D-lactic acid found in human physiological fluids originates from bacterial production in the intestinal tract, from D-lactate ingestion, or from endogenous production by the methylglyoxylase pathway. D-lactic acidosis, first described as a disease by Oh et al in 1979, has been described in short bowel syndrome due to either surgical resection of the intestine or intestinal bypass surgery for treatment of obesity, and due to chronic pancreatic insufficiency. D-lactic acidosis may be more common than is thought and should be looked for in cases of metabolic acidosis in which the cause of acidosis is not apparent. The clinical presentation is characterised by episodes of unusual neurological manifestations and severe metabolic acidosis. The mechanism of D-lactic acidosis is still unknown, and there is no effective treatment.

We present a case of D-lactic acidosis secondary to short bowel syndrome. The patient had undergone extensive intestinal resection due to volvulus. In this report we review the clinical presentation, metabolism of D-lactate, pathophysiology, and discuss treatment options.

CASE REPORT

A 12 year old boy presented on 24 October 2001 with 11 episodes of weakness, ataxia, nausea, slurred speech, dehydration, and sometimes severe lethargy bordering on coma. A year previously the boy had small intestinal resections leaving 20 cm of small bowel remaining. D-lactic acidosis was diagnosed on the basis of a D-lactate level of 5.23 mmol/l. The clinical presentation of the disease is recurrent episodes of unusual neurological manifestations and severe metabolic acidosis. The diagnosis is dependent on the presentations and the plasma D-lactate level. Development of the syndrome seems to be the effect of the accumulation of D-lactic acid.

Anion gap = sodium – chloride – bicarbonate.

Anion gap = sodium chloride bicarbonate.

Table 1
Characteristics of the patient on admission

<table>
<thead>
<tr>
<th>Symptoms and signs</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness, nausea, slurred speech, lethargic and hostile, blood pressure 75/50 mm Hg on sitting, ataxia, dehydrogenation, asterixis</td>
<td>pH 7.21</td>
</tr>
<tr>
<td>Potassium 4.9 mmol/l</td>
<td></td>
</tr>
<tr>
<td>Sodium 140 mmol/l</td>
<td></td>
</tr>
<tr>
<td>Chloride 110 mmol/l</td>
<td></td>
</tr>
<tr>
<td>Bicarbonate 6 mmol/l</td>
<td></td>
</tr>
<tr>
<td>D(−)-lactate level 5.23 mmol/l</td>
<td></td>
</tr>
<tr>
<td>Anion gap 24*</td>
<td></td>
</tr>
</tbody>
</table>

*Anion gap = sodium–chloride–bicarbonate.

Aniseed, milk, orange juice, and yoghurt. No more attacks happened in two months of follow up.

Method of measuring lactate

Enzymatic measurement of L(+) -lactate was done by a standard method using lactate dehydrogenase from rabbit muscle. Enzymatic analysis of D(−)-lactate was done the same way except that the L(+) -lactate standard and L(+) -lactate dehydrogenase were substituted by D(−)-lactate and D(−)-lactate dehydrogenase respectively (obtained from Sigma Chemical Co, St Louis, Missouri).

DISCUSSION

Clinical presentations

The clinical presentation is characterised by recurrent episodes of unusual neurological manifestations and severe

D-lactic acidosis secondary to short bowel syndrome

D L Zhang, Z W Jiang, J Jiang, B Cao, J S Li


A 12 year old boy presented on 24 October 2001 with 11 episodes of weakness, ataxia, nausea, slurred speech, dehydration, and sometimes severe lethargy bordering on coma. A year previously the boy had small intestinal resections leaving 20 cm of small bowel remaining. D-lactic acidosis was diagnosed on the basis of a D-lactate level of 5.23 mmol/l. The clinical presentation of the disease is recurrent episodes of unusual neurological manifestations and severe metabolic acidosis. The diagnosis is dependent on the presentations and the plasma D-lactate level. Development of the syndrome seems to be the effect of the accumulation of D-lactic acid.
metabolic acidosis. These episodes often last from a few hours to several days. The patient often has short bowel syndrome, mainly due to surgical resection of intestine or intestinal bypass surgery for treatment of obesity. Another underlying condition is chronic exocrine pancreatic insufficiency. D-lactic acidosis can present from a few months to 23 years after the underlying condition.\(^3\) Neurological manifestations are nearly always present in 26 out of 27 cases, and usually present from patient to patient. Common features include slurred speech, confusion, inability to concentrate, somnolence, hallucinations, clumsiness, weakness, ataxia, unsteady gait, nystagmus, irritability, and abusive behaviour.\(^1\) In this report, the patient had short bowel syndrome due to surgical resection of his intestine. D-lactic acidosis presented nearly a year later. His main symptoms were episodes of weakness, ataxia, nausea, slurred speech, dehydration, and sometimes severe lethargy bordering on coma. The patient presented with systemic acidosis; however, there have been reports of D-lactic acidosis without systemic acidosis.

**Metabolism of lactate**

D-lactate and L-lactate are optical isomers. D-lactic acid found in human physiological fluids originates from bacterial fermentation in the intestinal tract, from D-lactate ingestion, or in human physiological fluids. D-lactic acid is formed in sour milk by lactic acid bacteria and is fermented to produce organic acids. This results in a progressive decrease in intraluminal pH, which alters the intestinal microenvironment favouring the overgrowth of acid-resistant bacteria such as *Lactobacillus acidophilus*, *Lactobacillus fermenti*, and streptococcus. These are the main bacteria that produce D-lactate in both animals and humans.\(^4\)\(^5\) Secondly, stool flora show a preponderance of Gram positive anaerobes, which are the major lactate producers. The effect of poorly absorbed oral antibiotic was good in most patients with D-lactic acidosis. Finally, the symptoms of D-lactic acidosis may also occur after patients ingest a large amount of carbohydrate. Diminished colonic motility that allows time for nutrients in the colon to undergo bacterial fermentation, deficiency of thiamine,\(^10\) impaired D-lactate metabolism may be other reasons for the development of D-lactic acidosis.

Why does D-lactic acidosis bring about neurological symptoms? It is difficult to explain them by the acidosis itself, as patients with other types of acidosis of comparable severity do not have such presentations. It is possible that D-lactic acidosis is toxic to the brain. The brain apparently lacks D-2-hydroxyacid dehydrogenase, and D-lactic acid may accumulate excessively there. High D-lactic acid level may alter intraneuronal pH. Low pH inhibits pyruvate decarboxylation by interfering with the pyruvate dehydrogenase complex and therefore decreases production of acetyl CoA and adenosine triphosphate, an outcome that leads to altered neurotransmitter production. Because the cerebellum contains minimal pyruvate dehydrogenase reserves over that needed for normal metabolism, cerebellar manifestations may be especially prominent in D-lactic acidosis.\(^11\) Acquired and congenital disorders of pyruvate metabolism generally present with central nervous system symptoms.\(^12\) However, some men acting as controls in a test didn't have neurological symptoms when their plasma D-lactic acid levels reached 3.5 mmol/l.\(^2\) It is likely that there are some other reasons for the cause of the patient's neurological presentation.

**Diagnosis**

Noticeably, there needs to be emphasis on the fact that the colon needs to be present for D-lactic acidosis to occur. If the patient has short bowel syndrome or chronic exocrine pancreatic insufficiency with a high level of D-lactate, we should suspect D-lactic acidosis. However there are no universal reference values for D-lactate at present. L-lactic acidosis is commonly defined by a serum level of lactate greater than 5 mmol/l.\(^2\) In contrast, D-lactate is normally undetectable, and the measured concentration of D-lactate in excess of 3 mmol/l contributes greatly to the acidosis.\(^2\)

**Treatment**

So far there are no effective therapies. In some cases antibiotics can control symptoms and prevent recurrences of the syndrome, but have no effect in other patients. Indeed, some
patients presented with the above syndrome while taking antibiotics.\(^21\)\(^,\)\(^22\) This may be because antibiotics promote the overgrowth of D-lactate-producing bacteria at the expense of other competing bowel flora. We recommend that the treatment methods should include a low carbohydrate diet, bicarbonate given intravenously as well as rehydration, correction of the underlying conditions if possible, a saline enema if constipated, and poorly absorbed oral antibiotics when necessary. Administration of insulin to diminish fatty acid levels and enhance D-lactate clearance may be a treatment option during an episodes of acidosis.\(^21\)\(^,\)\(^22\) If the patient is in a critical condition, haemodialysis is also likely to be an effective therapy.

**Key points**

- D-lactic acidosis should be looked for in cases of metabolic acidosis in which the identity of acidosis is not apparent and the patient has short bowel syndrome or chronic exocrine pancreatic insufficiency with high level of D-lactate.
- The clinical presentation is characterised by episodes of peculiar neurological manifestations and severe metabolic acidosis.
- In this patient D-lactic acidosis was diagnosed on the basis of D-lactate level of 5 mmol/l and clinical presentations.
- Low carbohydrate diets, bicarbonate given intravenously as well as rehydration, and taking poorly absorbed oral antibiotics may be helpful to control symptoms.

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