known medical illness prior to his first presentation to healthcare in 2014 with a 1-month history of rapid progressive worsening signs and symptoms of renal failure. Vasculitis screening and renal biopsy revealed pauci-immune crescentic glomerulonephritis with perinuclear antineutrophil cytoplasmic antibodies (p-ANCA) pattern. Unfortunately, the ultrasound scan and renal biopsy at the time showed his kidneys already had significant chronicity changes. After shared decision-making with the patient, the risks of immunosuppressants were deemed to outweigh any possible benefits. Of note, 2 years later, the patient had survived a life-threatening episode of pulseless ventricular tachycardia during one of his fistuloplasty procedures; subsequently, a coronary angiogram demonstrated right coronary artery and left circumflex artery stenosis, which was treated conservatively with single antiplatelet therapy. Thereafter, he remained asymptomatic with medical therapy and had regular cardiology follow-up. His latest medication list includes: aspirin 75 mg once daily, ranitidine 150 mg once daily, isosorbide mononitrate 60 mg once daily, atorvastatin 40 mg once daily and amlodipine 10 mg once daily, with a calcium supplement and haematinics.

The patient had been on a non-cuffed temporary right internal jugular catheter after recent thrombosis of right brachiocephalic fistula. He was admitted for an elective, apparently uneventful left tunnelled cuffed central venous catheter (14 Fr/28 cm) insertion *via* the left internal jugular vein into the atriocaval junction under fluoroscopic guidance. However, during the first haemodialysis session after the catheter insertion, the patient complained of sudden onset left-sided chest pain. Physical examination was unremarkable except for a slight reduction of air entry over the left hemithorax. There was no radial-radial or radial-femoral delay and heart sounds were normal. Electrocardiogram demonstrated new T wave inversions and ST segment depressions over lateral leads. Echocardiography revealed global hypokinesia of the left ventricle with an impaired left ventricular ejection fraction of only 39%. In view of the underlying ischaemic heart disease with new evolving electrocardiogram changes, the patient was given double antiplatelets (aspirin and clopidogrel) and anticoagulation. Cardiac enzymes were not raised. Despite 3 days of acute coronary syndrome treatment, the patient further developed respiratory distress with hypoxaemia. Saturation on room air was 90% and air entry remained reduced over the left hemithorax. Arterial blood gas on room air showed pH 7.417, oxygen tension 65.9 mmHg, carbon dioxide tension 28.8 mmHg and bicarbonate 18.1 mmol·L^{-1}. A chest radiograph was performed (figure 1).

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Acute chest pain and breathlessness in a haemodialysis patient is a common but challenging clinical scenario, can you diagnose and manage it? http://bit.ly/2Qf1mXr

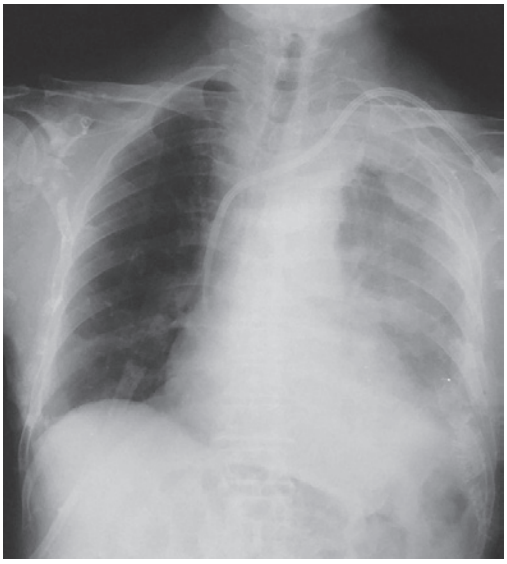

Figure 1 *Chest radiograph.*

Task 1
Describe the chest radiograph in figure 1.

Answer 1
The chest radiograph demonstrated diffuse opacity over the left hemithorax with obliteration of diaphragmatic outline and costophrenic angle. Left tunnelled cuffed central venous catheter *in situ* with the catheter tip in a good position.

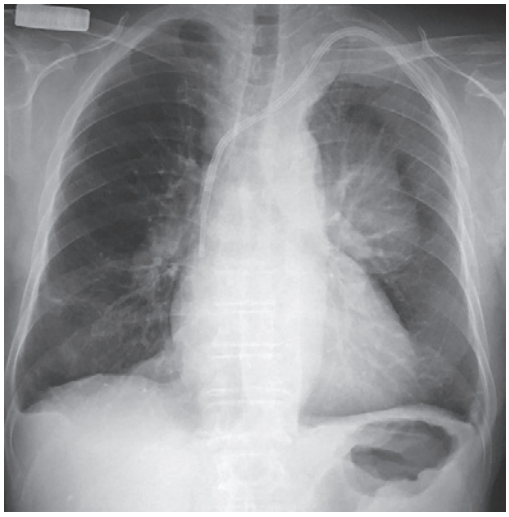

Figure 2 *Left loculated pleural collection with hilar overlay sign.*

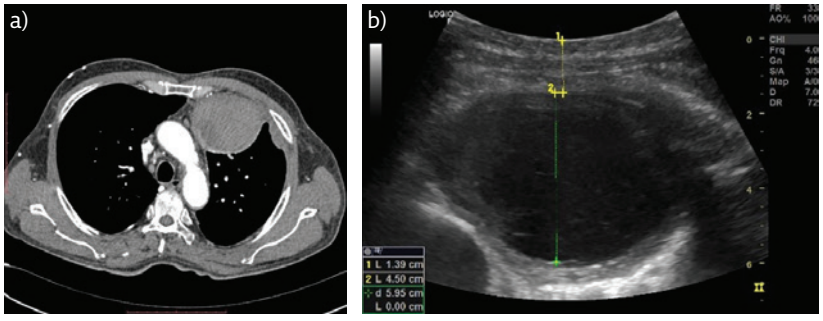

Figure 3 *a) CT of the thorax showing loculated pleural effusion and b) transthoracic ultrasound revealing hyperechoic pleural collection anteriorly.*

On further review of his history, the left-sided chest pain was pleuritic in nature. A bedside transthoracic ultrasound was performed by the managing team over the left lateral hemithorax which revealed only minimal pleural effusion. In view of the raised total white cell count (to $16.84\times10^{3}\cdot\mu L^{-1}$) and new chest radiograph changes, empirical antibiotic therapy was initiated for nosocomial pneumonia. However, despite antimicrobial therapy and adequate dialysis, a repeated chest radiograph 1 week later, although improved somewhat, showed pleural collection now loculated superiorly with hilar overlay sign (figure 2). The patient was subsequently referred to the respiratory team for further assessment. His vital signs were stable and air entry had improved. However, subcutaneous swelling and bruising was noted around the tunnelled cuffed central venous catheter insertion site. A review of serial investigations noted his haemoglobin had dropped from 10 $g\cdot dL^{-1}$ to 8.9 $g\cdot dL^{-1}$ during the current admission. Computed tomography (CT) of the chest was arranged which showed an enhancing multi-loculated high density pleural fluid with Hounsfield Unit of 60 at the left apical and anterior–medial pleural lining, consistent with loculated complex pleural effusion. A systematic transthoracic ultrasound examination of the left hemithorax now confirmed a hyperechoic pleural collection in the left anterior hemithorax at the second intercostal space, measuring 4.5 cm in depth (figure 3). When diagnosis is uncertain, a loculated pleural effusion should be aspirated for investigation. As the only possible entry point was anteriorly, clopidogrel was withheld for 1 week to prevent further bleeding complications, and diagnostic thoracocentesis planned 1 week thence. By then the patient was well and pain-free and was therefore was allowed home in the meantime.

Task 2
What would be the next investigation of choice? What are the expected findings?

Answer 2
Ultrasound-guided diagnostic thoracocentesis. Either stale blood would be aspirated, or a dry tap if the blood had already clotted.

A repeat ultrasound examination a week later revealed unchanged pleural collection and the patient's clinical condition remained static. Thus, elective pleural aspiration proceeded as planned at the mid-clavicular line, in the second intercostal space. Under direct ultrasound guidance, visible vessels were identified and avoided. However, during infiltration with local anaesthesia *via* 21G needle, no fluid was aspirated. Thoracocentesis was then attempted *via* a 16G branula; however, only 10 cc of stale blood was obtained despite vigorous aspiration.

Task 3
What is the clinical diagnosis?

Answer 3
Iatrogenic clotted haemothorax, probably from the tunnelled cuffed catheter insertion.

A clotted haemothorax will eventually progress to a trapped lung if left unevacuated. In view of multiple comorbidities and recent acute coronary syndrome, the patient was deemed to be high surgical risk for thoracotomy and clot evacuation. Furthermore, he was haemodynamically stable. Options were discussed with patient and the decision was to undertake a trial of percutaneous drainage. Under real-time ultrasound guidance, a 14 Fr pleural catheter was inserted, using the Seldinger method, into the anterior collection (figure 4b). As anticipated, there was still no fluid aspirated from the pleural catheter, hence placement was confirmed by flushing agitated saline into the catheter, allowing visualisation of the whole length of the catheter (figure 4c). However, despite daily flushing and aspiration *via* the pleural catheter, drainage was minimal and the chest radiograph remained static (figure 4a). Transthoracic ultrasound also demonstrated persistent collection anteriorly.

Task 4
What would be the next most appropriate course of management?

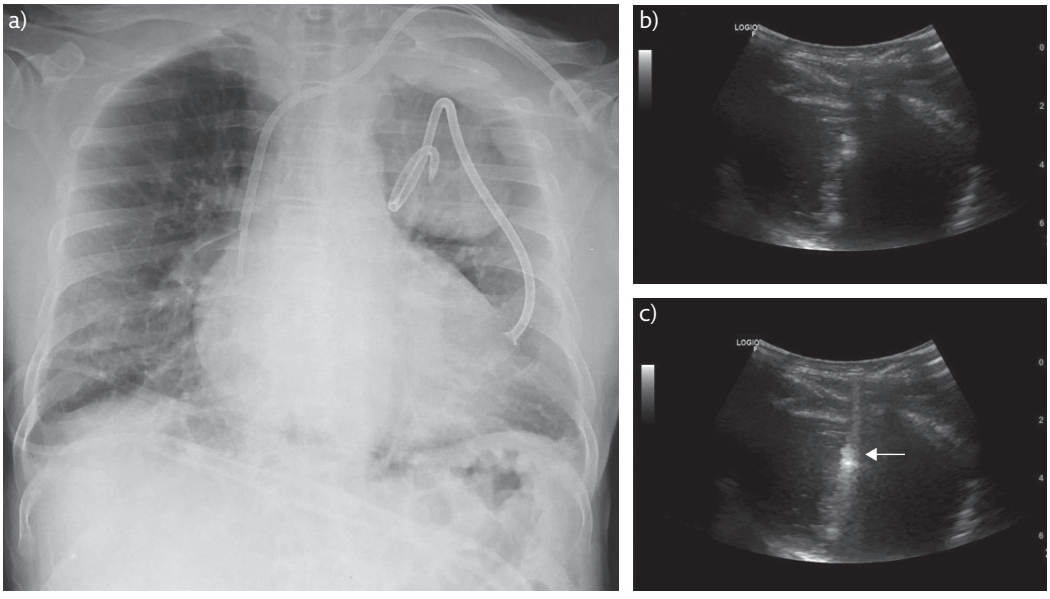

Figure 4 *a) Chest radiograph post-pleural catheter insertion anteriorly; b) insertion of the pleural catheter under real-time ultrasound guidance; c) visualisation of the pleural catheter by flushing with agitated saline (white arrow).*

Answer 4
Trial of intrapleural fibrinolytic therapy

Table 1 *Pleural catheter drain output chart*

Treatment day	Haemodialysis	Intrapleural fibrinolytic	24-h drain output mL	Cumulative drain output mL
1	Haemodialysis		0	0
2		Streptokinase x 1	100	100
3	Haemodialysis		0	100
4		Streptokinase x 1	50	150
5		Streptokinase x 1	100	250
6	Haemodialysis		100	350
7		Streptokinase x 2	200	550
8	Haemodialysis		100	650
9			0	650

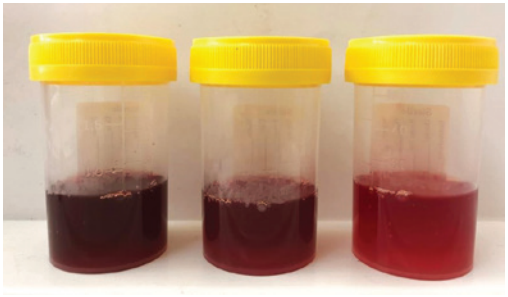

Figure 5 *Pleural fluid demonstrated reducing haemorrhagic component over time with intrapleural streptokinase instillation.*

As drainage was minimal and the patient was a high surgical risk, the risk and benefit of intrapleural fibrinolytic therapy was discussed with patient. In view of the high bleeding risk (recent acute coronary syndrome and end-stage renal failure on haemodialysis), a more vigilant protocol of intrapleural fibrinolytic therapy was adopted: intrapleural streptokinase 250000 units (diluted in 50 mL of normal saline) was given only on non-haemodialysis days with close observation for evidence of bleeding and monitoring of vital signs. The pleural catheter was clamped for 4 h after each instillation of streptokinase, then unclamped to allow drainage of the pleural effusion. Fortunately, the amount drained increased after several doses of intrapleural streptokinase (table 1), while haemoglobin and coagulation profile remained static throughout the intrapleural fibrinolytic therapy. The patient also remained haemodynamically stable throughout the fibrinolytic therapy. The nature of haemoserous drain output demonstrated a reducing haemorrhagic component over time (figure 5). By the fifth dose of intrapleural streptokinase (cumulative dose of 1.25 million IU), a cumulative total amount of 650 mL of stale blood had been drained, and the output trend was decreasing. A repeat chest radiograph now demonstrated almost complete resolution of the pleural collection and an ultrasound of the thorax also revealed normal lung sliding with only minimal pleural thickening (figure 6). Haemodialysis was continued *via* the tunnelled cuffed central venous catheter and no further bleeding episode was observed. The patient was discharged uneventfully and double antiplatelets were resumed until a coronary angiogram a month later showed stable double vessel disease, with fractional flow reserve below the angioplasty threshold. The patient was subsequently deescalated to single antiplatelet therapy again.

Discussion

Acute breathlessness in haemodialysis patients can be caused by various conditions such as acute coronary syndrome, catheter-related infection, pneumonia and pericardial effusion, as well as a reaction to the dialyser or medication given during dialysis [1]. Hence, clinical acumen remains integral in evaluation of acute breathlessness in this group

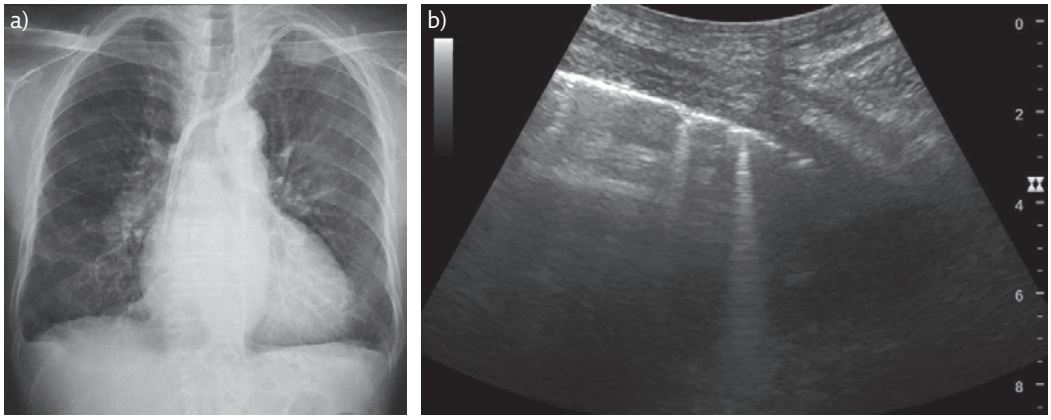

Figure 6 *a) Complete resolution of pleural collection after intrapleural fibrinolytic; b) Ultrasound of the hemithorax revealed only residual pleural thickening with normal lung sliding.*

of patients. Although our patient was of high risk for cardiac events and infection, the temporal relationship of symptom onset with central venous catheter insertion should have suggested that the cause of the acute breathlessness was probably a procedure-related complication. Massive haemothorax is a known complication of central venous catheterisation, and can be related to the insertion, advancement and maintenance of the catheter [2]. Hence, a chest radiograph immediately after central venous catheter insertion and at appropriate intervals thereafter is essential [2]. This was illustrated in our case in which the procedure was performed under seemingly uneventful fluoroscopic guidance, with unfortunately no immediate control chest radiograph, but in which a delayed complication probably set in after commencement of haemodialysis *via* the newly placed catheter.

A neglected haemothorax poses several problems. First, the neglected haemothorax will eventually clot and organise within ~10 days, which would promote further angioblastic and fibroblastic proliferation within the pleural cavity, resulting in trapped lung [3]. This happens in about 10.9% of retained traumatic haemothoraces [4]. This was demonstrated in our case with the progression of chest radiographs from figure 1, which showed a unilateral homogeneous pleural opacity, to figure 2, where the blood had clotted into a locule. Furthermore, a neglected haemothorax acts as medium for infection, especially in immunocompromised patients as in our case. Dubose *et al.* [5] demonstrated that empyema and pneumonia could develop in 26.8% and 19.5%, respectively, of patients with retained traumatic haemothorax.

Ultrasound has a good diagnostic performance in comparison to CT for patients suspected of clotted haemothorax [6]. Moreover, ultrasound is a point-of-care test that can provide immediate visual feedback to the operator as well as guide therapeutic intervention as shown in our case. This therapeutic guidance is particularly important as evacuation of a clotted haemothorax is difficult, and major clinical guidelines recommend that, in the event that free air or fluid cannot be aspirated at the time of local anaesthesia infiltration, a chest drain should be inserted with imaging guidance [7].

For clotted haemothorax, a surgical approach with either video-assisted thoracoscopic surgery (VATS) or thoracotomy is the preferred choice in haemodynamically unstable patients; however, in stable patients, a trial of intrapleural fibrinolytic therapy can be offered [3]. Although VATS reduces the length of hospital stay and future thoracotomies, it is not without risk, especially in patients with significant comorbidities [4]. Transient hypoxaemia or reversible cardiac arrhythmias are the most common complications of VATS, and this could be disastrous for our patient who had a history of pulseless ventricular tachycardia [8].

Intrapleural fibrinolytic therapy in clotted haemothorax was first described using fibrinolysin in the 1960s [9]. Cangir *et al.* [10] demonstrated the efficacy of intrapleural fibrinolytic therapy in enhancing clot resolution and reducing pleural thickening in an animal model with experimentally induced minimal clotted haemothorax. Since then, various reports have demonstrated the efficacy of intrapleural fibrinolytics in adult human patients with clotted haemothorax [8, 11–12]. Intrapleural fibrinolysis using streptokinase or urokinase showed an overall success rate of around 92% in a small series of clotted haemothorax patients, with no complication or mortality [11–12]. Tissue plasminogen activator as an intrapleural fibrinolysis agent was also shown to be safe and useful in complicated pleural effusion including retained haemothorax [13]. Despite the concern about bleeding, allergic and other adverse events while using intrapleural fibrinolytic therpay, various studies have determined its safety with a low risk of adverse events [14]. Davies *et al.* [15] have also demonstrated that a cumulative dose of intrapleural streptokinase up to 1.5 million IU has no significant effect on activation of systemic fibrinolysis. This was reflected in our case where even in a patient with high bleeding risk, intrapleural streptokinase up to a cumulative dose of 1.25 million IU did not cause any systemic bleeding complication.

To sum up, there are a few lessons to be learned from this case. First, the importance of post-catheter insertion chest radiographs, even with fluoroscopic procedures. Secondly, the importance of attention to signs and symptoms, in this case the onset timing, the pleuritic nature of the pain and the surrounding bruising should have been early clues. Timelier diagnosis could have allowed more simple drainage before clotting. Thirdly, the key role of confident diagnostic and therapeutic thoracic ultrasound, with the assurance to place a pleural drain despite dry tap. And finally, the efficacy of pleurolysis with streptokinase.

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Author contributions

S.S. Kho initiated the idea for case reporting. S.S. Kho and S.K. Chan prepared the final copy of the manuscript. S.S. Kho was involved in pleural catheter insertion, administration and monitoring of the intrapleural fibrinolytic in this case. S.K. Chan and V.E. Phui were involved in the overall patient management. S.T. Tie supervised the whole management process and reviewed the final manuscript. All authors have read and approved the final manuscript.

Conflict of interest

None declared.

References

1. Suraj K, Qi Q. 84 year-old woman with hemodialysis-associated shortness of breath. *Mayo Clin Proc* 2009; 84: 187–190.
2. Lossos IS, Putterman C, Mainer Z. Massive haemothorax from central venous catheterization: a note of caution. *Arch Emerg Med* 1992; 9: 335–338.
3. Boersma WG, Stigt JA, Smit HJM. Treatment of haemothorax. *Respir Med* 2010; 104: 1583–1587.
4. Oğuzkaya F, Akcali Y, Bilgin M. Videothoracoscopy *versus* intrapleural streptokinase for management of post traumatic retained hemothorax: a retrospective study of 65 cases. *Injury* 2005; 36: 526–529.
5. Dubose J, Inaba K, Demetriades D, *et al*. Management of post-traumatic retained hemothorax: a prospective, observational, multicenter AAST study. *J Trauma Acute Care Surg* 2012; 72: 11–22.
6. Poveda TS, Uribe CHM, Loaiza JR, *et al*. Chest ultrasonography *versus* chest CT for diagnosis of posttruamtic residual hemothorax. *Rev Colomb Radiol* 2012; 23: 3464–3468.
7. Laws D, Neville E, Duffy J, *et al*. BTS guidelines for the insertion of a chest drain. *Thorax* 2003; 58: Suppl. 2, ii53–ii59.
8. Agarwal R, Aggarwal AN, Gupta D. Intrapleural fibrinolysis in clotted hemothorax. *Singapore Med J* 2006; 47: 984–986.
9. Hardin CA, Leo W. Treatment of clotted hemothorax with fibrinolysin. *Dis Chest* 1959; 36: 37–40.
10. Cangir AK, Yuksel C, Dakak M, *et al*. Use of intrapleural streptokinase in experimental minimal clotted hemothorax. *Eur J Cardiothorac Surg* 2005; 27: 667–670.
11. Incil I, Ozcelik C, Ulkii, *et al*. Intrapleural fibrinolytic treatment of traumatic clotted hemothorax. *Chest* 1998; 1: 160–165.
12. Kimbrell BJ, Yamzon J, Petrone P, *et al*. Intrapleural thrombolysis for the management of undrained traumatic hemothorax: a prospective observational study. *J Trauma* 2007; 62: 1175–1178.
13. Skeete DA, Rutherford EJ, Schlidt SA, *et al*. Intrapleural tissue plasminogen activator for complicated pleural effusions. *J Trauma* 2004; 57: 1178–1183.
14. Hunt I, Thakar C, Southon S, *et al*. Establishing a role for intra-pleural fibrinolysis in managing traumatic haemothoraces. *J Interact Cardiovasc Thorac Surg* 2009; 8: 129–133.
15. Davies CW, Lok S, Davies RJ. The systemic fibrinolytic activity of intrapleural streptokinase. *Am J Respir Crit Care Med* 1998; 157: 328–330.