CASE REPORT

Sigmoid volvulus in a patient with mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS): a rare occurrence

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SUMMARY

Mitochondrial diseases are rare and devastating, with a wide spectrum of clinical presentations and systemic symptoms. The majority of the published literature focuses on the neuromuscular manifestations and genetic components of this mitochondrial cytopathy, however, cardiac, renal, endocrine and gastrointestinal manifestations may also be present. The authors report a case detailing a 56-year-old woman's final hospitalisation from the gastrointestinal sequelae of mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS) (Co Q10 deficiency variant). She presented with abdominal pain and distension associated with lactic acidosis, and was shown on imaging to have a colon perforation. This resulted in emergent surgery at which a necrotic colon secondary to a sigmoid colon was identified. Following four subsequent operations, and the development of multiorgan failure, care was eventually withdrawn. Practitioners of patients with MELAS should be cognisant of the rare but devastating gastrointestinal consequences of mitochondrial diseases.

BACKGROUND

Mitochondrial diseases are among the most common inherited genetic diseases. They have the potential to present acutely or chronically in nearly every organ system. Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS) are components of a neurodegenerative disease caused by mitochondrial point mutations.¹ Mitochondrial cytopathies vary considerably in their manifestations, leading to uncertainty about diagnosis and classification. However, some of the main findings include varying degrees of cognitive impairment and dementia, lactic acidosis, strokes and transient ischaemic attacks, hearing loss, gastrointestinal (GI) dysmotility and weight loss.² There is no absolute prevalence of the m3243A gene mutation, which is commonly associated with MELAS; yet, Schaefer *et al*³ suggest a minimum prevalence of 1 in 5000.

CASE PRESENTATION

A 56-year-old woman presented to our hospital as a direct transfer to the surgical intensive care unit (ICU). The patient's transfer was prompted by progressive abdominal pain and distension along with marked colonic dilation, free fluid and free air on CT scan of the abdomen and pelvis (figures 1 and 2). She was vomiting with severe diffuse abdominal

pain that she rated at 10/10. Her symptoms had been present for 3 days and getting progressively worse. She also reported of nausea, headache and blurred vision, yet still coherent and able to communicate with staff and consent for her medical care.

The patient had been diagnosed with MELAS in 2001. She had first begun experiencing GI dysmotility and intestinal pseudo-obstructive episodes in the 1970's. Eventually, her GI dysmotility became severe enough that a vagotomy and pyloroplasty were performed in 1987, after an episode of gastric outlet obstruction. She was subsequently started on total parenteral nutrition in 1988. Stroke-like episodes requiring close management by a neurologist began in the 1980's and persisted on a frequent basis.

Her initial physical examination was remarkable for a rigid and markedly distended abdomen,

Figure 1 Representative image of the initial CT scan. The massively dilated loops of colon and pneumoperitoneum demonstrated on coronal view contributed to the decision for hospital transfer and emergent abdominal exploration.

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which on palpation was peritonitic. Intra-abdominal pressure was increased to the point where she had absent sensation below her nipples, and her feet were dusky and mottled. Her vital signs were blood pressure of 105/75 mm Hg, sinus tachycardia of 130 bpm and respiratory rate of 28 breaths/min on a 4 L nasal cannula.

INVESTIGATIONS

The patient was profoundly acidotic with a pH of 6.84 and a pCO₂ of 48 mm Hg. She had a low intravascular volume with low urine output, a base excess of -24 mmol/L and a high lactate of 19 mg/dL. Additionally, she was found to be anaemic with haemoglobin of 7.2 g/dL, and her telemetry displayed atrial fibrillation. A Foley catheter was placed with minimal urine output, and a nasogastric tube was inserted with a moderate amount of faeculent output.

DIFFERENTIAL DIAGNOSIS

- ▶ Bowel obstruction
- ▶ Pancreatitis
- ▶ Acute mesenteric ischaemia

TREATMENT

The patient was resuscitated and underwent an emergent exploratory laparotomy. Immediately on entering the abdomen, copious murky, foul smelling fluid was noted from a massively distended, necrotic colon (figures 3 and 4). On further inspection of the abdomen, a sigmoid volvulus was noted and appeared to

be the cause of the colonic distension. A total colectomy was performed with end ileostomy formation, as none of the colon was viable. There was marked bleeding from all the cut surfaces and a coagulation profile showed a prothrombin time of 21.2 s, prothrombin international normalised ratio of 1.9, activated partial thromboplastin time of 111.5 and D-dimer of >35 200 ng/mL fibrinogen equivalent unit (FEU), consistent with a diagnosis of disseminated intravascular coagulopathy (DIC). After obtaining the best haemostasis possible given the DIC, the patient was returned to the ICU, intubated, with a plan to resuscitate her and further correct the coagulopathy and hypothermia.

OUTCOME AND FOLLOW-UP

Twelve hours later, the patient was noted to have a rigid abdomen with increased ventilatory support requirements, consistent with an abdominal compartment syndrome. She was taken to the operating room for abdominal exploration. On opening the prior laparotomy incision, 5 L of gelatinous haematoma were discovered and evacuated. The gallbladder was noted to be necrotic at this time and was also excised. The abdomen was packed with gauze towels and covered with an ABThera (Kinetic Concept, Inc; San Antonio, Texas, USA) open abdomen negative pressure therapy system. The patient returned to the operating room 2 days later for a planned re-exploration. At this time, the ileostomy was found to be necrotic, and was excised, with reapplication of the ABThera system. Continued physiological deterioration prompted re-exploration a further 2 days later. Intraoperative findings included a necrotic small bowel with multiple nodules on its serosal surface; all frankly ischaemic bowel sections were excised. Two more attempts at septic source control through abdominal explorations resulted in the resection of further non-viable small bowel. The remaining

Figure 2 Representative image of the initial CT scan. The massively dilated loops of colon and pneumoperitoneum demonstrated on sagittal view contributed to the decision for hospital transfer and emergent abdominal exploration.

Figure 3 Intraoperative photo demonstrating mega colon encountered on the initial emergent exploratory laparotomy on hospital day 1.

Figure 4 Intraoperative photo demonstrating mega colon encountered on the initial emergency exploratory laparotomy on hospital day 1.

intestine consisted of two islands of proximal jejunum measuring 165 cm in total. Of note, on final exploration, the patient's abdomen was noted to have increased ileal necrosis and a dark, irregular film over the bowel (figure 5). This was excised and pathological review of this specimen identified invasive Candidiasis. Over six additional days of hospitalisation, her condition worsened due to the progression of multiorgan system failure requiring continuous haemodialysis, ventilation and

Figure 5 Intraoperative photo demonstrating Candidiasis colonisation of the necrotic ileum, which was encountered during the final abdominal re-exploration on hospital day 10.

vasopressor support. Despite these extensive efforts, the prognosis remained extremely poor and the patient's family decided not to pursue any further interventions, and the patient passed away shortly after comfort measures were initiated.

DISCUSSION

The case presented here precedes the first publication regarding the diagnostic criteria for MELAS in 1992.⁴ Retrospectively, this patient's initial presentation, both GI and neurological, began around the time of the first reported cases of MELAS in 1975,^{5,6} well before the acronym MELAS was coined in 1984.⁷ This case demonstrates a patient who was shown to have low coenzyme Q10 activity, however, she was negative for the MELAS 3243 point mutation and for mitochondrial DNA gene deletion. A muscle biopsy was never performed due to the strong clinical evidence of disease (neurological and GI) and the belief that a histopathological analysis would not change the management of the patient. This strategy is supported by similar reports of clinically diagnosed MELAS cases where the biopsy and genetic analysis both lacked MELAS characteristics.²

The association of ischaemic colitis and chronic intestinal pseudo-obstruction in MELAS has been well established and characterised. Hess *et al* reported a case of ischaemia at the splenic flexure of a patient with MELAS in 1995. Hess *et al*⁸ hypothesised a higher fraction of abnormal mitochondria at the splenic flexure leading to impaired energy metabolism and subsequent ischaemia. Investigation of the mechanism and prevalence of GI manifestations of mitochondrial diseases progressed over the years and led to retrospective reviews such as that by Sekino *et al* in 2012,⁹ who reported that 40% of patients with MELAS develop chronic intestinal pseudo-obstruction.

However, we believe this case is the first reported death due to the GI manifestations of the disease and sigmoid volvulus. Our patient presented with a sigmoid volvulus, which has not previously been described in a patient with MELAS. Likely, MELAS predisposes a patient to sigmoid volvulus due to the ongoing pseudo-obstructions, GI dysfunction and dilated colon. This can be a devastating consequence, requiring vigilant care, for patients presenting with acute abdominal pain and MELAS.

Learning points

- ▶ Patients with established mitochondrial diseases may present with acute issues involving the gastrointestinal tract.
- ▶ Patients presenting with a constellation of seemingly unrelated symptoms in multiple organ systems may have underlying mitochondrial pathology.
- ▶ Abdominal pain and radiological findings of a progressively dilating colon in patients with underlying mitochondrial disease should prompt close observation with a low threshold for operative intervention.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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