Unusual association of diseases/symptoms

Salmonella enteritidis induced myocarditis in a 16-year-old girl

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Correspondence to Dr Lucy Childs, lucychilds@doctors.org.uk**Summary**

Myocarditis typically presents with non-specific clinical symptoms, and can easily be missed in the absence of a high index of clinical suspicion. Myocarditis caused by bacterial pathogens is rare in immunocompetent individuals, more commonly seen following viral infection. Although more classically associated with typhoid fever and gastroenteritis, *Salmonella* species are a rare cause of myocarditis. We report a case of *Salmonella enteritidis*-induced myocarditis after gastrointestinal infection in a 16 year-old girl, and discuss the diagnostic tools currently utilised to ascertain the diagnosis.

BACKGROUND

Myocarditis is defined as inflammation of the heart muscle. It often presents with a variety of non-specific symptoms, which can hinder diagnosis. Causative agents commonly include viruses, classically Coxsackie and adenovirus infections in the UK and Europe, infrequently, bacterial infections are implicated. *Salmonella* species remain a rare cause of myocarditis. We discuss the diagnostic strategies that may aid the clinician to establish a diagnosis, and also highlight this rare disease as one not to miss.

CASE PRESENTATION

A 16-year-old girl presented to accident and emergency with a 3-day history of profuse watery diarrhoea, vomiting and fever. She also described anorexia and mild dyspnoea. Four days prior to admission she had eaten at a fast-food restaurant with her family. Two family members also experienced mild diarrhoea and nausea following the meal; however, their symptoms were short lived. No blood was found in her stool, and no other systemic symptoms were present at this time.

On further questioning she had no recent travel, and was usually fit and well. She took no regular medications and had no significant family history of bowel disease or other illness.

On examination the girl was clinically dehydrated and pyrexial at 37.9°C. She was tachycardic (102 beats/min), and tachypnoeic (respiratory rate 24 breaths/min) with oxygen saturations of 95% on room inspired air (figure 1). She had fine bilateral crepitations in the lung bases, and mild peripheral ankle oedema bilaterally. Mild epigastric abdominal tenderness was present with highly active bowel sounds, but no associated guarding or rigidity.

The differential diagnoses at this point included: bacterial gastroenteritis, viral gastroenteritis, inflammatory bowel disease and more broadly sepsis with systemic inflammatory response syndrome.

INVESTIGATIONS

Initial blood tests showed Hb 9.6 g/dl (MCV 87.4×10^9 /l), WCC 10.4×10^9 /l (neutrophils 9.2×10^9 /l), CRP 206 mg/l, Na 140 mmol/l, K 4.4 mmol/l, Cr 120 mmol/l, Ur 6.2 mmol/l and liver function was normal. Arterial blood gas analysis on 4L O₂ showed: pH 7.45, pO₂ 7.3, pCO₂ 2.2, BE -9, HCO₃ 14.5. Her admission ECG demonstrated sinus tachycardia but was otherwise unremarkable. An abdominal radiograph demonstrated a normal bowel gas pattern. Review of the admission chest x-ray revealed loss of the costophrenic angles bilaterally and mild bilateral pulmonary alveolar infiltrates consistent with pulmonary oedema. Blood culture was sterile after 48 h; however, her stool culture confirmed *Salmonella enteritidis* infection.

TREATMENT

Initial management was with careful intravenous fluid rehydration. Over the following 12 h the patient clinically deteriorated. She became increasingly tachypnoeic and tachycardic, and developed oliguria (urine output 10–20 ml/h). Reassessment revealed her to be hypoxic, with a pO₂ of 7.3, pCO₂ 2.2, BE -9, pH 7.45 (on 4LO₂ via nasal cannulae). A Repeat ECG demonstrated significant change compared with her admission ECG, with the development of deep 'T'-wave inversion throughout the antero-lateral chest leads and a continuing tachycardia (figure 2). Her troponin was 'intermediate' measuring 50–100 ng/l. A repeat chest radiograph demonstrated gross pulmonary oedema and bilateral pleural effusions (figure 3). An urgent bedside echocardiogram (ECHO) visualised a dilated left ventricle with globally reduced systolic contractility, mild mitral regurgitation, tricuspid regurgitation and a small pericardial effusion. Her IV ejection fraction was mildly impaired at 47% (normal=>55%). A diagnosis of *Salmonella*-induced myocarditis was suspected.

The patient was transferred to the intensive care unit for close monitoring and fluid balance. Central venous access was obtained and intravenous ceftriaxone initiated to treat *Salmonella* infection. Intravenous frusemide and glyceryl

Figure 1 Admission ECG demonstrating sinus tachycardia.

trinitrate (GTN) infusions were commenced to remedy fluid overload. Bisoprolol and ramipril were introduced in a stepwise approach. The patient gradually improved over the following days and the diarrhoea abated. She was discharged home 11 days after admission. At 3-month follow-up she appeared well with a repeat ECHO now within normal limits, preserved left ventricular systolic function and normalisation of all blood parameters. ECG abnormalities also resolved. Bisoprolol and ramipril were gradually withdrawn over the following few months given the young age and complete recovery of the patient.

DISCUSSION

Myocarditis is clinically defined as inflammation of the heart muscle. It may present with a constellation of non-specific symptoms, including chest pain, dyspnoea and palpitations. Many cases are believed to be asymptomatic with no long-term sequelae, conversely evidence of myocardial inflammation has been identified in 9% of routine postmortem examinations, with myocarditis suggested to be accountable for 12–20% of sudden deaths in young adults under the age of 40 years.^{1 2} From a clinical investigation perspective, patients may have ECG changes, arrhythmias, congestive cardiac failure and cardiogenic shock. The variability in clinical presentation and patient outcome make it a diagnosis requiring a high index of clinical suspicion. Myocarditis may be found in conjunction with other seemingly unconnected clinical scenarios, notably gastroenteritis as in our particular case.

Myocarditis has many causes including infection, immune-mediated inflammation and direct toxin effect to name a few. Cocksackie and adenovirus' have well-established causative association with myocarditis in medical literature; however, bacterial infections are comparatively rare. Various different species of *Salmonella* have been linked with myocarditis, with variable clinical manifestations and time courses.^{3 4}

Myocarditis associated with *Salmonella* spp. infection was first described in 1884 by Volz, where haemorrhagic pericarditis was noted at postmortem in a case of typhoid fever.⁵ Similarly, Theler-Ballmer *et al* found that 8 out of 103 patients with Salmonellosis had ECG abnormalities suggestive of myocarditis.⁶ *Salmonella* more commonly causes endocarditis, although autopsy case-reports of *Salmonella* endocarditis have revealed that the myocardium is often involved in the inflammatory process.⁷ Since its recognition *Salmonella*-associated myocarditis has been described in rare but increasing numbers of case reports, possibly reflecting its recognition and learned association with myocarditis or improved diagnostics.^{8–10}

ECG changes although non-specific are of significant use in diagnosis and also prognosis. The presence of Q-waves and the development of left bundle branch block having been associated with poorer prognosis.¹¹

ECHO is a valuable diagnostic tool in cases of myocarditis. Findings are typically non-specific with pericardial effusion, global/segmental wall movement abnormalities and dilated, hypertrophic and restrictive ventricular

Figure 2 ECG on day 9 showing anterolateral T-wave inversion.

patterns described. Evidence of ventricular dysfunction is associated with future cardiac transplantation and risk of death.¹² Findings on ECHO can help to differentiate cases of myocarditis from myocardial infarction, and allow direct comparison over time. Differences in outcome have also been described based on ECHO findings, comparing fulminant and acute myocarditis. The former typically showing absence of ventricular dilatation and full return

of normal ventricular function as in our specific case.¹³ Fulminant myocarditis is less likely to progress to dilated cardiomyopathy (DCM) compared with acute myocarditis, where progression to persistent cardiac dilatation, and subsequently a DCM more frequently occurs. In a similar case of *Salmonella enteritidis* myocarditis described by Franczuk *et al* the resolution of echocardiological findings after antimicrobial treatment was suggested to be evidence of a causative association.¹⁴

As myocarditis presents with a myriad of clinical manifestations, endomyocardial biopsy (EMB) remains the gold standard for diagnostic evaluation. EMB is however hindered by a number of drawbacks, and is very rarely performed. Sampling errors, inter-interpret variability, complications associated with the procedure and low sensitivity of the investigation (10–22%) limits its suitability in practice.⁴ EMB was not felt to be indicated in our case as the diagnosis was apparent.

The advent of new imaging modalities such as cardiac magnetic resonance imaging (CMR), in the assessment of myocardial tissue characterisation, offers a unique combination of safe imaging, anatomical clarity and quantitative accuracy.¹⁵ CMR can be used to guide EMB sampling or be used as a diagnostic tool in its own right. Results of diagnostic accuracy in CMR are encouraging and arguably the investigation of choice for myocarditis due to the breadth of information obtained.

Although *Salmonella* gastroenteritis is not routinely treated with antibiotics, the development of systemic complications, such as myocarditis arguably warrants

Figure 3 Anteroposterior chest radiograph demonstrating pulmonary oedema.

prompt initiation of antimicrobial therapy. This might represent an opportunity to potentially reduce the risk of progression to long-term complications such as DCM.

Learning points

- ▶ Myocarditis manifests non-specifically and requires a high index of clinical suspicion for diagnosis.
- ▶ *Salmonella* spp. are rare bacterial causes of myocarditis, but a diagnosis not to miss.
- ▶ Early initiation of antimicrobial therapy may prevent future morbidity in myocarditis related to bacterial infection.
- ▶ Endomyocardial biopsy remains the gold standard diagnostic test for myocarditis; however, newer imaging modalities such as cardiac magnetic resonance imaging are proving to be safer and produce reliable, accurate results.

Competing interests None.

Patient consent Obtained.

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