

Fever in a Patient with a Previous Gastrectomy

A 64-year-old male retiree developed fever, vomiting and lethargy over 1 day. He had a significant past history of gastric adenocarcinoma (stage T3N0) and underwent a laparoscopic proximal gastrectomy with intracorporeal anastomosis 1 year ago, followed by adjuvant chemotherapy. In addition, he had Child's B liver cirrhosis complicated by oesophageal varices which were ligated. On presentation to the emergency department, he had a low grade fever of 37.9°C and was hypotensive with a blood pressure of 70/40 mmHg. Heart rate was 78 beats per minute, respiratory rate was 17 breaths per minute, and oxygen saturation was 98% on room air. He had distended neck veins, muffled heart sounds, and pulsus paradoxus. Abdominal examination was unremarkable.

Electrocardiogram (ECG) documented low electrical voltages with >1 mm saddle-shaped ST-segment elevations in multiple leads (Fig. 1). Bedside echocardiography confirmed a large pericardial effusion with tamponade physiology. On the full blood count, the white cell count was elevated at $14 \times 10^9/L$ with predominance of neutrophils (92%), and C-reactive protein was elevated at 68 mg/L.

In view of persistent hypotension despite multiple fluid boluses, intravenous dopamine was initiated, followed by an urgent pericardiocentesis in the coronary care unit. We aspirated a total of 300 mL of foul-smelling purulent pericardial fluid.



Fig. 1. Electrocardiogram (ECG) performed in the emergency department showing a combination of saddle-shaped ST-segment elevations in the precordial and limb leads, as well as small QRS complexes globally. There is no electrical alternans.

We made the primary diagnosis of purulent pericarditis causing cardiac tamponade. Intravenous (IV) ceftriaxone was started empirically. After pericardial drainage, transthoracic echocardiography (Fig. 2) showed a normal ejection fraction of 60%, and a small to moderate residual pericardial effusion containing echogenic material.

Analysis of the pericardial fluid revealed an exudative picture: fluid glucose was low at <1.1 g/mmol; fluid protein to serum protein ratio was >0.5. Nucleated cell count was high at 50190/ μL , with 96% neutrophils. Gram stain smear showed gram-positive cocci, and occasional gram-negative rods and yeast cells. Acid-fast bacillus stain was negative. Pericardial fluid culture grew multiple micro-organisms which included: a) Methicillin-sensitive *Staphylococcus aureus*, sensitive to cloxacillin; b) *Viridans streptococci*, sensitive to penicillin; c) *Haemophilus parahaemolyticus*, sensitive to amoxicillin/clavulanate; and d) *Candida albicans* – sensitive to fluconazole.

The antimicrobial therapy was thus escalated to a broad-spectrum combination of IV amoxicillin/clavulanate 1.2 g 6-hourly, IV ceftazidime 2 g 8-hourly, and IV fluconazole 200 mg 12-hourly.

The pericardial cytology obtained was highly unusual, demonstrating the presence of squamous cells normally found in the upper oesophagus.

A computed tomography (CT) scan of the thorax was obtained (Fig. 3). It showed non-specific oesophageal thickening, a fluid-filled and distended oesophagus, and a large complicated pericardial effusion with pneumopericardium.

What is/are the most likely underlying cause(s) of purulent pericarditis in this patient?

- Recurrence of gastric carcinoma causing a fistula
- Oesophago-pericardial fistula as a complication of proximal gastrectomy
- Infective endocarditis
- Biliary tract infection
- Myocardial abscess

Answer: A or B

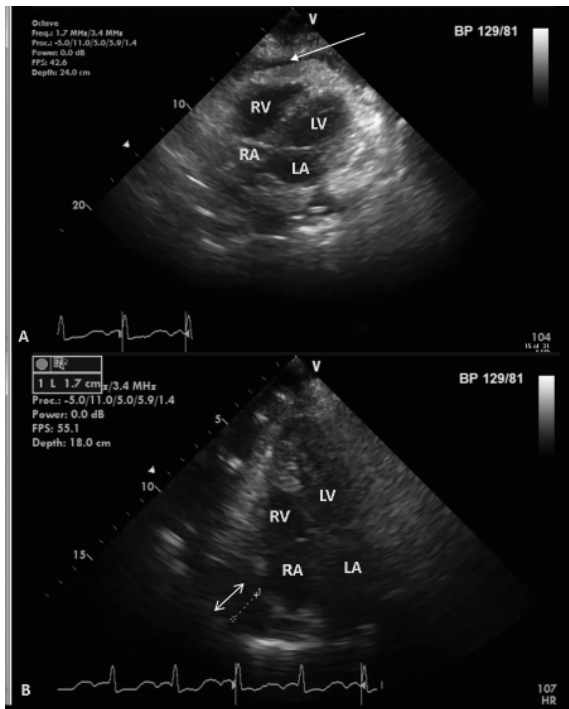


Fig. 2. A) shows the post-pericardiocentesis transthoracic echocardiography with modified apical 4-chamber view. Arrow points to fibrinous deposits within the pericardium, and a small echo-free space anterior to the heart. At B), the transthoracic echocardiography with apical 4-chamber view is shown. Arrow points to small to moderate echo-free space lateral to the right atrium. The pericardium appears irregular due to fibrin deposits.

The upper gastrointestinal surgery team was consulted and the plan was for an oesophagogastrroduodenoscopy when the patient was more stable.

Unfortunately, the patient developed progressive septic shock and disseminated intravascular coagulation not responding to supportive therapy. He demised 5 days into admission. The coroner's report concluded septicaemia with multi-organ failure due to infective pericarditis, on a background history of gastric adenocarcinoma. No postmortem was performed.

Discussion

Purulent pericarditis is defined as a localised infection of the pericardial space with gross pus in the pericardium, or microscopic purulence with more than 20 leukocytes per high power field. Although rare, mortality rates can reach 40% in treated patients.¹

Common predisposing factors, present in our patient, include chronic alcohol abuse, immunosuppression and malignancy.^{1,2} Less than a quarter of cases are attributable to a primary infectious focus, such as pneumonia.²

There are 5 main modes of spread of infection to the pericardial space; most commonly contiguous spread from

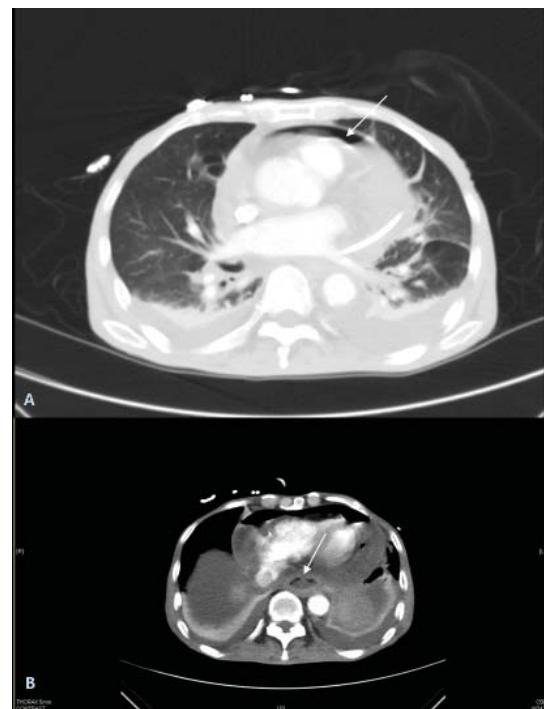


Fig. 3. A) presents the CT thorax (lung window) post-pericardiocentesis showing pneumopericardium (arrow) and a large pericardial effusion with heterogeneously dense appearance, suggesting a complicated effusion. B) presents the CT thorax (abdominal window) showing a fluid-filled oesophagus (arrow) with non-specific thickening without features suggesting possible abscess.

an intrathoracic focus. Other modes of spread include hematogenous, pericardial perforation from injury/surgery, extension from the myocardium, and subdiaphragmatic extension. In our patient, the likely mode of spread is contiguous; either from partial breakdown of surgical gastro-oesophageal anastomosis causing fistulation into the pericardium, or recurrence of the carcinoma invading into the pericardium.

All 4 micro-organisms isolated from our patient's pericardial fluid are common flora of the mouth and nasopharynx. *Staphylococcus aureus* is most common, with up to 36% of cases over a period of 60 years.^{3,4} *Viridans streptococcal* pericarditis may present subacutely, and may originate from mediastinitis caused by oesophageal perforation, thoracic surgery or pneumonia. *Hemophilus parahaemolyticus* is a gram-negative commensal of the nasopharynx. It may cause serious infections such as aspiration pneumonia, but had not previously been described in purulent pericarditis. *Candida* species causing purulent pericarditis are often fatal, especially in immunocompromised and those with previous oesophagogastrrectomy.⁵

Typical symptoms of purulent pericarditis include high fever, tachycardia, cough, and chest pain. However,

presentation may be atypical, such as that in our patient (low grade fever and lethargy).

ECG features include those of acute pericarditis, such as diffuse ST-segment elevation (present in our patient), as well as PR-segment depression in the first 2 weeks. This is followed by normalisation of these segments within 3 weeks, then widespread T-wave inversions and subsequent normalisation. If a large pericardial effusion is present, QRS complexes appear small with voltages of less than 0.5 mV in the limb leads and less than 1 mV in the precordial leads. Electrical alternans may be noted in large effusions. Transthoracic echocardiography will determine the size of the pericardial effusion, but cannot distinguish between purulent collections and sterile inflammatory effusions.

The diagnosis is established by echocardiography-guided pericardiocentesis, yielding a sample with high protein, glucose less than 2 mmol/L, and leukocyte count of 6000 to 240,000 cells/ μ mol.

Immediate management requires urgent pericardial drainage. Pericardiocentesis with percutaneous catheter drainage is quickest; however thick pericardial fluid may loculate, resulting in constrictive pericarditis. Surgical options include pericardiotomy (pericardial “window”) or pericardiectomy (removal of the pericardium). Intrapericardial fibrinolysis is an alternative to surgery, but pericardiectomy is indicated if there is failure of complete drainage despite repeated fibrinolysis attempts.⁶

Initial empiric antibiotic therapy should target *Staphylococcus aureus*, especially in the immunocompromised, with some experts proposing vancomycin, targeting methicillin-resistant *Staphylococcus aureus* (MRSA). Anaerobes and gram-negative bacteria should be targeted if a gastrointestinal origin is suspect. Empiric antibiotic regimens include vancomycin + ceftriaxone, imipenem, piperacillin/tazobactam, or cefepime. Empiric IV fluconazole is usually added in the severely immunocompromised or those with recent intensive care unit (ICU) stay. Further antibiotic adjustments should be guided by pericardial culture. Antibiotic therapy is recommended for 3 to 6 weeks depending on fever resolution and normalisation of white cell count.

Long-term complications include constrictive pericarditis and persistent purulent pericarditis. Pericardiectomy at this stage is difficult due to multiple adhesions.

Oesophago-pericardial fistula is very rare, with fatality up to 76% in the first month.⁷ Most fistulae are from benign oesophageal disease, with a quarter of cases from oesophageal malignancies.⁸ Benign oesophageal causes include ulcers, foreign body perforation, and iatrogenic surgical site breakdown. Clinical symptoms include fever, dyspnoea and retrosternal pain. A systolic “waterwheel” murmur may be heard if pyopneumopericardium develops.^{9,10}

Pneumopericardium is the most common radiologic finding in an oesophago-pericardial fistula, apparent in our patient. An oesophago-pericardial fistula is best demonstrated by oesophagogastroscopy. Administering oral gastrograffin may demonstrate filling of the pericardial sac through the fistula. This is done after adequate pericardial fluid drainage, to prevent cardiac tamponade.¹⁰ CT may also demonstrate gastrograffin in the pericardial space.

We strongly suspected an oesophago-pericardial fistula in our patient because of upper oesophageal pathogens on pericardial fluid culture, and squamous cells on cytology. As he was drowsy, administering gastrograffin would pose an unacceptably high aspiration risk.

Little has been described about treating an oesophago-pericardial fistula. Strategies involve early diagnosis, pericardial drainage, and targeted anti-microbial therapy, then early operative closure of the fistula. Endoscopic stenting may temporarily seal off the fistula before definitive surgery. A recent case report described management of Barrett’s oesophago-pericardial fistula, with temporary oesophageal stenting, closing of the fistula with an autologous pericardial patch and a feeding jejunostomy.¹¹

Conclusion

Clinicians should be aware of the potentially fatal condition of purulent pericarditis. Early diagnosis and drainage is critical. Oesophago-pericardial fistula as the cause should be suspected in a patient with a history of upper gastrointestinal carcinoma and ECG changes of pericarditis.

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Debra GF Seow, ¹*MBBS*, Po Fun Chan, ¹*MBBS, MRCP*,
Boon Lock Chia, ¹*MBBS, FRACP, FAMS*, Joshua PY Loh, ¹*MBBS*,

MMed (Int Med), MRCP

¹Cardiac Department, National University Heart Centre, Singapore

Address for Correspondence: Dr Joshua Loh, Cardiac Department, National University Heart Centre, Singapore, 1E Kent Ridge Road, Level 9, NUHS Tower Block, Singapore 119228.
Email: joshua_py_loh@nuhs.edu.sg