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CASE REPORT
Heart failure

Gas in the myocardium: a fatal presentation of *Clostridium perfringens*: a case report

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Background *Clostridium perfringens* is a well-known cause of gas gangrene with a very high mortality rate. Multiple cases of internal organs have been reported in the literature; however, non-traumatic spontaneous gas gangrene due to *C. perfringens* with solely cardiac involvement in a patient without any risk factors has not been reported before.

Case Summary A 52-year-old male presented to the emergency department with chest pain and exertional dyspnoea for three days. The patient was haemodynamically stable initially, and the physical examination was unremarkable. Initial laboratory workup revealed elevated D-dimer and troponin levels. Computerized tomography (CT) of the chest was negative for pulmonary embolism but showed a hypodense focus in the cardiac silhouette. Acute coronary syndrome protocol was initiated; however, invasive cardiac workup was negative. The patient had rapid clinical deterioration with development of respiratory failure, shock, and multiorgan failure within 24 h. A transesophageal echocardiogram demonstrated an abnormal echogenic focus, corresponding to CT chest area. Despite aggressive treatment, the patient passed away within 36 h. Later, the patient's blood culture grew *C. perfringens*. A limited autopsy showed an abscess cavity in the interventricular septum, pathology of which revealed acute myocarditis and fibrinous pericarditis.

Discussion Unlike other reported cases of *C. perfringens* with cardiac abscess, our patient had no known risk factors, and no other organs were involved. We conclude from this case that an air focus on the CT scan in the myocardium can be suggestive of a spontaneous gas gangrene of the myocardium, and the patients should be treated accordingly.

Keywords Emphysematous • Gas gangrene • Myocardial abscess • *Clostridium perfringens* • Case report

ESC curriculum 2.2 Echocardiography • 2.4 Cardiac computed tomography • 7.3 Critically ill cardiac patient • 2.1 Imaging modalities

Learning points

- Spontaneous gas gangrene with *Clostridium perfringens* can present in an atypical fashion as acute coronary syndrome in patients with solely cardiac involvement.
- In patient with atypical presentation, air density in the myocardium on CT scan should prompt diagnosis of gas gangrene.
- Mysterious, undiagnosed, and understood cases should be investigated by autopsy to clarify the diagnosis and course of diseases.

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Introduction

Clostridium perfringens (*C. perfringens*) is an anaerobic Gram-positive bacillus with five types (A–E) based upon the type of toxin. All these types produce hemolytic α-toxin leading to tissue hypoxia.[1] *C. perfringens* can present with gastroenteritis, necrotizing enteritis, gas gangrene, bacteraemia, and septic shock.[2] Gas gangrene is one of the fatal manifestations that present after trauma or gastrointestinal surgeries; however, spontaneous gas gangrene (SGG) can occur in immunocompromised individuals and patients with colon cancer, leukaemia, and vascular disease.[3] Although *C. perfringens* gas gangrene involving various organs has been reported in the literature, to the best of our knowledge, solely cardiac involvement has never been reported.

We present a case report of a patient who died within 48 h of admission due to septic shock secondary to a myocardial abscess caused by *C. perfringens*.

Timeline

Time	Event
Day 1 admission, 0–3 h	Presented with chest pain, dyspnoea, diaphoresis, fatigue, and chills. Physical examination was unremarkable except borderline heart rate of 100 beats/min. Elevated D-dimer with negative CT scan for pulmonary embolism. CT showed a hypodense area of unknown clinical significance in the cardiac septum. Acute coronary syndrome protocol initiated.
Day 1 admission, 3–12 h	Dynamic ST-T changes and up trending troponins along with worsening chest pain leading to cardiac catheterization which revealed normal coronary arteries. The clinical condition further deteriorated with hypoxia, confusion, and agitation requiring intubated and mechanical ventilation.
Day 1 admission, 12–24 h	The patient developed fever, tachycardia, and hypotension. Lab work showed elevated c-reactive protein, leucocytosis, and lactic acidosis. The septic protocol was initiated with broad spectrum antibiotics. Septic work with CT abdomen and pelvis, lumbar puncture, and microbiology were negative at 24 h. Transoesophageal echocardiogram showed an abnormal area of unknown significance at the interventricular septum.
Day 2 admission, 24–36 h	Despite aggressive therapy with antibiotic, pressors, and ventilation support, the patient developed cardiopulmonary arrest with asystole rhythm and could not survive.
Day 2 admission, 48 h	Blood cultures showed *Clostridium perfringens* growth from the cardiac abscess which was later confirmed by autopsy and histopathology.

Case presentation

A 52-year-old male with a past medical history of morbid obesity, diabetes mellitus, essential hypertension, and hyperlipidemia presented to the emergency department with intermittent chest pain for 3 days. The chest pain was substernal, 8/10 in intensity, dull in character, radiating to the neck and jaw, without aggravating or relieving factors, and was associated with exertional dyspnoea and diaphoresis. Home medications included metformin 500 mg twice a day, lisinopril 5 mg once a day, and atorvastatin 20 mg once a day. The review of systems was pertinent for fatigue, headache, and chills. Upon presentation, the vital signs and physical examination were unremarkable.

Upon further evaluation, the electrocardiogram and chest radiography were unremarkable. The initial laboratory revealed mild anaemia, mild thrombocytopenia, elevated D-dimer of 3.85 mg/L (normal range, 0.19–0.52), and troponin-I of 3.1 ng/mL (normal, <0.06). The temporal trends of laboratory parameters are listed in *Table 1*.

Given elevated D-dimer values and the presence of dyspnoea and chest pain, a computed tomography (CT) of chest was performed which excluded a significant pulmonary embolism; however, it did reveal a hypodense area in the centre of the cardiac silhouette which was reported as a possible artefact vs. the presence of air containing cavity (*Figure 1*).

The patient was admitted with acute coronary syndrome (ACS) protocol and pharmacotherapy with aspirin, statin, beta-blocker, intravenous nitroglycerin, and unfractionated heparin was initiated. Within the following few hours, the patient developed worsening chest pain, dyspnoea, and hypoxia requiring 4–5 liters of oxygen through a nasal cannula. A repeat electrocardiogram showed diffuse ST depressions, elevations in aVR and V1, and elevated troponin-I of 4.8 ng/mL. Emergency cardiac catheterization (see Supplementary material online, *Figure S1*) revealed non-obstructive coronary artery disease and normal ejection fraction with elevated end-diastolic pressure of 32 mmHg.

During the procedure, the patient's condition deteriorated with worsening hypoxia, confusion, and agitation requiring endotracheal intubation. Over the next 12 h, the patient had temperature spikes up to 39.1° C, tachycardia with heart rate above 140 bpm, and hypotension with mean arterial pressure less than 50 mmHg. The septic shock protocol which included intravenous fluids administration at 30 mL/kg and broad-spectrum antibiotics was initiated after the blood, urine, and sputum cultures were drawn. The patient was started on anti-microbial therapy including anaerobic coverage with vancomycin, aztreonam, and metronidazole. Prophylactic antiviral therapy with acyclovir was also given for possible encephalitis.

Further investigation revealed an elevated C-reactive protein of 30 mg/dL (normal, <0.9), leucocytosis, lactic acidosis, and worsening kidney functions. A transoesophageal echocardiogram (TEE) was negative for infective endocarditis but demonstrated an abnormal echogenic focus of unknown significance in the mid and basal septal wall (corresponding abnormal area of the CT chest) (*Figure 2*; see Supplementary material online, *Videos S1* and *S2*). CT abdomen and pelvis with contrast was negative for any focus of infection. The lumbar puncture had elevated total white blood cell count (18, normal range 0–7) but was negative for bacterial or viral growth suggestive of cerebritis. Blood, urine, and sputum cultures were negative after 24 h from admission.

Despite aggressive treatment modalities with antibiotics, pressor support, and mechanical ventilation, the patient continued to deteriorate with multi-organ failure. The patient developed cardiopulmonary arrest with asystole rhythm and could not survive.

The following day, the patient's blood culture grew *C. perfringens*, which opened questions regarding the source of infection and the presence of an abnormal area of focus on imaging modalities.

Table 1 Trends in laboratory tests

Lab value	Trends
Haemoglobin (g/dL)	9.5 > 9.8 > 9.9 > 9.5
White cell count ($\times 10^9$ per mm^3)	8 > 12.5 > 20.8 > 27.1
Platelets (10^9/L)	89 > 63 > 97 > 109
BUN (mg/dL)	32 > 55/71/89/86
Creatinine (mg/dL)	1.5 > 3.37 > 3.7 > 4.7 > 5.13
Sodium (mEq/L)	139 > 142 > 143
Potassium (mE/L)	4.7 > 4.5 > 4.9 > 5.3
CRP (mg/L)	27
ALT (IU/L)	93 > 82 > 94 > 94 > 71
AST (IU/L)	65 > 124 > 181 > 185 > 154
Bilirubin (mg/dL)	2.8 > 4.5 > 6.5 > 4.3 > 4.2
Lactic acid (mmol/L)	2.6 > 2.4 > 3.7 > 2.4 > 2.1 > 3.3 > 4.3 > 8.2
D-dimers (mcg/mL)	3.85
Troponins I (ng/mL)	4.7–18.8–18.8–12.8
Cerebrospinal fluid total WBC (<3)	18
	(Polymorphonuclear lymphocytes 95%, lymphocytes 0%, monocytes 5%, eosinophils 0, basophils 0%)
Cerebrospinal fluid glucose (45–63 mg/L)	213 mg/dL
Cerebrospinal fluid protein (18–45 mg/dL)	31 mg/dL
Cerebrospinal fluid culture	No growth

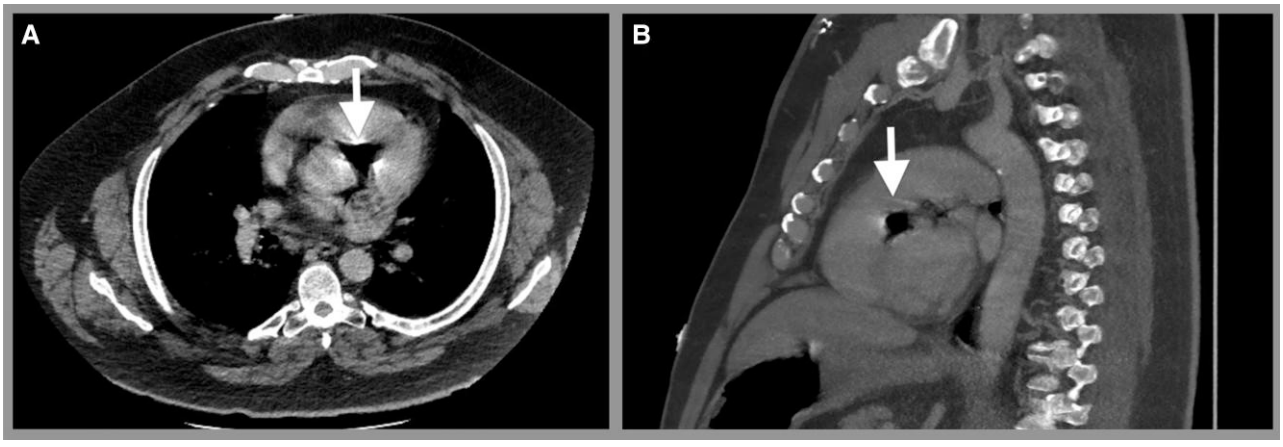

Figure 1 Computerized tomography scan showing an abnormal hypodense area in the centre of the cardiac silhouette.

Therefore, we requested an autopsy after a discussion with the family. The cardiac autopsy revealed an abscess containing cavity in the interventricular septum, communicating both with the right and left ventricles (*Figure 3*). The pathology of the myocardium showed significant neutrophils in the interstitium, abscess formation, and active myocyte damage consistent with acute myocarditis. The pericardium had extensive deposition of the fibrin admixed with neutrophils consistent with fibrinous pericarditis (*Figure 4*). No other finding known to be associated with increased risk of gas gangrene was noted on autopsy. Moreover, a retrospective discussion of the CT chest with the radiologist concluded that the hypodense air density lesion in the heart was most likely an emphysematous abscess of the interventricular septum.

Discussion

Gas gangrene caused by *C. perfringens* is a fatal necrotizing infection that usually occurs after a trauma or surgery. Cases of SGG are usually caused by *C. septicum*; however, *C. perfringens* has also been reported to be the cause.[3] The disease spreads rapidly and can present within 6–8 h after the trauma. It can spread several centimeters in the surrounding tissues and multiple organs within minutes to hours (see Supplementary material online, *Table S1*).[3] The rapid spread is generally referred to as the fast growth cycle of *C. perfringens* (8–10 min), which is accompanied by gas production.[4]

The presence of a prosthetic valve can be a risk factor in people with *C. perfringens* infective endocarditis,[5] but the exact mechanism of

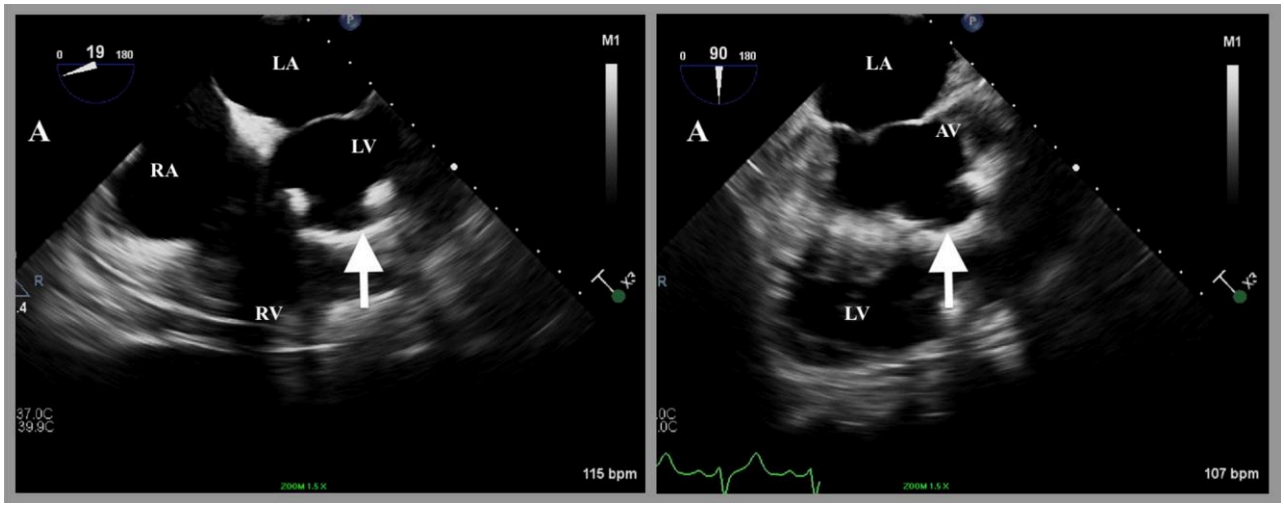

Figure 2 Transoesophageal echocardiogram showing an abnormal cavity at basal and mid inter ventricular septum.

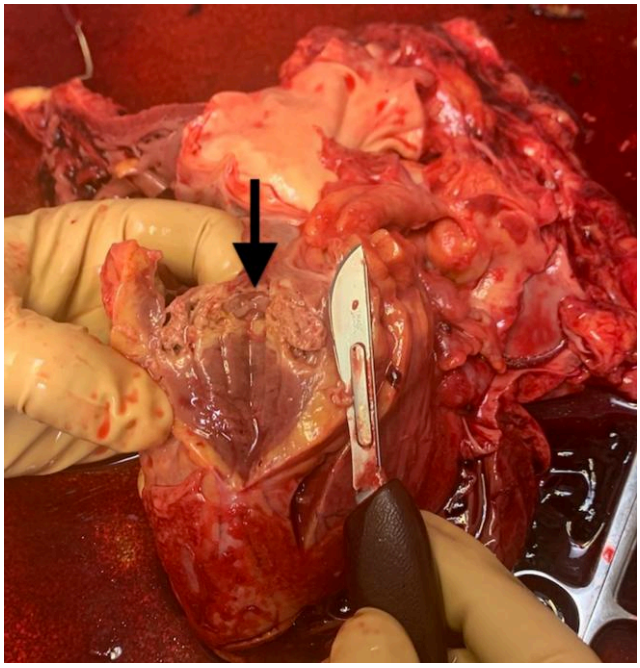

Figure 3 Pathological specimen of the heart showing infectious cavity at the level of interventricular septum.

myocardial involvement is not known. Immunosuppression is one of the risk factors in disseminated infections caused by *C. perfringens*.[6] Our patient was middle-aged and had no risk factors.

The presentation of SGG usually depends on the organ involved.[3, 4] In our patient, ACS was the main presentation likely due to solely cardiac involvement. Keese *et al.*[3] reported another case of SGG with ACS presentation; however, the first presentation was pain and swelling in the groin, leucocytosis, and elevated inflammatory markers which were not present in our patient. That patient also developed arrest within 48 h and was found to have emphysematous abscesses in multiple organs.

Roberts *et al.*[7] reported a series of 17 patients with *C. perfringens* septicemia, 9 of which had cardiac involvement. This study also highlighted that patients with a history of chemotherapy, steroids, and long-term antibiotics use were more prone to have disseminated infections.

Early surgical debridement and antibiotic therapy are the mainstays of treatment to prevent complications and decrease mortality.[8] Penicillin plus tetracycline or clindamycin are the definitive treatment in this setting once a diagnosis is confirmed. Metronidazole has shown anti-microbial activity against *C. perfringens* in in-vitro settings; however, no human studies are available.[8] Our patient did receive metronidazole, but penicillin was not part of the therapy due to atypical presentation.

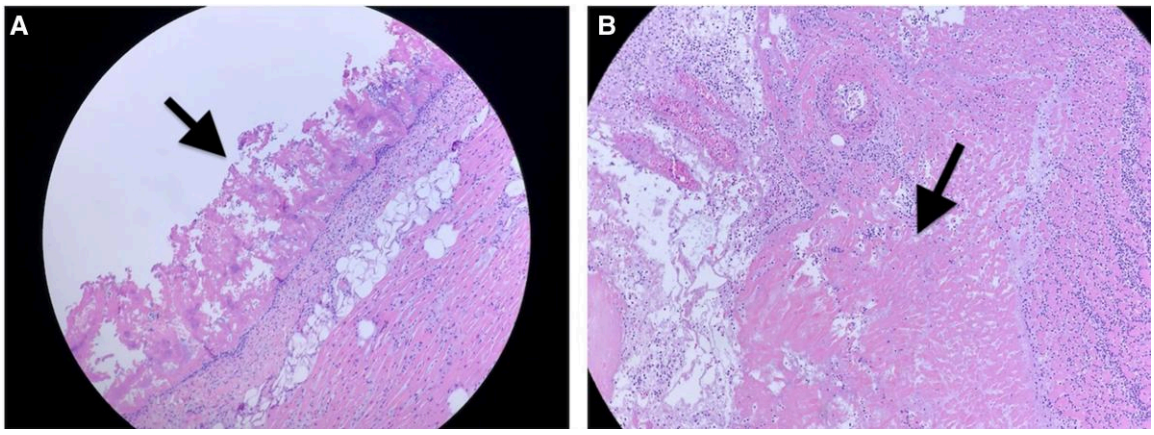

Figure 4 The pericardium pathological examination showed an extensive deposition of the fibrin admixed with neutrophils consistent with fibrinous pericarditis (*A*). The pathology of the myocardium showed significant neutrophils in the interstitium, abscess formation, and active myocyte damage consistent with acute myocarditis (*B*).

SGG has high mortality range between 67% and 100%, with most of the deaths within the first 24 h.[9]

Conclusions

SGG can also present with solely cardiac involvement. In patients with an atypical presentation, an air-containing cavity on CT and TEE should be considered highly suspicious for emphysematous infection. Prompt diagnosis and treatment may prevent fatal outcomes.

Lead author biography

Hafiz Muhammad Waqas Khan, MD, is a cardiovascular disease fellow at Michigan State University/McLaren. He earned his Bachelor of Medicine and Surgery degree from Kind Edward Medical University, Pakistan. After completion of medical school, he pursued his career in USA and joined cardiovascular disease fellowship programme after completing Internal Medicine residency. He is soon starting his Interventional Cardiology at Icahn School of Medicine at Mount Sinai Morningside and plan to subspecialize in Structural Heart Disease in the future.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including imaging and associated text has been obtained from the patient's family in line with COPE guidance.

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References

1. Sakaue M, Ota K, Nakamura E, Nitta M, Oka M, Oishi Y, *et al.* Type A fulminant *Clostridium perfringens* sepsis indicated RBC/Hb discrepancy; a case report. *BMC Infect Dis* 2019;**19**:719.
2. Fujita H, Nishimura S, Kurosawa S, Akiya I, Nakamura-Uchiyama F, Ohnishi K. Clinical and epidemiological features of *Clostridium perfringens* bacteremia: a review of 18 cases over 8 year-period in a tertiary care center in metropolitan Tokyo area in Japan. *Intern Med* 2010;**49**:2433–2437.
3. Keese M, Nichterlein T, Hahn M, Magdeburg R, Karaorman M, Back W, *et al.* Gas gangrene pyaemia with myocardial abscess formation–fatal outcome from a rare infection nowadays. *Resuscitation* 2003;**58**:219–225.
4. Stevens DL, Bryant AE. The role of clostridial toxins in the pathogenesis of gas gangrene. *Clin Infect Dis* 2002;**35**:S93–S100.
5. Huang CY, Wang MC. *Clostridium perfringens* bacteremia associated with colorectal cancer in an elderly woman. *Turk J Gastroenterol* 2020;**31**:960–961.
6. Kitterer D, Braun N, Jehs MC, Schulte B, Alscher MD, Latus J. Gas gangrene caused by *Clostridium perfringens* involving the liver, spleen, and heart in a man 20 years after an orthotopic liver transplant: a case report. *Exp Clin Transplant* 2014;**12**:165–168.
7. Roberts WC, Berard CW. Gas gangrene of the heart in Clostridial septicemia. *Am Heart J* 1967;**74**:482–488.
8. Lorber B. Gas gangrene and other Clostridium-associated diseases. In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and Practice of Infectious Diseases*. 6th ed, Philadelphia: Churchill Livingstone 2005. p. 2828
9. Nordkild P, Crone P. Spontaneous clostridial myonecrosis. A collective review and report of a case. *Ann Chir Gynaecol* 1986;**75**:274–279.
10. Rives C, Chaudhari D, Patel P, Swenson J, Reddy C, Young M. *Clostridium perfringens* liver abscess complicated with bacteremia: 836. *Am Coll Gastroenterol* 2015;**110**:S363.
11. Mishra R, Sinha N, Duncalf R. Beta lactamase producing *Clostridium perfringens* bacteremia in an elderly man with acute pancreatitis. *Case Rep Crit Care* 2016;**2016**:7078180.
12. Yong CH, Lam M. Discitis and *Clostridium perfringens* bacteraemia. *BMJ Case Rep* 2017;**2017**:bcr2017220646.
13. Jing HD, Li L, Tian JY, Jiang DP. Clostridium septicum-induced gangrene in the right lower extremity complicating pneumatosis in the right ventricle and the pulmonary artery and occlusion of right femoral artery: a case report. *BMC Infect Dis* 2021;**21**:957.