Absence of the interstitial cells of Cajal in a neonate with segmental dilatation of ileum

Tatsuma Sakaguchi*, Yoshinori Hamada, Yusuke Nakamura, Hiroshi Hamada, A-Hon Kwon

Department of Surgery, Kansai Medical University, 2-5-1 Hirakata, Osaka 573-1191, Japan

Article info
Article history:
Received 24 November 2015
Received in revised form
28 December 2015
Accepted 28 December 2015

Key words:
Segmental dilatation of the ileum
Immunohistochemistry
Interstitial cells of Cajal
c-kit

Abstract
Segmental dilatation of intestine (SD) is a congenital disease characterized by localized bowel dilatation with normal ganglion cells. Clinically, small intestinal type of SD frequently occurs in the neonatal period with pseudo-obstruction. Though many theories have been proposed regarding the pathogenesis, the disease etiology is unclear. Interstitial cells of Cajal (ICCs) have been ascribed as the pacemaker cells that coordinate peristaltic behavior and its disorder is the possible cause of intestinal pseudo-obstruction. Here, we report a rare case of SD observed the absence of ICCs in the dilated segment. A male neonate suffered abdominal distention and vomiting underwent segmental resection of the diluted ileum on the third day after birth. He was diagnosed with SD and his clinical course after surgery was uneventful. Immunohistochemically, c-kit positive cell was not identified around the ganglion cells in the resected specimen.

© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Case report
A neonate was referred to our department for surgical indication. A cystic mass in the right upper quadrant was identified at 36 weeks gestation by antenatal ultrasonography and magnetic resonance imaging (Fig. 1). He was born at 36 weeks. His birth weight was 2585 g and Apgar score was 7 at 1 min and 9 at 5 min. He presented bilious vomiting by the first day after birth. Physical examination demonstrated a right-sided intra-abdominal mass but the abdomen was otherwise soft and non-tender. X-ray imaging showed localized bowel distention (Fig. 2a). Computed tomography demonstrated limited dilatation of ileum with a three to fourfold increase in size without intestinal atresia (Fig. 2b). This sign was typical for segmental dilatation. Furthermore, congenital diverticulum and duplication of the intestine were given for differential diagnosis. Surgery was performed on the third day. Surgical findings showed limited bowel dilatation measuring 6.0 × 5.5 cm at 10 cm from the distal end of the ileum (Fig. 3). No adhesion or stenosis resulted in mechanical intestinal obstruction were observed. Segmental resection of the dilated bowel and end-to-end anastomosis were performed and his clinical course after surgery was uneventful. Histologically, the muscle layer was thickened in the diluted segment but no heterotopic tissue was observed (Fig. 4). Antibody for S-100 (Leica #NCL-L-S100p) and c-kit (DAKO #A4502) were used for immunohistochemical staining. Ganglion cells were stained normally by S-100, however, c-kit positive cells (interstitial cells of Cajal: ICCs) around the Auerbach’s plexus was deficit (Fig. 5).

2. Discussion
SD was first described by Swenson and Rathauzer [1] in 1959 as a “new entity.” Common segment of dilatation is ileum and colon,
Fig. 1. Antenatal images at 36 weeks gestation. (a) Ultrasonography showed a cyst (arrow) in the abdomen measured 2.6 × 1.5 cm. (b) Magnetic resonance imaging showed a dilated bowel (arrow) below the liver.

Fig. 2. Images after birth. (a) Plain radiograph showed a dilated bowel (arrow) in the right side of the abdomen. (b) Computed tomography showed a dilated ileum (arrow) without atresia.

Fig. 3. (a) Surgical finding. Locally dilated ileum with overswelling vessels above the serosa was observed. (b) Resected specimen.
but any segment from duodenal to rectum. Common symptom is abdominal distension, vomiting and chronic constipation. Melena [2] and severe malnutrition [3] had been also described in some previous reports. Clinical course can be treated by resection of the dilated bowel. Pathologically, abnormality of muscle layer as thinning or thickening, and ectopic pancreatic or gastric tissues have been reported [4]. Diagnostic criteria are as follows; (a) limited bowel dilatation with a three to fourfold increase in size, (b) an abrupt transition between the dilated and normal bowel, (c) no intrinsic or extrinsic barrier distal to the dilatation, (d) a clinical picture of intestinal occlusion or sub-occlusion, (e) a normality of the neuronal plexus, (f) complete recovery after resection of the affected segment [1,5]. We did not definitively rule out the differential diagnosis of congenital diverticulum and duplication of the intestine. In diagnosing of SD, we prioritized the anatomical features mentioned above.

Various theories have been proposed regarding the pathogenesis, such as an extrinsic intrauterine intestinal compression [6], aberrations of ectopic tissue [6], congenital damage of the myenteric plexus [7], and a disturbance during splitting of the notochord from the endoderm [8]. These theories are mostly depending on the histological findings of hematoxylin and eosin (HE) staining. Clinically, small intestinal type of SD frequently shows the signs of pseudo-obstruction [4]. Pathogenesis of intestinal pseudo-obstruction is generally classified into myopathies, neuropathies, and/or mesenchymopathies, and to detect the abnormalities, a systematic immunohistochemistry is useful [9]. However, few reports of SD have been used the technique of immunohistochemistry. To the best of our knowledge, immunohistological investigation for SD had done in only 4 reports (Table 1) [5,10–12]. They used S-100 [10,12], Ret [10] or MAP5 [10] for nervous marker and c-kit [5,10–12] for mesenchymal marker. As Amiot et al. had indicated that known muscle markers are useless to detect the myopathy, and fibrosis or vacuolization of HE staining is the sign that demonstrate the myopathy [9]. As a result of the immunohistochemical examination of SD, 2 reports identified the disorder of ICCs [5,11] and 3 reports concluded the pathogenesis local myopathy [10–12]. ICCs have been ascribed as the pacemaker cells that coordinate peristaltic behavior [13] and the loss or decrease of ICCs has been implicated in several disorders of human intestinal motility [14] such as Hirschsprung’s disease and chronic pseudo-obstruction [15]. Lack of normal pacemaker activity, usually generated by ICCs, could account for the apparent obstruction [16]. ICCs were immunohistochemically identified using an antibody for c-kit, a tyrosine kinase receptor expressing ICCs [14]. The different pathological findings from myopathy to disorder of ICCs suggest that there are different types of SD. The difference of the clinical features between them is unknown.

In this case, the muscle layer of the dilated segment was thickened, but there was no sign of fibrosis or vacuolization that demonstrate the myopathy. We also denied the local neuropathy because antibody for S-100 stained ganglion cells normally. We could not examine the distribution of ICCs in other segment. However, the clinical course after surgery was uneventful so that it is clear to consider that the function of ICCs in other segment has been usual. We concluded that the pathogenesis of

<table>
<thead>
<tr>
<th>No.</th>
<th>Author</th>
<th>Year</th>
<th>Segment</th>
<th>Immunohistochemical marker</th>
<th>Pathogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cheng [10]</td>
<td>2001</td>
<td>Jejunum</td>
<td>S-100, Ret, MAP5, c-kit</td>
<td>Myopathy</td>
</tr>
<tr>
<td>2</td>
<td>Okada [11]</td>
<td>2010</td>
<td>Duodenum to jejunum</td>
<td>c-kit</td>
<td>Disorder of ICCs and/or myopathy</td>
</tr>
<tr>
<td>3</td>
<td>Katsura [5]</td>
<td>2011</td>
<td>Duodenum</td>
<td>c-kit</td>
<td>Decreased number of ICCs</td>
</tr>
<tr>
<td>4</td>
<td>Soyer [12]</td>
<td>2015</td>
<td>Ileum</td>
<td>S-100, c-kit</td>
<td>Myopathy</td>
</tr>
<tr>
<td>5</td>
<td>This case</td>
<td>2015</td>
<td>Ileum</td>
<td>S-100, c-kit</td>
<td>Absence of ICCs</td>
</tr>
</tbody>
</table>

Fig. 4. Histological finding stained by HE. Muscle layer was thickened without fibrosis or vacuolization.

Fig. 5. Immunohistochemical finding. (a) Ganglion cells (arrow) were stained normally by antibody for S-100. (b) c-kit staining showed absence of ICCs. Brown cells (circle) scattering around the inner circular muscle and submucosa were mast cell.
pseudo-obstruction was mesenchymopathy and the local absence of ICCs was the specific finding of our case.

3. Conclusion

We report a case of SD with the absence of ICCs in the dilated ileum. We concluded the pathogenesis is mesenchymopathy and hypothesized that local absence of ICCs resulted in SD.

References