CASE REPORT

Metabolic acidosis in short bowel syndrome: think D-lactic acid acidosis

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Accepted 30 April 2018

SUMMARY

Short bowel syndrome (SBS) is a condition when a person's gastrointestinal function is insufficient to supply the body with essential nutrients and hydration. Patients with SBS suffer from diarrhoea and symptoms of malabsorption such as weight loss, electrolyte disturbances and vitamin deficiencies. Long-term management of this condition can be complicated by the underlying disease, the abnormal bowel function and issues related to treatment like administration of parenteral nutrition and the use of a central venous catheter. Here, we describe a case of D-lactic acid acidosis, a rarer complication of SBS, presenting with generalised weakness and severe metabolic acidosis.

BACKGROUND

D-lactic acid is a stereoisomer of L-lactic acid. In patients with short bowel syndrome (SBS), there can be an overgrowth of anaerobe bacteria such as *Lactobacilli*, which can produce large amounts of both L-lactate and D-lactate.[1] Furthermore, there is less absorption of carbohydrates which remain in the colon and provide more substrate for the anaerobe bacteria to produce lactate.

The breakdown of D-lactic acid is much slower than the breakdown of physiologically occurring L-lactic acid. The latter is catalysed by L-lactate dehydrogenase which is not effective on D-lactic acid. Humans lack D-lactate dehydrogenase; therefore, the rate at which they metabolise D-lactate is estimated to be five times slower than for L-lactate.[2]

There are also other situations in which D-lactic acid can accumulate, including rapid infusion of drugs dissolved in propylene glycol (lorazepam, diazepam),[3] ingestion of propylene glycol[4 5] and diabetic ketoacidosis.[6]

D-lactic acid acidosis presents as episodic neurological symptoms, usually following high carbohydrate meals.[7] The manifestations are very variable, usually consisting of altered mental status (from mild drowsiness to coma) and a variety of other symptoms such as slurred speech, gait disturbances, weakness and impaired coordination. This is thought to be secondary to other organic acids produced in the colon, substances which are generated and absorbed in parallel to D-lactic acid, rather than by D-lactic acid itself, as cerebral spinal fluid (CSF) concentrations of D-lactate do not correlate with plasma concentrations and it is not possible to reproduce the symptoms by administering D-lactic acid in normal subjects.[7]

This condition should always be suspected in patients with SBS or other malabsorption conditions and typically requires the presence of a relatively intact colon. Due to the lack of specificity of the symptoms, D-lactic acidosis can be missed; therefore, there is a need of awareness of this condition for people caring for this patient population in order to suspect it and test for it.

Most pathology laboratories are unable to measure D-lactic acid; therefore, samples need to be sent to a reference laboratory.

CASE PRESENTATION

A 65-year-old man with a history of essential thrombocythaemia complicated by mesenteric ischaemia which required extensive small bowel resection was receiving home parenteral nutrition for short bowel syndrome. He presented to the hospital feeling unwell for the previous few weeks, mainly complaining of muscle weakness. He denied any fevers or rigours and any change in bowel habit or vomiting. He did not report any memory or mood problems.

Physical examination was remarkable for profound lethargy but otherwise he was fully orientated, stable haemodynamically, without any significant clinical signs, including no focal neurological deficit.

INVESTIGATIONS

Blood tests on admission were remarkable for a severe metabolic acidosis pH 7.20, HCO_3 11.3, base excess −17 with a normal lactate of 1. He was also noted to have a creatinine of 205 µmol/L (baseline 130). Inflammatory markers were in the normal value white cell count (WCC) 4.5, Creactive protein <0.2. Repeated septic screens consisting of urinalysis, chest X-ray and blood cultures did not reveal a source of infection. Ultrasound of the renal tract showed no signs of hydronephrosis.

DIFFERENTIAL DIAGNOSIS

He was first considered to be suffering from acute kidney injury with uraemic acidosis. He was given supplemental intravenous fluids and sodium bicarbonate and his renal function soon improved and the patient felt well. However, even despite being given 1 g of sodium bicarbonate twice a day, his plasma pH was 7.25, bicarbonate 14, with a lactate of 1.2 on the blood gas analyser.

Other causes of metabolic acidosis were considered and a D-lactic acid was requested. The value

To cite: Stanciu S, De Silva A. *BMJ Case Rep* Published Online First: [*please include* Day Month Year]. doi:10.1136/bcr-2018-224221

of the D-lactic acid came back at 784 mmol/L, well beyond the normal high limit of 19.

TREATMENT

He was started on rifaximin 550 mg twice a day for bacterial overgrowth and he was advised to reduce the carbohydrate load of his diet.

Intravenous sodium bicarbonate was administered to compensate the severe metabolic acidosis. This was later switched to oral bicarbonate with occasional intravenous infusions.

OUTCOME AND FOLLOW-UP

After being discharged, he was seen in the clinic after 2 weeks and was feeling well, mobilising normally, not feeling any weakness.

DISCUSSION

This was a typical patient with SBS being given parenteral nutrition (PN). His initial presentation did not have any specific neurological manifestations. In a case series of 29 patients with D-lactic acidosis, all patients had a diminished level of consciousness (from mild drowsiness to coma), 65% had dysarthria and 45% had ataxia.[7] Some case reports described violent behaviour while others suggested a presentation similar to acute alcohol intoxication. The patient presented here had only marked general weakness but no diminished level of consciousness.

Another particularity worth pointing out was that the profound metabolic acidosis did not have a high anion gap, as it would be expected when large quantities of D-lactate are added to the plasma. This is largely explained by the fact that D-lactate is readily excreted by the kidneys, even more efficiently than L-lactate. The excretion of D-lactate is coupled with the excretion of sodium, potassium and water, which leaves the chloride compartment to contract due to volume depletion and account for the hyperchloraemic (normal anion gap) metabolic acidosis.[8]

In terms of differential diagnosis, it is important to mention that accumulation of D-lactic acid can arise in several other clinical situations. D-lactate is a product of propylene glycol metabolism and ingestion[4] or intravenous administration of this substance may lead to the syndrome described above. Propylene glycol is used as a solvent for a variety of medications to make them suitable for intravenous administration and infusion of lorazepam has been described to lead to D-lactic acid acidosis.[3] Lastly, diabetic ketoacidosis has been shown to be associated with accumulation of D-lactic acid from breakdown of ketones.[6]

In the acute setting, if the acidosis is severe, sodium bicarbonate can be administered.[1] Antibiotics that target the D-lactate producing gut bacteria such as rifaximin, metronidazole, neomycin or vancomycin are often useful and may need to continue long term in patients with recurrent symptoms. A low-carbohydrate diet also helps diminish the amount of substrate delivered to the bacteria in the colon. Some fermented foods such as sour milk, yoghourt and pickles have D-lactate and should be avoided.

Some issues regarding measuring D-lactic acid levels are important to mention for clinical practice. First of all, not many laboratories are suited to measure D-lactate and a reference laboratory needs to be contacted. The patient does not need any specific preparation but the sample collected needs to be immediately centrifuged and/or frozen. Therefore, if the patient is mobile enough, it would be more practical to take the sample near the pathology laboratory where this can be done rapidly.

Patient's perspective

The patient's perspective can be seen reflected in this thank-you e-mail written to the Nutrition Support Team: 'I went to St Marks today—it is a year since the last time I saw them. They were very impressed at the treatment I have received at RBH, particularly the diagnosis of the acidosis. They said this is a very rare condition, only now starting to be understood, and that they themselves, despite their depth of specialism, could well have taken several weeks to have diagnosed the problem. So the fact that you diagnosed it relatively quickly was quite something. They endorsed the treatment I am on (Rifaximin)—in fact they recommended no changes whatsoever to my treatment. So I owe you a big "thank you".'

Learning points

- Consider testing for D-lactic acid in a patient with short bowel syndrome (SBS) and unexplained acidosis (either high anion gap or hyperchloraemic).
- Also consider D-lactic acid acidosis in a patient with SBS with altered mental state or other neurological signs.
- Treatment is aimed at reducing the D-lactate producing over-represented gut bacteria.

Contributors SS collected the data regarding this case report by searching the clinical notes and computerised health records, interpreted and analysed the data, compared it with available literature, conducted literature searches concerning the condition of D-lactic acidosis, its pathophysiology, clinical manifestations and treatment and wrote the article. ADS conceived the case report and made corrections to the first and second draft.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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