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Case Reports and Series

A case of invasive meningococcal disease presenting as myopericarditis

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ABSTRACT

Background: Neisseria meningitidis is a universally-feared Gram negative diplococcus, and infection confers high rates of morbidity and mortality despite effective antimicrobial therapy. Invasive meningococcal disease most commonly presents with meningococcaemia or meningococcal meningitis.
Case report: 72-year-old female, previously fit and well, was admitted with chest pain, and associated breathlessness and diarrhoea. The clinical picture was of a myopericarditis.
Results: Initial electrocardiogram (ECG) changes and elevated troponin were consistent with myopericarditis. *Neisseria meningitidis* W135 was cultured from blood, and subsequently from cerebrospinal fluid (CSF). Leptomeningeal meningitis and ventriculitis was evident on magnetic resonance imaging (MRI) of the brain. Treatment was commenced with intravenous ceftriaxone. The clinical course was complicated by pneumonia, influenza A infection, and fatal pulmonary embolism.
Conclusions: This case demonstrates the range of clinical features of invasive meningococcal disease, highlighting in particular that meningococcal bacteraemia can present clinically as myopericarditis, which may be present in a substantial proportion of cases. Prompt antimicrobial therapy, as well as an awareness of potential complications, are paramount in the clinical management of meningococcal myopericarditis.

Introduction

Neisseria meningitidis is a Gram-negative, aerobic, encapsulated diplococcus bacterium, first isolated and characterised in 1887 by Weichselbaum (Weichselbaum, 1887), and the causative organism for meningococcal disease, initially described by Vieusseux (Vieusseux, 1805) in 1805. Non-pathogenic *N. meningitidis* is carried asymptomatically in the nasopharyngeal tissues of 8–25% of healthy adults, with respiratory droplet spread, and thirteen capsular serogroups are known to exist; for the most part, carriage does not result in disease (Read, 2019; Stephens et al., 2007; Stephens, 2009). There is variable meningococcal disease incidence dependent on epidemic and endemic transmission (particularly in areas of overcrowding), and immunity derived from vaccination campaigns, amongst other potential risk factors (Read, 2019; Stephens et al., 2007; Stephens, 2009; Rosenstein et al., 2001). In the UK, invasive meningococcal disease due to serogroup C is diminishing due to widespread vaccination, with 80% of clinical cases due to serogroup B, and an increase since 2009 of serogroup W-135 cases (England, 2016). W-135 outbreaks were associated with pilgrims returning from the Hajj in 2000 (Stephens et al., 2007). Preventive vaccines now exist for *N. meningitidis* serogroups A, B, C, X, Y and W-135 (Read, 2019). The 2016 schedule provides recommendations for routine childhood vaccination and immunisation of at-risk individuals (England, 2016).

Invasive meningococcal disease (IMD) carries a high morbidity and mortality, and may present not just with "textbook" signs of meningitis, but also with cardiac and rheumatological complications (Stephens et al., 2007; Rosenstein et al., 2001). Here we present a fatal case of invasive meningococcal disease presenting as myopericarditis, with several other complications illustrative of severe disease.

Case report

A 72-year-old Caucasian female, previously fit and well with no documented medical co-morbidities and no history of tobacco smoking, presented by ambulance to a tertiary heart attack treatment centre in a UK hospital with a 4-hour history of gradual-onset central chest pain, described as a feeling of pressure, worsened on inspiration and on

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changing positions. The patient also reported 2 days of fatigue, loss of appetite, vomiting, diarrhoea, and some abdominal discomfort.

Initial bloods showed Hb 123 g/L, WCC 5.7 $\times$ 10^9 cells/L, platelets 298 $\times$ 10^9/L eGFR 29 mL/min, urea 16.4 mmol/L, and C-reactive protein of 500 mg/L, HIV serology negative. Electrocardiogram showed widespread saddle ST-segment elevation, and troponin-I rose from 13 to $>$ 10,000 ng/mL over the first 24 h of admission (Fig. 1). Transthoracic cardiac V-scan on day 1 showed no abnormalities, and on day 10 showed a small global pericardial effusion with preserved left ventricular ejection fraction.

The patient was noted to be mildly confused, presumed secondary to delirium, and developed a fever of 38.3 °C at 6 h post-admission. Computed tomography (CT) brain imaging showed no acute intracranial pathology. Blood cultures were taken and empirical ceftriaxone 2 g IV once daily and metronidazole 500 mg IV three times daily were commenced to cover infection of unknown origin; 36 h post-admission, the blood cultures grew *Neisseria meningitidis.* The isolate was sent to the national reference laboratory and identified as *N. menigitidis* W135 type 2a. The ceftriaxone dose was increased to 2 g IV twice daily and metronidazole stopped.

The patient's confusion worsened and cerebrospinal fluid (CSF) was collected by lumbar puncture (day 7), which showed 298 WBCs/cm^3 (70% polymorphs, 30% mononuclear cells), glucose 2.3 mmol/L (low compared with serum glucose), total protein of 1.48 g/L (raised) and LDH 142 IU/L. Magnetic resonance imaging (MRI) of the brain (day 20) showed meningitis with leptomeningeal involvement and ventriculitis. She was noted to be thrombocytopenic on day 2 (platelet count 60 $\times$ 10^9/L), but this resolved by day 7 and low molecular weight heparin (LMWH) at a thromboprophylactic dose was commenced (day 11).

On day 14, after 13 days of ceftriaxone, the patient developed a cough and fever; ceftriaxone was stopped, and she was commenced on a 5-day course of piperacillin/tazobactam IV 4.5 g three times daily to cover hospital-acquired pneumonia. A respiratory swab was positive for influenza A (hospital-acquired), and she was treated with 5 days of oseltamivir 75 mg orally twice daily. Her oxygen requirement and inflammatory markers continued to worsen (WCC 15x10^9/mL, CRP 200). Chest X-ray showed bilateral pleural effusions and upper zone patchy infiltration. Piperacillin/tazobactam 4.5 g IV three times daily was recommenced and a left-sided chest drain was inserted. Despite these interventions, she continued to deteriorate and on day 31, was transferred to the intensive care unit, where she required intubation and ventilation. CT angiogram (Fig. 2) showed extensive bilateral pulmonary emboli with evidence of right heart strain. Thrombolysis was unsuccessful and the patient died the same day. A timeline summary of events during admission is shown in Fig. 3.

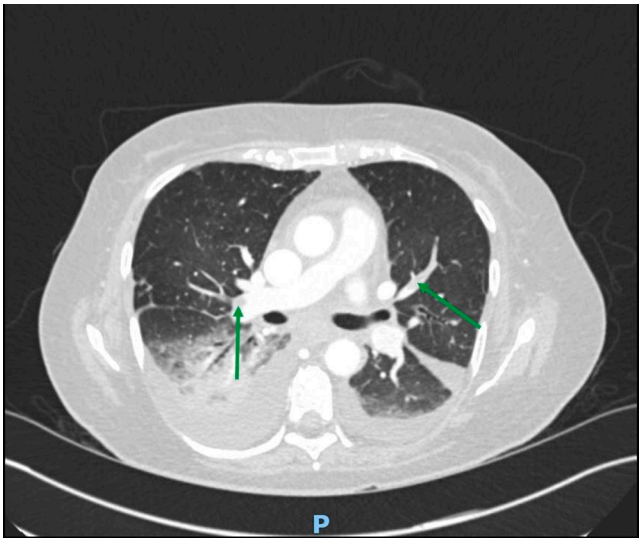

Fig. 2. CT angiogram (day 31) showed extensive bilateral pulmonary emboli (arrows) with evidence of right heart strain.

Discussion

In the majority of cases (80–85%), meningococcal infection presents with meningism; the remaining 15–20% mostly present with bacteraemia or pneumonia. Pericarditis, urethritis, conjunctivitis and arthritis remain rare presentations (Al-Tawfiq et al., 2010). In our case, the patient presented with myopericarditis. Prior to antibiotic therapy, meningococcal disease resulted in a 70% mortality; despite treatments, death rates remain high at 9–12%, and up to 40% in meningococcaemia (Rosenstein et al., 2001). Various host susceptibility factors exist for invasive disease, particularly defects in the mannose-binding lectin (MBL) pathway and complement cascades (deficiencies of which may be present in up to 20% of affected adults), as well as instances of immunosuppression as with hypo- or asplenism, tobacco smoking, nephrotic syndrome, hypogammaglobulinaemia, and HIV infection (Stephens et al., 2007; Stephens, 2009). Respiratory tract infections including influenza may increase susceptibility to invasive meningococcal disease through direct mucosal damage; (Stephens, 2009) but in this case meningococcal infection preceded influenza. Even in vaccinated adults

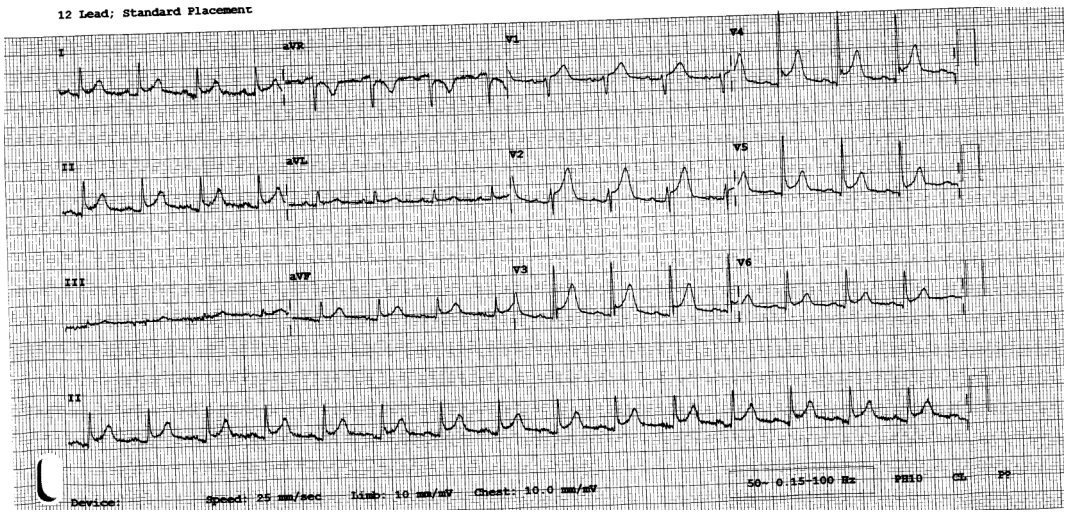

Fig. 1. ECG on admission (Day 1).

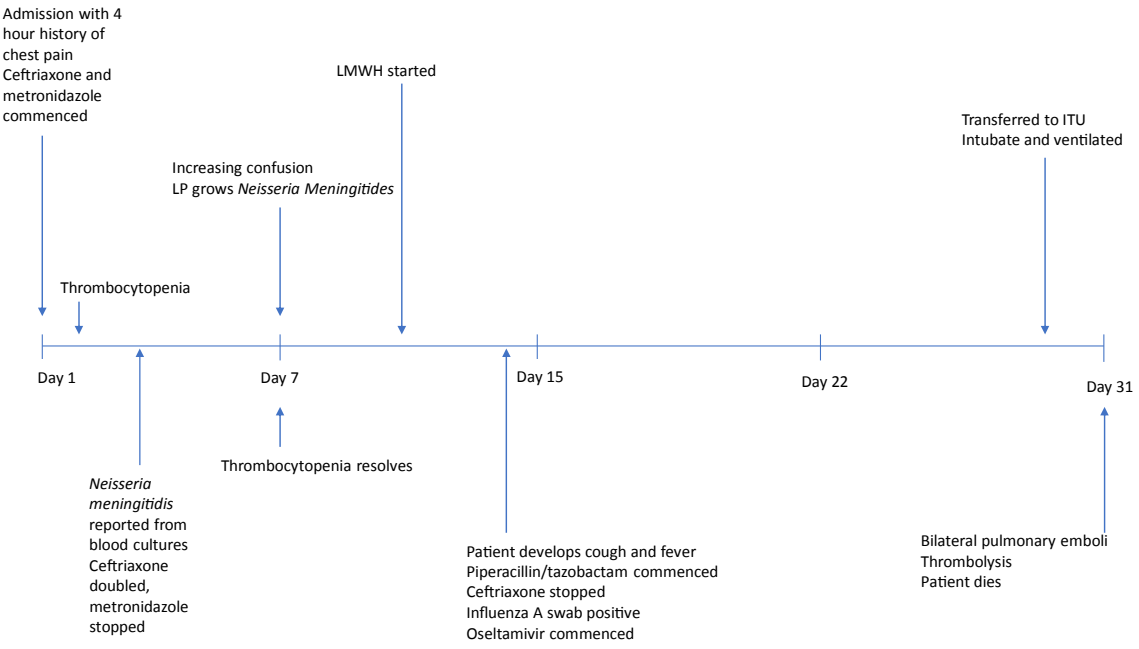

Fig. 3. Timeline of events post-admission (Day 1).

with putatively-protective meningococcal antibody levels, infection may still occur and immunity wane (Stephens, 2009). In this case, further workup of the patient to identify such risk factors would have been prudent had they survived.

Meningococcal bacteraemia presenting with primary myopericarditis is rare, with 7 clear cases published (Dawson et al., 2018). Myopericarditis classically presents with dyspnoea and pleuritic chest pain, extant in this case; heart sounds may be muffled, and a pericardial friction rub heard on auscultation (Finkelstein et al., 1997). In a previous report on meningococcal myocarditis, pathological examination demonstrated a haemorrhagic fibrinous exudative pericardial effusion, myofibril destruction and necrosis, and intracellular Gram-negative diplococcic (Saphir, 1936).

A classification of the aetiology of pericarditis in meningococcal disease has been proposed by Finkelstein *et al.* (Finkelstein et al., 1997):

- *Disseminated meningococcal disease with pericarditis* (DMP), with early haematogenous spread and direct bacterial pericardial invasion.
- *Isolated meningococcal pericarditis* (IMP), with positive identification of *N. meningitidis* in purulent pericardial fluid or blood culture, without signs of meningococcaemia or meningitis.
- *Reactive meningococcal pericarditis* (RMP), an immune-complex mediated inflammatory reaction that can lead to cardiac tamponade and aseptic inflammation elsewhere (such as the pleura, joints and skin), and which is difficult to treat.

In our case, the initial presentation was consistent with DMP, with subsequent deterioration due to RMP and/or alternative pathology (bacterial superinfection, post-viral changes, pulmonary embolism, cardiac failure). Such crossover between the above three categories of meningococcal myopericarditis has been previously described. One case described a patient with *N. meningitidis* infection, where both direct myopericarditis (*Neisseria menigitidis* PCR positive pericardial aspirate) and also a prolonged steroid-responsive post-infective inflammatory syndrome was reported (Keeley et al., 2018). Immune-mediated reactive post-meningococcal pericarditis may still rarely recur despite appropriate therapy, and may be more severe than the initial episode (Akinosoglou et al., 2016).

Meningococcal myopericarditis is under-diagnosed, likely due to under-recognition of the complication (Dawson et al., 2018). It carries an extremely poor prognosis with high mortality, (Bouneb et al., 2018) and is histopathologically identified in a significant proportion of fatal cases of invasive meningococcal disease. Hardman & Earle (Hardman and Earle, 1969) found a prevalence of myocarditis of 78% among 200 fatal cases of meningococcal infection, with more indication of severe features (necrosis) in adults than children. A Brazilian study found myocarditis in 41.9% of cases of childhood death from meningococcal disease (Garcia et al., 1999).

Meningococcal disease is feared due to the potential for abrupt deterioration, despite management guidelines detailing principles of investigation and treatment (Stephens et al., 2007; McGill et al., 2016). Clinical management of meningococcal myopericarditis involves early antibiotic use; appropriate exclusion of cardiac tamponade, and drainage if required; confirmatory sampling if advised; and careful attention to the haemodynamic state of the patient throughout their disease course (Keeley et al., 2018). An awareness of the potential reactive sequelae is required to plan for management of decompensation.

Meningococcaemia can cause impaired fibrinolysis, consumption of clotting factors, and thrombocytopaenia, as here; and vascular endothelial dysfunction promotes thrombosis, which in this instance proved fatal (Stephens et al., 2007). Anticoagulation treatment has not been shown to improve outcomes in invasive meningococcal disease (Stephens et al., 2007). Capillary leak with extravascular shifts of albumin and water, vasodilatation, and reduced myocardial function result in circulatory collapse, (Stephens et al., 2007) and contributed to the severity of this case.

In summary, this case reminds the physician that invasive meningococcal disease may present as myopericarditis. Further studies are required to determine the degree to which myopericarditis may be a presenting feature of invasive meningococcal disease in the present day. In all such cases, prompt antimicrobial administration and careful monitoring, as well as an awareness of potential complications, are required to guide patient care.

CRediT authorship contribution statement

Simon M. Durkin: Writing - original draft, Writing - review & editing. **Clemency Britton:** Writing - original draft, Writing - review & editing. **Graham S. Cooke:** Conceptualization, Writing - review &

editing, Supervision. **Ravi Mehta:** Conceptualization, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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