Meconium ileus in the absence of cystic fibrosis

Khoulood Fakhoury, Peter R Durie, Henry Levison, Gerard J Canny

Abstract
Although meconium ileus in the absence of cystic fibrosis is considered a rare event, it was found that eight of 37 (21.6%) newborn infants with meconium ileus had no laboratory or clinical evidence of cystic fibrosis.

(Arch Dis Child 1992;67:1204–6)

Meconium ileus is the earliest clinical manifestation of cystic fibrosis in 10–20% of affected patients (1.3–4% at this clinic),1 but it is a rare phenomenon in patients who do not have this condition. We report eight neonates with meconium ileus, who had no clinical or laboratory evidence of cystic fibrosis.

Patients, methods, and results
During the six year period, 1986–91, 37 neonates with meconium ileus were seen at the Hospital for Sick Children, Toronto. Eight (four boys) of these 37 patients (21.6%) were subsequently shown to have no laboratory evidence of cystic fibrosis, and they form the basis of this report.

The patients’ characteristics are summarised in the table. Four of the eight infants were delivered prematurely (that is, less than 37 weeks’ gestation), three of whom required intubation and mechanical ventilation at birth. Maternal complications included polyhydramnios (patients 4 and 7) and pre-eclampsia (patient 6), but there was no family history of cystic fibrosis. All presented with signs of intestinal obstruction with abdominal distension (with the exception of patient 5), and failure to pass meconium, and four infants developed ileal perforation. All except patient 5 required laparotomy, and three infants required bowel resection. Complications noted at surgery included ileal perforation, meconium peritonitis, meconium pseudocysts, ileal volvulus, and ileal atresia (table). Histopathology of the surgically resected specimens of small bowel revealed necrosis and haemorrhage, but lesions typical of cystic fibrosis or Hirschsprung’s disease were not identified. Pilocarpine iontophoresis sweat chloride tests were normal on two occasions in all patients. Genetic studies were performed on six subjects, none of whom had the ΔF508 deletion, which is present in 68% of patients with cystic fibrosis at this clinic.3 Six of the eight infants had a favourable outcome and developed no gastrointestinal, nutritional, or pulmonary complications.

Patient 2, who was born at 30 weeks’ gestation, required mechanical ventilation for 17 days and developed mild bronchopulmonary dysplasia. Patient 6 required continuous mechanical ventilation for 106 days for the respiratory distress syndrome, which resulted

Clinical data of the eight patients

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Sex</th>
<th>Gestational age (weeks)</th>
<th>Age at presentation</th>
<th>Birth weight (g)</th>
<th>Clinical presentation</th>
<th>Abdominal radiograph</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>36</td>
<td>Day 2</td>
<td>2730</td>
<td>Formula feeds for 24 hours, abdominal distension, vomiting (bilious drainage by nasogastric tube).</td>
<td>Distended loops with air-fluid levels, no air in colon. Barium enema: microcolon, 7 distal small bowel atresia</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>30</td>
<td>Day 3</td>
<td>730</td>
<td>Ventilated for RDS (17 days): not fed, developed abdominal distension, periumbilical erythema.</td>
<td>Dilated loops (day 1), free air in the abdomen (day 3)</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>40</td>
<td>At birth</td>
<td>3210</td>
<td>Not fed, developed abdominal distension. No meconium passed; bilious drainage by nasogastric tube.</td>
<td>No abdominal gas; microcolon; calcification in RIF. 7 Meconium cyst</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>35</td>
<td>Day 2</td>
<td>2630</td>
<td>Low APgar scores—ventilated for 24 hours: not fed, developed ascites and raised serum transaminase values on day 2.</td>
<td>No abdominal gas. Barium enema: malrotation, proximal dilation of small bowel with free air in the abdomen</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>40</td>
<td>12 hours</td>
<td>3120</td>
<td>Breast fed, bilious vomiting. No meconium passed</td>
<td>Barium meal: masses in RIF, barium enema: patchy filling defects in colon and the last 10 cm of ileum</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>27</td>
<td>Day 2</td>
<td>870</td>
<td>Ventilated for RDS (106 days): not fed, abdominal distension. No meconium passed by day 3</td>
<td>Dilated bowel loops. Barium enema: microcolon</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>39</td>
<td>At birth</td>
<td>3500</td>
<td>Not fed, abdominal distension, bilious gastric aspirate</td>
<td>Air bubble in the stomach, no air in the rest of the bowel. Barium enema: proximal bowel dilatation microcolon Paucity of air in the abdomen, free air under diaphragm</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>40</td>
<td>7 hours</td>
<td>3000</td>
<td>Breast fed, abdominal distension, bilious vomiting</td>
<td></td>
</tr>
</tbody>
</table>
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in the development of bronchopulmonary dysplasia. Despite irrigation of the bowel with N-acetylcysteine at laparotomy, no meconium was passed, and further surgery was required at day 14 of life after a rectal perforation. Several attempts at extubation failed and this baby died at 4 months of age from lower respiratory infection, superimposed on chronic lung disease. With the exception of patients 2 and 6, all infants in our series had normal chest radiographs.

Discussion

Although all of the newborns described presented with meconium obstruction of the terminal ileum, none had clinical or labora-
tory evidence of cystic fibrosis. Meconium intestinal obstruction in the neonatal period can be due to three conditions (1) meconium ileus; (2) meconium plug syndrome; and (3) meconium disease (inspissated meconium syndrome).

Meconium ileus is due to mechanical obstruction of the terminal ileum with thick, viscid meconium, and in about 50% of cases is complicated by volvulus, atresia, or meconium peritonitis. In cystic fibrosis, meconium ileus is thought to result from abnormal mucus production in the intestine and/or impaired pancreatic enzyme or fluid secretion. Meconium ileus rarely occurs in infants without cystic fibrosis, but has been reported with pancreatic duct stenosis, partial pancreatic aplasia, ileoceleal atresia as a familial condition and a functional disorder in preterm babies. The meconium plug syndrome has also been reported in cystic fibrosis. In this condition, transient obstruction of the distal colon occurs, although meconium plugs in the ileum may cause complications, requiring surgery. Meconium disease has been described in premature infants with very low birth weight and is not associated with cystic fibrosis. In this condition meconium plugs are found in the distal ileum and proximal colon and the resulting obstruction can generally be relieved by enemas.

Although overlap between the three causes of meconium obstruction may occur, the cases we report most closely resemble meconium ileus. In addition, typical complications of meconium ileus occurred in five of our cases, necessitating surgical intervention. However, sweat tests were negative in all of our patients, none had clinical or laboratory evidence of pancreatic insufficiency, and the most common deletion associated with cystic fibrosis (ΔF508) was not present in the six infants who had genetic studies. We feel confident, therefore, that our patients did not have cystic fibrosis.

Meconium ileus in the absence of cystic fibrosis is considered a rare event and has been reported in only a few cases. However, 21-6% of our patients with meconium ileus did not have cystic fibrosis. Although the exact cause of meconium ileus is unclear, four out of eight of the babies described were born prematurely (<37 weeks' gestation), three of whom required mechanical ventilation. It is possible that reduced intestinal motility may have contributed to the development of meconium ileus in these infants.

In summary, our report indicates that a significantly greater number of newborn infants with meconium ileus will not have cystic fibrosis than has been previously described. Definitive parental counselling should, therefore, be delayed until accurate sweat chloride tests can be obtained.

The authors thank J Chay for secretarial assistance.


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<table>
<thead>
<tr>
<th>Operative findings</th>
<th>Genetic analysis</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meconium ileus, meconium obstructing the ileocaecal valve. No atresia</td>
<td>Not done</td>
<td>Bowel flushed with N-acetylcysteine</td>
<td>No complications. Normal faecal fat and bentiromide study</td>
</tr>
<tr>
<td>Meconium ileus with perforation of mid-ileum</td>
<td>Negative for ΔF508</td>
<td>5 cm ileal resection and end to end anastomosis</td>
<td>No nutritional or gastrointestinal problems. Serum trypsinogen normal. Mild BPD</td>
</tr>
<tr>
<td>Meconium peritonitis. Meconium cyst: ileal atresia with perforation</td>
<td>Negative for ΔF508</td>
<td>10 cm small bowel resection, and ileostomy</td>
<td>No nutritional, gastrointestinal, or respiratory problems</td>
</tr>
<tr>
<td>Meconium ileus with mid-ileal volvulus and perforation</td>
<td>Not done</td>
<td>10 cm small bowel resection with end to end anastomosis and irrigation of distal bowel with N-acetylcysteine</td>
<td>Jejunostomy required for small bowel dehiscence. No nutritional or respiratory problems</td>
</tr>
<tr>
<td>No surgery</td>
<td>Negative for ΔF508</td>
<td>N-acetylcysteine by nasogastric tube and enema</td>
<td>No nutritional or respiratory problems. Normal faecal fat study and serum trypsinogen</td>
</tr>
<tr>
<td>Meconium ileus, microcolon</td>
<td>Negative for ΔF508</td>
<td>Bowel flushed with N-acetylcysteine</td>
<td>Severe BPD. Rectal perforation day 14. Died from respiratory failure at 4 months</td>
</tr>
<tr>
<td>Segmental ileal volvulus at mid-ileum meconium cyst, and associated ileal atresia</td>
<td>Negative for ΔF508</td>
<td>Meconium cyst resection, side to side anastomosis</td>
<td>Normal trypsinogen value</td>
</tr>
<tr>
<td>Perforated distal ileum, meconium peritonitis</td>
<td>Negative for ΔF508</td>
<td>Ileostomy, no bowel resection</td>
<td>Raised trypsinogen value</td>
</tr>
</tbody>
</table>
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