A Novel Strategy to Reveal Latent Liver Abnormalities in Human Embryonic Stages from a Large Embryo Collection

The cause of spontaneous abortion of normal conceptuses remains unknown in most embryos because of the difficulty of diagnosing too small embryos. We aimed to reveal latent liver abnormalities using novel phase-contrast radiographic computed tomography (PXCT). Embryos with liver volumes $\pm 2$ SD above or below the mean for the stage of development were selected. Embryos with potentially abnormal livers were further analyzed by using PXCT. The PXCT data provide a resolution of $\geq 18$ μm/pixel, which enabled highly sensitive measurement, approximately $>1000$ times more sensitive than the conventional radiographic method using absorption contrast [6].

Liver abnormality was detected in 9 embryos after the procedure of our protocol (Fig. 1), which consisted of hepatic agenesis (2 embryos), hepatic hypogenensis (4), liver lobe defect (1), involvement of the liver to the thoracic cavity by diaphragm herniation (1), and other (1). Three embryos had only liver abnormalities and 6 exhibited complications in other organs. The prevalence of liver malformations in CS18 and CS21 in the intrauterine population of externally normal embryos is approximately 1.7%. Most of such liver abnormality embryos do not survive, as liver function becomes essential during development [7].

A representative embryo with liver agenesis is shown in Fig. 2. The size and gestational age were within the normal range for the embryo at CS 21. Obvious damage to, or anomalies of, the external forms were not present (Fig. 2a). The liver at CS21 usually occupies a large space in the abdominal cavity, which has a smooth surface due to the contact between the cranial surface and the diaphragm, and between the ventral surface and the abdominal wall [7]. In the present embryos, the liver was not detected in any of the serial plane sections (Fig. 2b). The locations of all intrahepatic, retroperitoneal, and intra-abdominal organs were reconstructed in three dimensions (Fig. 2c). The absence of the liver had affected the locations of the other internal organs, especially the stomach, duodenum, and pancreas. The stomach was observed on the midsagittal plane sections at Th4, the diaphragm is indicated by arrow heads. Lung (Lu), c. Left anterior oblique view of the three-dimensional (3-D) PXCT reconstruction of the embryo using Amira software (Visage Imaging, Berlin, Germany), demonstrating the locations of all intrathoracic, retroperitoneal, and intra-abdominal organs.

The findings of note were as follows: agenesis of the liver; the stomach was deviated ventrally and cranially; the pancreas (Pa) was deviated ventrally, and the right mesoappendix (Ma) and genital ridge (Gd) were absent. Adrenal gland (Ad), splenomphysis (Mt), and heart (Ht).

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