Abnormal Intestinal Anatomy in Late-stage Human Fetuses: Three Case Series

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(Received April 15, 2020; Accepted July 14, 2020)

Objective: We reported three cases of fetuses with abnormal intestinal anatomy found during our recent study of the transverse mesocolon using 20 late-stage fetuses.
Cases: The first case (CRL: 328 mm) appeared to have a duodenum and transverse colon trapped in Winslow's foramen (foramen epiploicum) and the duodenum superior portion elongated rightward. The second case (CRL: 264 mm) had a transverse colon inserted deeply into a space between the right kidney and duodenum. The third case (CRL: 276 mm) had a descending colon that ran inferiorly through a deep space between the left kidney and duodenum. Each case had a greater omentum that was shifted leftward, but this is usual. These 3 abnormalities were not evident in the anterior view during dissection of the liver, stomach, jejunum, and ileum. With underdeveloped pancreatic ducts due to unknown reason other than the internal hernia, the first case seemed to be fatal after birth. However, the second and third cases could have recovered after birth because there was no evidence of definite malrotation and because of loose attachments of the intestines to surrounding structures.
Conclusions: The intestinal morphologies described here could cause some sort of symptoms, such as abdominal pain, whose cause might be difficult to determine.

Key words: Abnormal anatomy of intestines, mesocolon, duodenum, colon, peritoneal fusion, human fetus

INTRODUCTION

Many studies have identified the genetic bases of developmental abnormalities of the intestines [1, 2]. However, incidental mismatches of fetal topographical anatomy that result in the production of unusual mechanical stress between structures may also lead to intestinal abnormalities. Our recent report of liver agenesis described one example, in which capture or trapping of the jejunum by the foot during the early stage of physiological umbilical herniation led to abnormalities [3]. A well-known group of intestinal abnormalities — malrotation (including nonrotation, reversed rotation, and hyperrotation) — apparently occurs during the repackaging process following physiological herniation [4]. However, without malrotation, not only the ascending colon but the descending colon often enter the hernia sac, a morphology that is apparently not an abnormality, but within the range of usual variation [5, +Kim *et al,* 2020 +++]. We found abnormal intestinal anatomy in 3 fetuses during our recent study of the transverse mesocolon using 20 late-stage fetuses near term [6]. Here we report these 3 unique cases because each of them had an intermediate morphology between the usual anatomy and a real malrotation, which suggested a possibility of recovery from a transient abnormality *in utero.*

MATERIALS AND METHODS

The study was performed in accordance with the provisions of the 1995 Declaration of Helsinki (as revised in 2013), and the study protocol was approved by the ethics committee of the Universidad Complutense, Madrid (B08/374). We examined 17 late-stage fetuses (crown-rump length [CRL]: 250 to 325 mm, gestational age [GA]: 30 to 38 weeks). All specimens were part of the large collection kept at the Embryology Institute of Complutense University, and were from miscarriages and ectopic pregnancies at the Department of Obstetrics of the university, while there was no document writing details of the maternal or fetal factors as well as the family name and date. First, we observed the entire intestine during removal of most parts of the liver, stomach, jejunum, and ileum. During dissection, photographs were taken with Pentax K-1 camera using a 50 to 100 mm zoom lens. To avoid artificial sepa-

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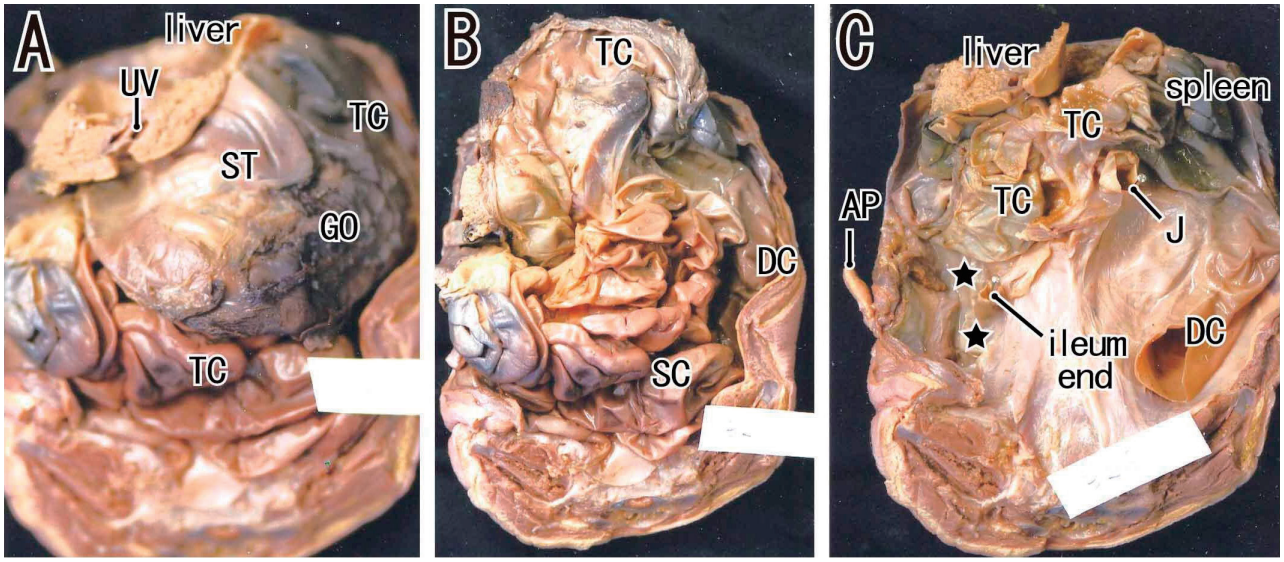

Fig. 1 Anterior macroscopic observations of the first specimen (CRL 328 mm).
Panel A shows the stomach and transverse colon after removal of major parts of the liver; the greater omentum was shifted leftward, and adhered to the dilated transverse colon (TC). Panel B shows the upward reflection of the transverse colon. Panel C shows the retroperitoneum after removal of the sigmoid colon and major parts of the jejunum (J) and ileum; removal of the transverse colon was difficult. Pins were inserted into the most proximal region of the jejunum and the ileum end. A band-like, thickened peritoneum (stars), fixed the ileum end at a higher position.
AP, appendix; DC, descending colon; GO, greater omentum; SC, sigmoid colon; ST, stomach; TC, transverse colon; UV, umbilical vein.

ration of the colon from the kidney, special attention was used to assure the colon remained at its original location.

After using routine procedures to prepare paraffin-embedded histological samples, the abdomen was sectioned horizontally at 50 to 100 μm intervals and stained with hematoxylin and eosin (H&E). The paraffin block contained the descending and ascending colon, left and right marginal parts of the transverse colon, the kidneys, and other retroperitoneal structures (including the aorta and parts of the posterior body wall muscles). Most photographs of histological samples were taken with a Nikon Eclipse 80. Photographs at ultra-low magnification (objective lens less than x1) were taken with a high-grade flat scanner using translucent illumination (Epson scanner GTX970). During observations of histological sections, we found 3 fetuses with abnormal course of the intestine, as reported here. The other 17 fetuses with usual morphologies had been used for a study of the topographical relation between the transverse colon and greater omentum [6].

RESULTS

Case 1: Candidate internal herniation of the duodenum and transverse colon into Winslow's foramen (CRL 328 mm)

The cecum and appendix were located at a higher level; the pancreatic head and duodenum were movable due to loose retroperitoneal fixation; and the transverse colon was dilated, folded, and tightly attached to the stomach (Fig. 1). The medial part of the transverse colon was folded and adhered to the duodenum and pylorus. A short band (thickened peritoneum) fixed the ileum end at a position higher than usual (Fig. 1C), but the lumen was not blocked beneath the band.

The histology indicated the superior portion of the duodenum was elongated rightward, and attached tightly to the left and inferior aspects of the hepatoduodenal ligament (Fig. 2A, B). The omental bursa (lesser sac) was occupied by the caudate lobe of the liver. The gastric cardia was dilated and attached to the left adrenal gland (Fig. 3A). The descending portion of the duodenum had a long meandering course along the anterior aspect of the right kidney, and turned back to the medially located greater papilla (Fig. 2C). There were no pancreatic ducts in the papilla or pancreatic parenchyma (Fig. 3B, D, E). Immediately below the pancreatic head, the duodenum passed horizontally toward the duodenojejunal junction. The pancreatic body was short and the tail appeared not to reach the spleen.

The jejunum extended upward, and occupied a large posterior space surrounded by the left kidney, stomach, and pancreas (Fig. 2C-E). The apical part of the left kidney was a slender process, and was sandwiched between the transverse colon and jejunum (Fig. 2C). Likewise, the right kidney was flattened beneath the folded and dilated colon (Fig. 2E). Smooth muscles were poorly developed or absent at several parts of the gastric and duodenal walls (Fig. 3A, D). Overall, the duodenum and transverse colon had been trapped in Winslow's foramen (foramen epiploicum), the passage that connects the lesser sac (omental bursa) and greater sac, behind the hepatoduodenal ligament.

Case 2: Insertion of transverse colon between the right kidney and duodenum (CRL 264 mm)

In macroscopic observations, a strong adhesion between the colon and pylorus was a limited abnormality (Fig. 4A, B).

The abnormal histological finding was limited to a course of the transverse colon: it had a sharp, wedge-

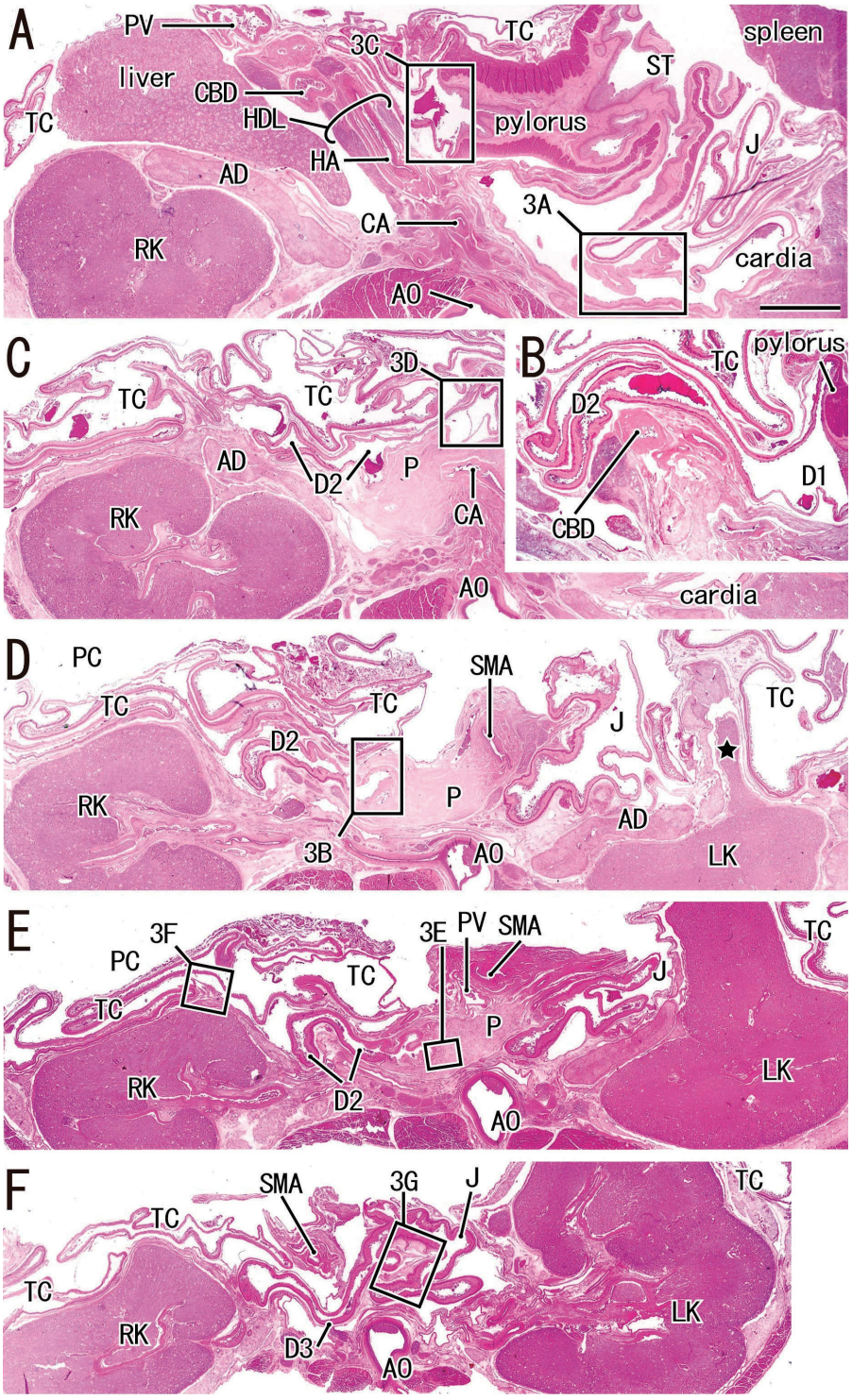

Fig. 2 Topohistology of the upper abdomen of the first specimen (CRL 328 mm).
Panel A shows the upper-most site, and panel E shows the lower-most site. The distances between the horizontal sections (50 to 100 μm) were 0.3 mm (A-B and B-C), 0.9 mm (C-D), 1.6 mm (D-E), and 3.5 mm (E-F). Panel A shows that the gastric cardia is highly dilated, and the superior portion of the duodenum (D1) extends anteriorly along the hepatoduodenal ligament (HDL). Panel B shows that the superior portion of the duodenum is highly folded and attached to the ligament. Panel C shows that the superior portion of the duodenum extends rightward on the right adrenal gland (AD). Panels D and E show that the duodenum meets the common bile duct (CBD) and, between the pancreas (P) and left kidney (LK), the jejunum (J) had a meandering course; the apex of the left kidney (LK) had an altered shape (star in panel D). Panel F shows that the duodenum is connected with the jejunum below the pancreas. Panels C to E show that the highly meandering course of the transverse colon. All panels are at the same magnification (scale bar in panel A: 5 mm). The seven rectangles within these panels appear at higher magnification in Fig. 3.
AO, aorta; D2, second (descending) part of the duodenum; D3, third (horizontal) part of the duodenum; HA, hepatic artery; P, pancreas; PC, peritoneal cavity; PV, portal vein; RK, right kidney; SMA, superior mesenteric artery; ST, stomach; TC, transverse colon.

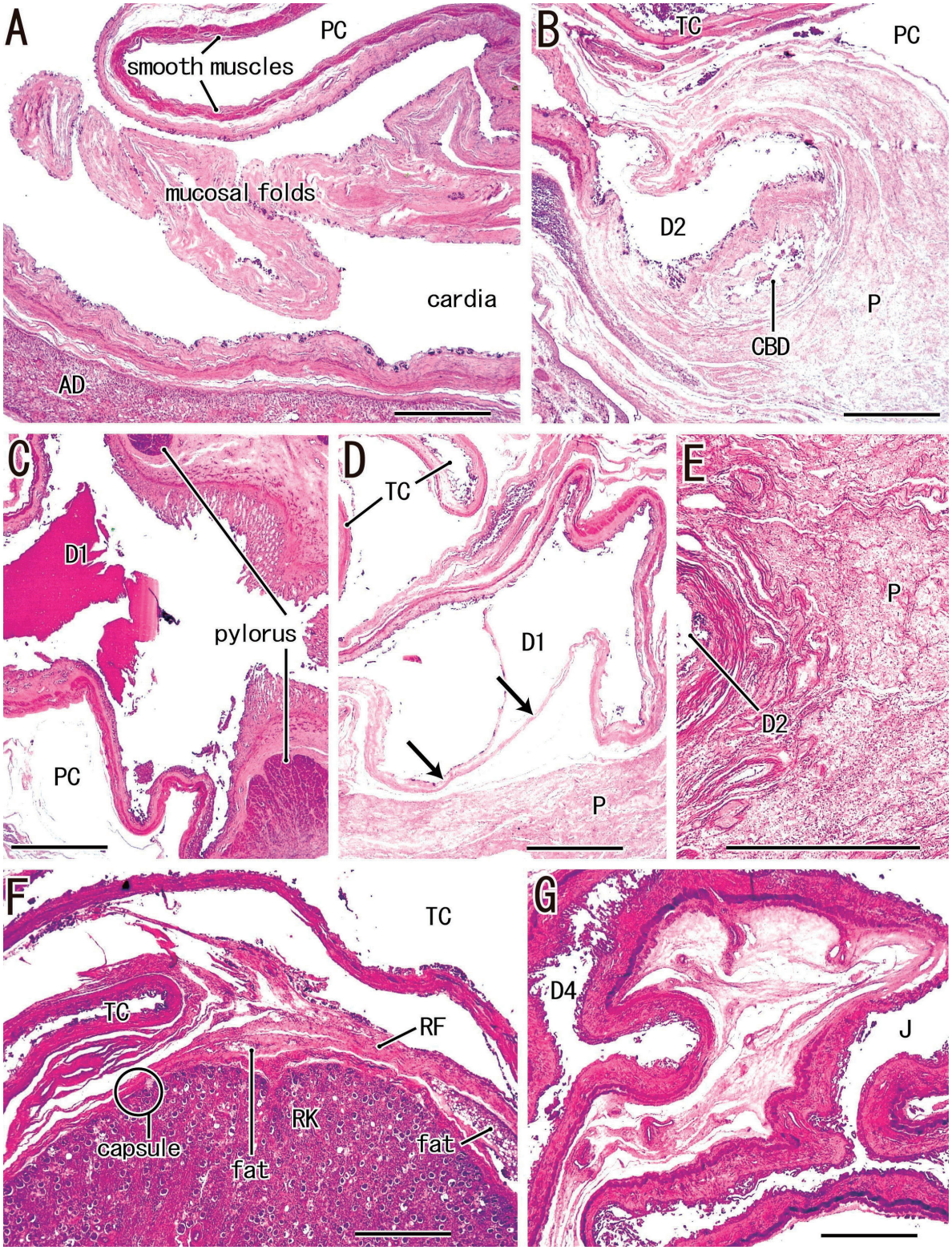

Fig. 3 High magnification observations of the upper abdomen (from Fig. 2) of the first specimen (CRL 328 mm).
Panel A (from Fig. 2A) shows poorly developed smooth muscles in the posterior wall of the gastric cardia. Panel B (from Fig. 2D) shows the common bile duct (CBD) in the major duodenal papilla. Panel C (from Fig. 2A) shows a border between the pylorus and the first (superior) duodenum (D1). Panel D (from Fig. 2C) shows the thin wall of the duodenum (arrows). Panel E (from Fig. 2E) and panel B show no pancreatic ducts in the pancreas (P). Panel F (from Fig. 2E) shows the renal capsule and renal fascia (RF) beneath the transverse colon (TC). Panel G (from Fig. 2F) shows the mesentery of the winding jejunum and duodenum in the posterior part of the abdominal cavity. Each scale bar: 1 mm.
AD, adrenal gland; D2, second (descending) part of the duodenum; D4, fourth (ascending) part of the duodenum; PC, peritoneal cavity; PV, portal vein; RF, renal fascia; RK, right kidney.

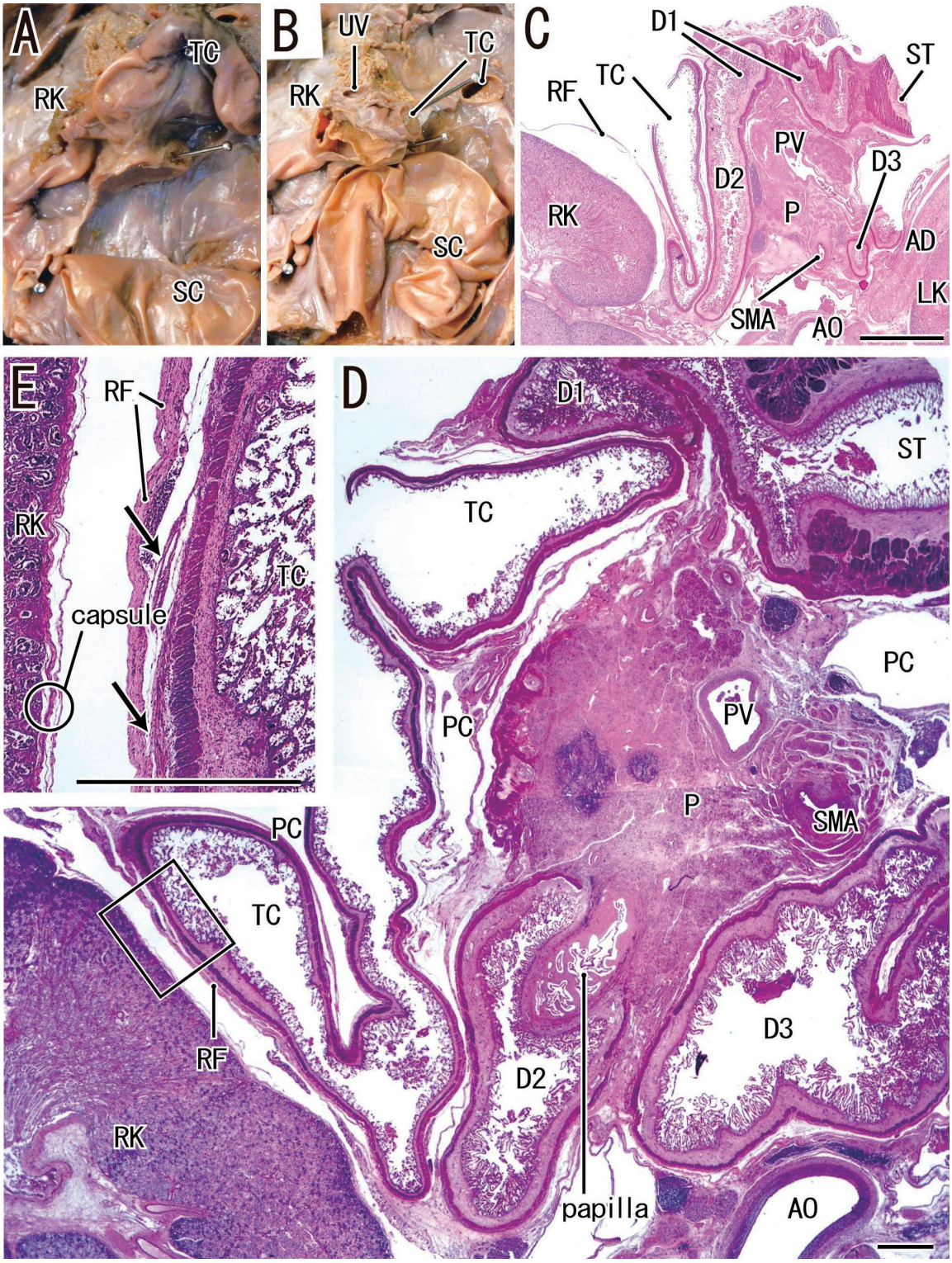

Fig. 4 Macroscopic and histologic observations of the second specimen (CRL 264 mm).
Panel A shows an anterior view of the transverse colon, which was reflected upward. Panel B shows the retroperitoneum after removal of major parts of the jejunum and ileum. In panels A and B, pins were inserted into the most proximal region of the jejunum and the end of the ileum; it was difficult to remove the transverse colon because the medial part (uppermost pin) adhered to the duodenum and pylorus. Panel C shows the transverse colon (TC), posterior to the second (descending) portion of the duodenum (D2). Panel D (a plane 0.5 mm below panel C) shows the major duodenal papilla and the abnormal transverse colon. Panel E (a higher magnification view of the rectangle in panel D) shows the renal capsule and a connection of the colon to the renal fascia (RF) by fibrous bands (arrows). Scale bar: 5 mm in panel C and 1 mm in panels D and E.
AD, adrenal gland; AO, aorta; D1, first (superior) part of the duodenum; D3, third (horizontal) part of the duodenum; LK, left kidney; P, pancreas; PC, peritoneal cavity; PV, portal vein; RK, right kidney; SC, sigmoid colon; SMA, superior mesenteric artery; ST, stomach; UV, umbilical vein.

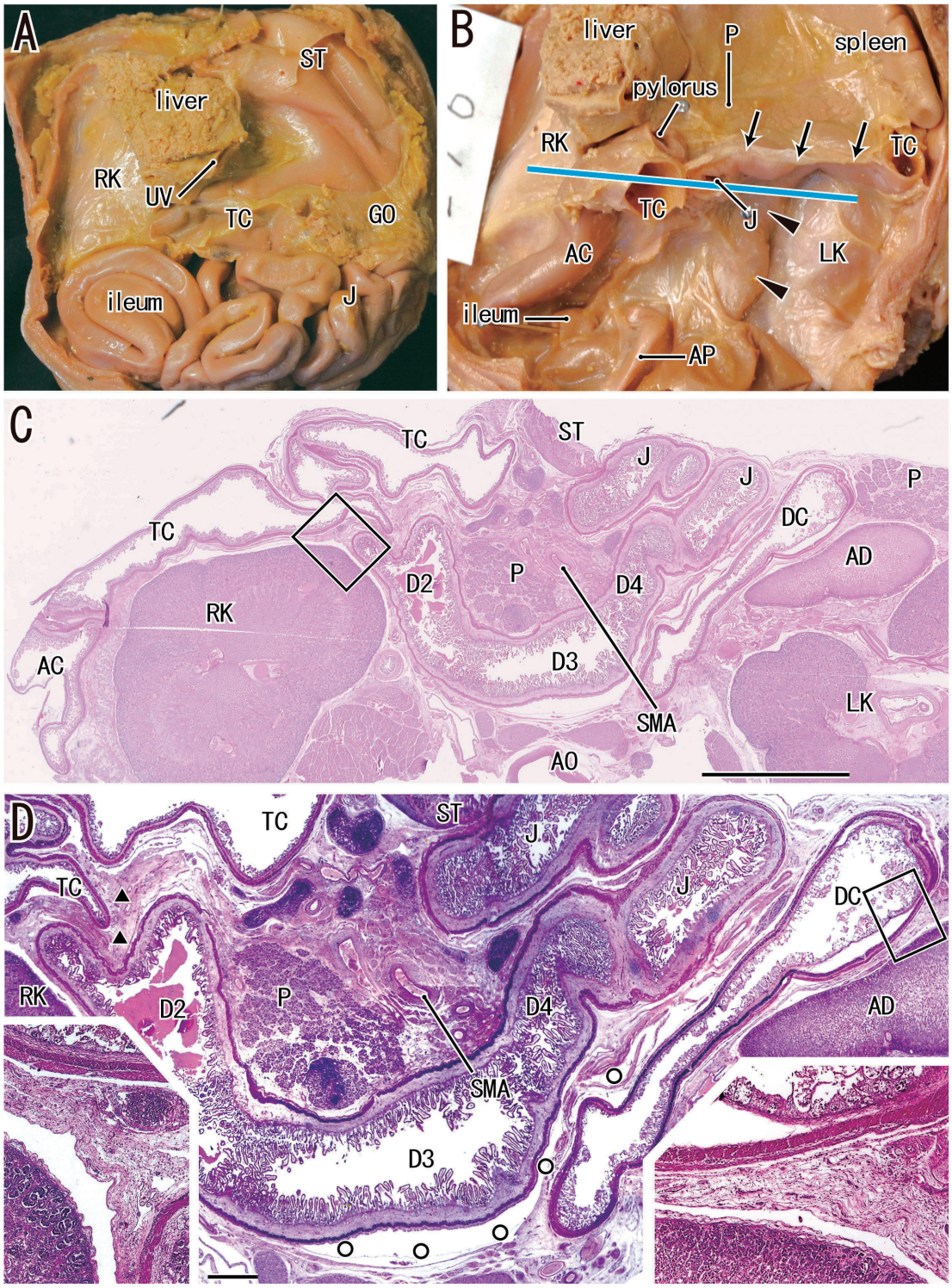

Fig. 5 Macroscopic and histologic observations of the third specimen (CRL 276 mm).
Panel A shows an anterior view after removal of a major part of the liver; the greater omentum (GO) extends inferiorly and leftward. Panel B shows a cut surface of the transverse mesocolon (arrows) after removal of major parts of the stomach, transverse colon (TC), jejunum (J), and ileum, and retroperitoneal swelling (arrowheads), in which the descending colon had an abnormal course. Panel C shows a horizontal section (blue line in panel B) in which the descending colon (DC) was inserted deeply between the left kidney (LK) and duodenum. Panel D (a higher magnification view of the rectangle in panel C) shows fascial relations along the duodenum. Between the transverse colon and duodenum (triangles) as well as between the descending colon and adrenal, a loose tissue is seen without any border (bottom corners of panel D); however, the duodenum was from retro-abdominal structures by a narrow peritoneal space (circles). Scale bars in panels C and D: 1 mm.
AC, ascending colon; AD, adrenal gland; AO, aorta; AP, appendix; D2, second (descending) part of the duodenum; D3, third (horizontal) part of the duodenum; D4, fourth (ascending) part of the duodenum; P, pancreas; RK, right kidney; SMA, superior mesenteric artery; ST, stomach.

like curve that inserted deeply into the space between the duodenum and right kidney (Fig. 4C, D). This curved region of the colon attached loosely to the duodenum and kidney, and there was a narrow space between the colon and renal fascia (Fig. 4E).

Case 3: Descending colon between the left kidney and duodenum (CRL 276 mm)

In macroscopic observations, an unusual morphology was limited to a retroperitoneal swelling present in the medial side of the left kidney (Fig. 5A, B).

The histology indicated the descending colon had a sharp and posterior turn near the future splenic flexure, and was inferior while passing through a deep space between the duodenum and left kidney (Fig. 5C). The duodenum and descending colon were loosely attached to the retroperitoneal structures, so there was a narrow space along the intestines facing the kidney, adrenal gland, retroperitoneal lymph nodes, inferior vena cava, and aorta. The descending colon resumed its original course below the left kidney, and connected to the dilated sigmoid colon.

DISCUSSION

Our first case (CRL 328 mm) had a candidate internal hernia of the duodenum and transverse colon into Winslow's foramen. However, this interpretation is simply based on the close topographical relationship of the duodenum and transverse colon with the hepatoduodenal ligament. The lesser sac was occupied by the liver caudate lobe, as during normal development, and the contents of the hepatoduodenal ligament and their topographical relations were also normal. Thus, we did not observe an actual hernia but the recovery process. However, because parts of the jejunum were in the left side of the gastric cardia, traction by the suspected internal hernia seemed to cause conduction of mechanical stress to the cardia and jejunum via the duodenum. Later during development, pressure from the unfixed intestines might have been so strong that it changed the morphology of both kidneys. With underdeveloped pancreatic ducts due to unknown reason other than the internal hernia, the first case seemed to be fatal after birth. Nevertheless, because a mass of the pancreatic parenchyma existed, the ducts had once developed but they might be secondarily degenerated.

An internal hernia passing through Winslow's foramen is very rare [7], and previous studies classified this condition as a left paraduodenal hernia [8–10]. However, in a group of the left paraduodenal hernia, a part of the intestines usually enters the lesser sac through a rupture of the gastrocolic ligament or other parts of the omentum, not through Winslow's foramen [11–13]. Moreover, in contrast to a report of a left internal hernia by Okino *et al.* [14], our case seemed have normal arrangement of the midgut mesenteries.

The second case (CRL 264 mm) had an abnormal transverse colon, in which a sharp wedge-like curve inserted into the space between the right kidney and duodenum. In contrast, the third case (CRL 276 mm) had an abnormal descending colon, with a relatively long course and a medial shift. Thus, the second case may have had a temporal and spotty mechanical stress directed posteriorly, whereas the third case may have had a slight error in the repackaging process from physiological herniation. Neither of these cases had a band-like structure that fixed or trapped the colon. In the second case, a dilated sigmoid colon might have provided mechanical stress for pushing it posteriorly; in the third case, a delayed repackaging of the jejunum might have led to misdirection of the descending colon and medial fixation. It is likely that the descending colon is repackaged before the jejunum: such a reversed return seemed to be an usual variation according to Cho *et al.* [5]. In the second case, the deep insertion or hernia of the colon into a posterior space can be classified as a right paraduodenal hernia [8–10, 15].

In general, amniotic bands are considered major causes of defects in the limbs and/or body wall [16]. Likewise, Ladd bands are abnormal peritoneal structures in children that obstruct the intestine [17]. Abnormal tissue bands can lead to traction, fixation, and mechanical stress (possibly from the vitelline structures) and are considered a major cause of gastroschisis [18, 19]. An abnormal band may also lead to malpositioning of the descending colon [20]. However, we found none of these features in the three specimens described here. Indeed, we found a band at the ileum end in the first case (a candidate Winslow's foramen hernia), but it apparently did not cause the rightward elongation of the duodenum. In addition, a leftward shift of the greater omentum is present in normal morphology. Conversely, a widely and evenly extended omentum covering the entire jejunum and ileum is rare in late-stage fetuses [6].

Overall, because none of these cases had malrotation or loose retroperitoneal attachments, these unusual morphologies might not correspond to any classical categories of abnormalities. Rather, they might be likely to show the recovery process from a transient abnormality. In particular, the second and third cases seemed to be out of entities of any congenital diseases. However, after birth, these unusual morphologies might cause some sort of symptoms, such as abdominal pain, whose cause might be difficult to determine.

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