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Case report

A not so simple effusion

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ABSTRACT

We describe the case of a patient with an empyema, how it forms and what the evidence behind the treatment options are with specific reference to intrapleural thrombolytic therapy.

1. Case

A 54-year-old lady presented to the acute medical take with progressive dyspnoea over 3 weeks, purulent bronchitis and fevers. She was a non-smoker with no significant medical history.

Clinical examination was consistent with a right sided pleural effusion which was confirmed on PA and lateral chest radiograph (Figs. 1 and 2). C-reactive protein (CRP) was 352 mg/L, white cell count 23×10^9 L with a neutrophilia. Under ultrasound guidance, a chest drain was inserted and fluid analysis revealed a fluid pH of 7.16, Lactate Dehydrogenase (LDH) of 679 U/L (plasma LDH 304 U/L), fluid protein of 52 g/L (plasma protein 82) and fluid glucose of 2.3 mmol/L (plasma glucose 6.2 mmol/L). Gram stain was negative and no organisms were seen.

Two litres of straw coloured fluid drained promptly but, despite regular flushing with 0.9% saline to maintain drain patency, no further drainage occurred. The patient continued to exhibit an inflammatory response despite being on 1.2 g of co-amoxiclav and 400 mg of metronidazole intravenously, thrice daily. Repeat imaging with thoracic ultrasound showed residual pleural collections with marked septations present. A therapeutic intervention was performed culminating in further drainage and considerable clinical improvement. A CT scan of the chest was performed (Figs. 3–5) and the patient discharged home with early follow-up (Fig. 6).

2. Question

What diagnosis is suggested by the pleural fluid analysis?

2.1. Short answer

The analysis is in keeping with an exudative, complicated parapneumonic effusion.

2.2. Long answer

Classically, a pleural fluid protein >30 g/l suggests an exudative cause and <30 g/l a transudative cause. However, it has been known since 1976 that the reliability of absolute values is poor.[1] Hence, the application of Light's criteria is recommended in the interpretation of pleural fluid results.[2]

Pleural fluid is an exudate if one or more of the following criteria are met:

1. Pleural fluid protein divided by serum protein is >0.5.
2. Pleural fluid lactate dehydrogenase (LDH) divided by serum LDH is >0.6.
3. Pleural fluid LDH >2/3 the upper limits of laboratory normal value for serum LDH.

Light's criteria are nearly 100 percent sensitive at identifying exudates, but approximately 20 percent of patients with pleural effusion caused by heart failure may fulfil the criteria for an exudative effusion after receiving diuretics.[3]

An empyema is defined as pus in the pleural cavity. In this case the fluid was straw coloured but the clinical suspicion of pleural space infection was high. Therefore pH analysis was undertaken.

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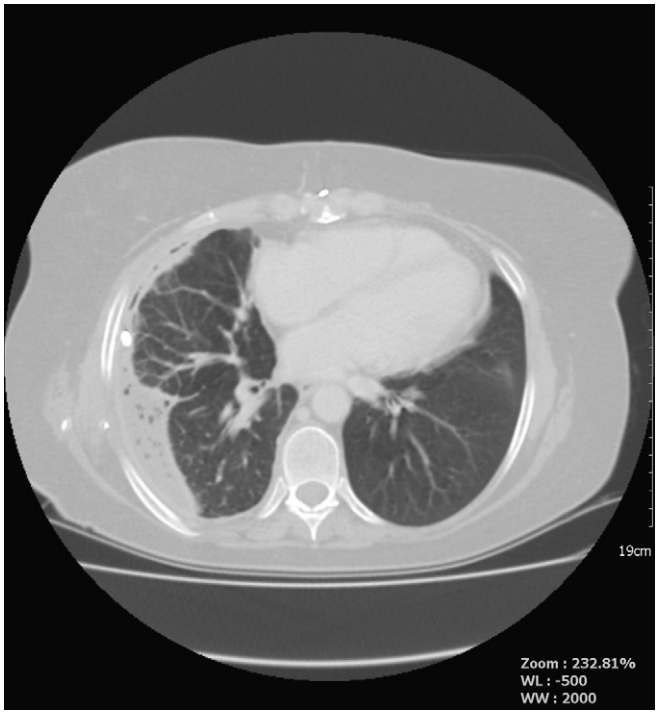

Fig. 1. CT scan showing a pleural collection of fluid and gas with pleural enhancement in keeping with presumed infection in the pleural space (empyema).

Pleural fluid acidosis is a marker of increased metabolic activity due to an increase in lactic acid and carbon dioxide production.[4] Increased consumption of glucose occurs also such that the pleural fluid glucose concentration is low.[5] Pleural fluid acidosis can also be associated with malignancy and connective tissue disease and should therefore be interpreted with the contemporary clinical picture.

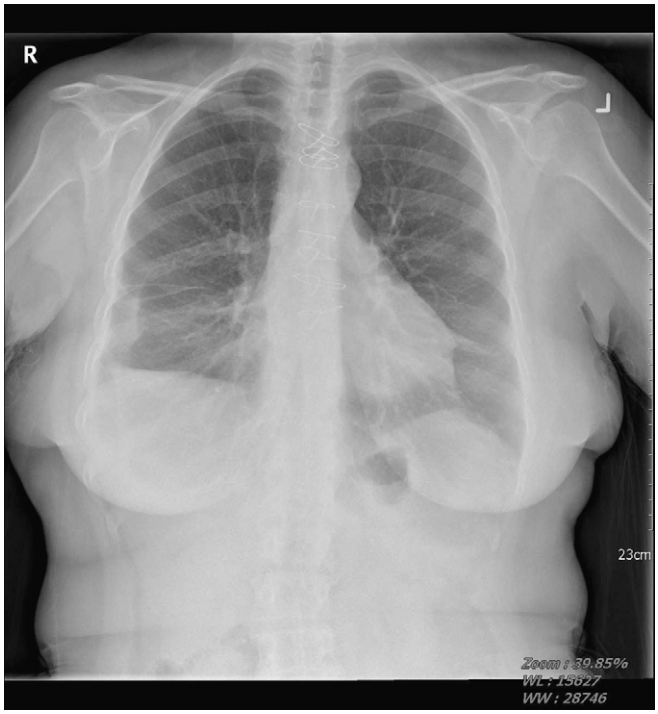

Fig. 2. CT scan showing a pleural collection of fluid and gas with pleural enhancement in keeping with presumed infection in the pleural space (empyema).

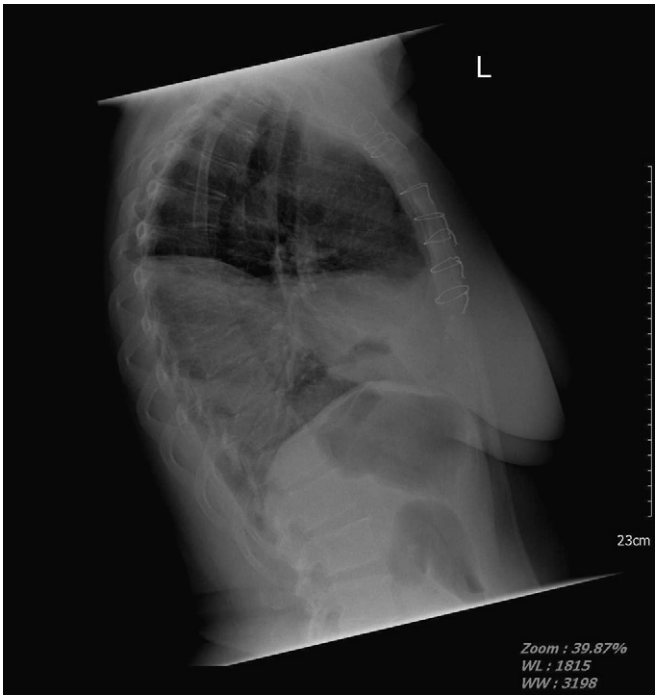

Fig. 3. CT scan showing a pleural collection of fluid and gas with pleural enhancement in keeping with presumed infection in the pleural space (empyema).

More importantly, a meta-analysis of studies examining pleural pH and the need for chest tube drainage or surgery in patients with parapneumonic effusions found that a pH < 7.2 was the most specific discriminator of complicated pleural infection and of the need for immediate chest drainage.[6] The current British Society Guidelines[7] support this and indicate that if pH measurement is not possible, a pleural fluid glucose level <3.4 mmol/l may be used as

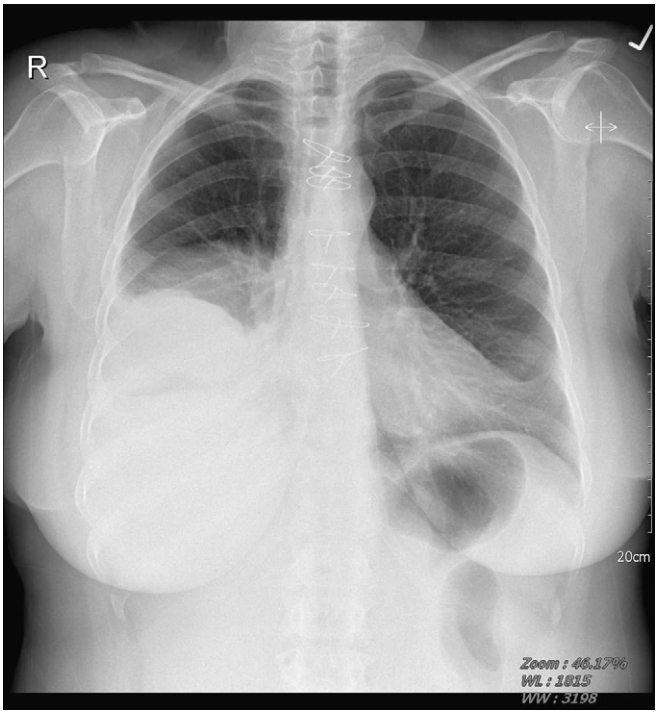

Fig. 4. Follow up film after 2 months showing only minor residual right basal pleural thickening.

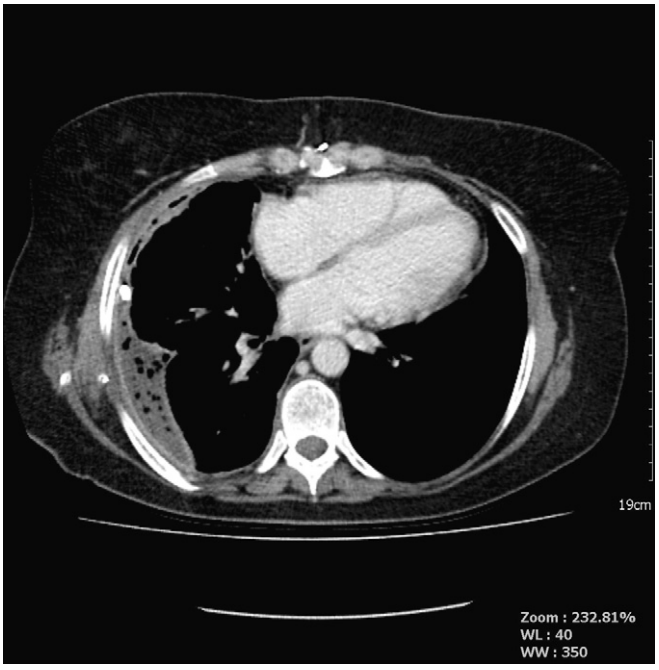

Fig. 5. Right sided pleural effusion.

an alternative marker to indicate a need for chest drain insertion, with the caveat that in certain other conditions like rheumatoid arthritis, the glucose level may be low too.

3. Question

What is the patho-physiology of this type of effusion?

3.1. Short answer

A progressive process occurs as a simple exudate transitions through a fibrino-purulent stage culminating in an organising stage with scar tissue formation.

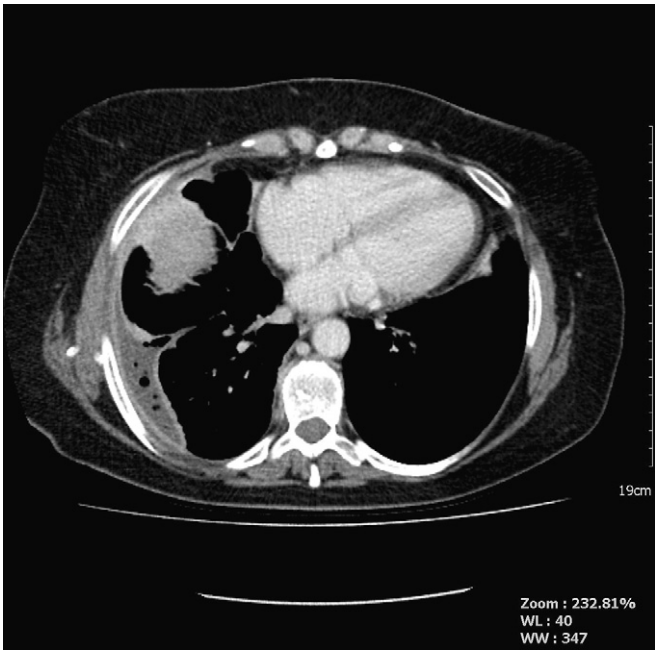

Fig. 6. Right sided pleural effusion.

3.2. Long answer

The normal volume of pleural fluid in humans is less than 1 ml and it forms a thin film between parietal and visceral pleura. In the early inflammatory phase, pro-inflammatory cytokines cause increased vascular permeability leading to fluid shift into the pleural space. This fluid is free flowing and has no bacteria within it. With ongoing damage to the endothelium, bacterial invasion can occur. This promotes further neutrophil migration and progression of the immune reaction. Moreover, there is activation of the coagulation cascade and depressed fibrinolytic activity, which leads to the formation of septations as a result of fibrin deposition.[8] A fibrino-purulent collection follows and is often associated with a paucity of organisms – as few as 25–30% of empyemas are actually culture positive.[7] The organising stage follows as fibroblasts create a solid fibrous pleural peel replacing the soft fibrin. This can prevent the re-expansion of the lung and create a persistent area of pleural thickening.[9]

4. Question

What was our therapeutic intervention?

4.1. Short answer

Intrapleural fibrinolytic drugs (streptokinase 250 000 IU twice daily for 3 days) were given.

4.2. Long answer

In the UK up to 20% of empyema patients come to surgery due to failed catheter drainage and, overall, 20% of patients with empyema die.[10] Intravenous antibiotics and chest tube drainage are the first line treatments. However, as outlined above, infected fluid can become septated and hence resist drainage. A meta-analysis from the Cochrane library[11] evaluated four trials[12–15] and concluded that fibrinolytics reduce hospital stay, shorten the period of fever, produce radiological improvement, and reduce the incidence of treatment failure (defined as death). However MIST 1, a large randomised trial of intrapleural streptokinase, failed to show any benefit in terms of mortality, rates of surgery, radiographic outcomes, or length of the hospital stay.[16] However, all infected effusions were included in this study from many centres with varying experience in their management and it is argued that streptokinase would not work in the effusions in the late organised stage with hard peels.[17] The patients were much older and had many more co-morbidities than in the previous trials. The effusions were also only treated with smaller chest tubes without image guidance. Our centre has considerable experience managing complicated parapenumonic effusions utilising image-guided drainage and intrapleural streptokinase. Streptokinase is adhesiolytic and complexes of streptokinase with human plasminogen can hydrolytically activate other unbound plasminogen to produce plasmin which breaks fibrin down. However, it is not bactericidal and does not reduce viscosity of pus which has a high DNA content from degranulated cells. It is plausible that a combination of agents that reduce pus viscosity (e.g., DNase) and those that break down loculations may be necessary to enhance pus drainage. Rahman et al.[18] found that intrapleural tissue plasminogen activator and DNase therapy improved fluid drainage in patients with pleural infection and reduced the frequency of surgical referral and the duration of the hospital stay. This was a study of 201 patients with pleural infection who received double placebo, intrapleural tissue plasminogen activator (t-PA) and DNase, t-PA and placebo, or DNase and placebo for 3 days. The primary outcome was the change

in pleural opacity and secondary outcomes included referral for surgery, duration of hospital stay, and adverse events.

Our patient had very effective drainage with marked clinical improvement.

5. Question

What was does the CT scan show?

5.1. Short answer

There is a pleural collection of fluid and gas with pleural enhancement in keeping with presumed infection in the pleural space (empyema).

5.2. Long answer

There is a pleural collection of fluid in the lower right thorax (low attenuation indicates fluid). There is pleural enhancement and haziness of the extra-pleural fat indicating inflammation. There are several bubbles of gas within the fluid that have not risen to the top as expected with gravity, indicating loculations within the fluid.

This appearance is in keeping with presumed infection in the pleural space (empyema).

The right sided percutaneous drain is present within the collection, but the tip was located anteriorly with the fluid predominantly postero-lateral. Slight reduction in volume of right lung is in keeping with secondary atelectasis of the lung adjacent to the pleural collection.

The drain was removed and the patient sent home to finish a 6 week course of antibiotics. No organisms were grown from the pleural fluid and she has made a complete clinical and radiological recovery.

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