**NOTE** *Pathology*

# Abdominal hamartoma with pancreatic and hepatic differentiation in a sow

Nanako USHIO[1)], James K. CHAMBERS[1)]*, Kennichi WATANABE[1)], Takuya E. KISHIMOTO[1)], Jun-You LI[2)], Hiroyuki NAKAYAMA[1)] and Kazuyuki UCHIDA[1)]

[1)]*Laboratory of Veterinary Pathology, Graduate School of Agricultural and Life Sciences, The University of Tokyo, Tokyo 113–8657, Japan*
[2)]*Animal Resource Science Center, Graduate School of Agricultural and Life Sciences, The University of Tokyo, Tokyo 113–8657, Japan*

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ABSTRACT. A 7-year-old Duroc sow exhibited emaciation, loss of appetite and rapid breathing, and was euthanized. Histopathological examination revealed mild to moderate fibrosis of the heart, cystic kidneys and ulcerative enteritis associated with *Balantidium* infection. Additionally, a small nodule was incidentally found in the peripancreatic fat tissue. The nodule consisted of disarranged cellular components: pancreatic islet cells (either insulin-, glucagon- or somatostatin-positive), pancreatic acinar cells, hepatocytes (human hepatocyte-positive) and ductal cells (cytokeratin 19-positive). Some of the human hepatocyte-positive cells were also positive for chromogranin A and cytokeratin 7, indicating that they were hepatic progenitor cells. The nodule was therefore diagnosed as hamartoma, probably originating from a fragment of the caudal verge of the liver bud, which contains hepatic and pancreatic progenitors.
KEY WORDS: abdominal hamartoma, liver, pancreas, sow

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Hamartoma is a focal overgrowth of endogenous mature cells in an organ [2, 4]. Pancreatic hamartoma in humans was divided into solid, and solid and cystic hamartoma in a previous report [6]. Solid pancreatic hamartoma is composed of three disarranged cellular components (acinar, islet and ductal cells) in the sclerotic stroma [6, 9]. Solid and cystic pancreatic hamartoma is a solid hamartoma with cystic lesions [6, 8]. Animal cases of pancreatic hamartoma, however, have not been reported. We observed a unique hamartoma lesion consisting of pancreatic and hepatic cells in a sow.

A 7-year-old Duroc sow exhibited emaciation, loss of appetite and rapid breathing, and was euthanized because of a poor prognosis. At necropsy, enlargement of the heart (right ventricular dilation and left ventricular hypertrophy) and polycystic kidneys was observed. Tissues from the heart, trachea, thyroid glands, lung, liver, spleen, pancreas, small intestines, large intestines and brain were fixed in 10% neutral-buffered formalin. The tissues were routinely embedded in paraffin, sectioned 4-$\mu$m thick and stained with periodic acid Schiff (PAS) as well as hematoxylin and eosin (HE).

Microscopically, mild to moderate fibrosis was found in the ventricular wall of the heart. In the small and large intestines, ulcerative enteritis associated with *Balantidium* infection was observed. A small nodule was incidentally found in the peripancreatic fat tissue (Fig. 1) composed of (i) cuboidal endocrine cells with an eosinophilic cytoplasm, a pale round nucleus and prominent nucleoli forming islet structures surrounded by thin connective tissue (Fig. 2, black arrows), (ii) columnar epithelial cells forming the duct (Fig. 2, green arrows), (iii) polygonal cells with an eosinophilic granular cytoplasm and an oval-shaped nucleus arranged in a trabecular pattern or a pseudo acinar structure (Fig. 3, arrows) and (iv) pancreatic exocrine cells with a hyperchromatic nucleus and PAS-positive zymogen granules in the cytoplasm forming the acinus (Figs. 2 and 3, arrowheads). All types of cells were mature and showed no nuclear or cytological atypia.

Immunohistochemistry was performed using the primary antibodies listed in Table 1. Reaction products were visualized using the EnVision+ System (Dako, Kyoto, Japan). The cuboidal cells (i) were positive for glucagon (Fig. 4), somatostatin (Fig. 5) or insulin (Fig. 6). The glucagon- or somatostatin-positive cells were located in the periphery of the islet structure (Figs. 4 and 5), and the insulin-positive cells were in the center (Fig. 6). Duct-forming columnar cells (ii) were immunopositive for cytokeratin (CK) 19 (Fig. 7). The large polygonal cells with eosinophilic granules (iii) were moderately to strongly immunopositive for human hepatocyte and chromogranin A, and partly immunopositive for CK 7 (Figs. 8–10), but negative for synaptophysin. Hepatocytes in the liver were positive for human hepatocyte and chromogranin A, and partly positive for CK 7, while ductal cells in the pancreas and liver were positive for CK 19. Islet cells in the pancreas were positive for glucagon, somatostatin, insulin and/or synaptophysin. Immunohistochemistry results are summarized in Table 2.

In the present study, the cellular components of the peripancreatic nodule indicated its pancreatic and hepatic differentiation. Differential diagnosis of the nodule included hamartoma, transdifferentiation of pancreatic cells to hepatic cells and ectopic liver tissue in the pancreas. Transdifferentiation, known as metaplasia of pancreatic exocrine cells into hepatocytes, has been observed *in vitro* and in experiments during regeneration after massive injury [3, 5, 10–13, 15]. Glucocorticoid adminis-

*CORRESPONDENCE TO: CHAMBERS, J. K., Laboratory of Veterinary Pathology, Graduate School of Agricultural and Life Sciences, The University of Tokyo, 1–1–1 Yayoi, Bunkyo-ku, Tokyo113–8657, Japan. e-mail: achamber@mail.ecc.u-tokyo.ac.jp

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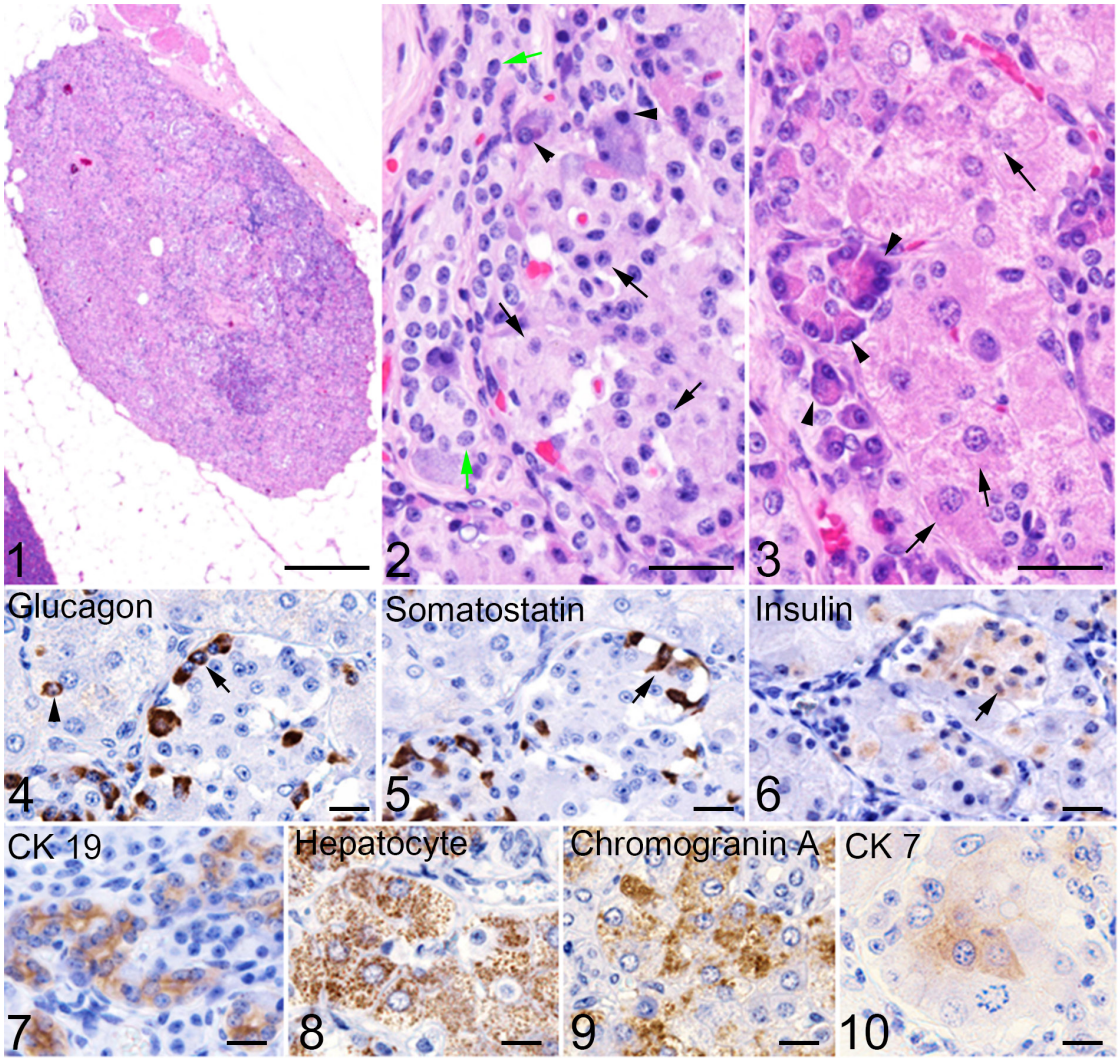


Fig. 1. A small nodule in the peripancreatic fat tissue. HE, Bar: 1 mm.
Fig. 2. Higher magnification of the nodule. Cuboidal endocrine cells with an eosinophilic cytoplasm, a pale round nucleus and prominent nucleoli, forming the islet structure surrounded by thin connective tissue (black arrows). Columnar epithelial cells forming the duct (green arrows). Pancreatic exocrine cells with zymogen granules (arrowheads). HE, Bar: 40 $\mu$m.
Fig. 3. Higher magnification of the nodule. Polygonal cells with an eosinophilic granular cytoplasm (arrows) arranged in a trabecular pattern. Pancreatic exocrine cells with zymogen granules in the cytoplasm forming the acinus (arrowheads) or scattered among other types of cells. HE, Bar: 30 $\mu$m.
Fig. 4. Glucagon-positive cells located in the periphery of the islet-like structure (arrow) and admixed with other types of cells (arrowhead). Hematoxylin counterstain, Bar: 20 $\mu$m.
Fig. 5. Somatostatin-positive cells located in the periphery of the islet-like structure (arrow). Hematoxylin counterstain, Bar: 20 $\mu$m.
Fig. 6. Insulin-positive cells located in the center of the islet-like structure (arrow). Hematoxylin counterstain, Bar: 20 $\mu$m.
Fig. 7. Duct-forming columnar cells positive for CK 19. Hematoxylin counterstain, Bar: 15 $\mu$m.
Fig. 8. Large polygonal cells positive for human hepatocyte. Hematoxylin counterstain, Bar: 15 $\mu$m.
Fig. 9. Large polygonal cells containing chromogranin A-positive granules. Hematoxylin counterstain, Bar: 15 $\mu$m.
Fig. 10. Some of the large polygonal cells positive for CK 7. Hematoxylin counterstain, Bar: 15 $\mu$m.

tration or copper deficiency can also induce transdifferentation of the pancreas to the liver [11, 12, 15]. In the present case, however, glucocorticoid administration was not conducted, and regeneration of the pancreas was not observed.

Immunohistochemical examinations revealed that insulin-, glucagon- and somatostatin-positive cells were arranged in the same pattern observed in the pancreatic islets of a pig [14]. However, some of the endocrine cells were scattered in the tissues without forming islets. Large polygonal cells were positive for human hepatocyte, and some of these cells were also positive for chromogranin A and CK 7 (Figs. 8–10). This staining pattern was consistent with that of he-

Table 1. Primary antibodies used in the present study

| Antibody | Clone | Dilution | Antigen retrieval | Source |
|---|---|---|---|---|
| Mouse monoclonal anti-human Hepatocyte | OCH1E5 | 1:200 | Autoclave ( pH 6.0) | Dako, Kyoto, Japan |
| Rabbit polyclonal anti-chromogranin A | | 1:2,000 | None | Yanaihara, Fujinomiya, Japan |
| Mouse monoclonal anti-CK 7 | OV-TL 12/30 | 1:100 | Protease K | Dako, Kyoto, Japan |
| Mouse monoclonal anti-synaptophysin | SY38 | 1:50 | Autoclave (pH 9.0) | Dako, Kyoto, Japan |
| Mouse monoclonal anti-CK 19 | b170 | Ready to use | Protease K | Leica Biosystems, Newcastle, U.K. |
| Rabbit polyclonal anti-glucagon | | 1:100 | None | Dako, Kyoto, Japan |
| Rabbit polyclonal anti-somatostatin | | 1:500 | None | Dako, Kyoto, Japan |
| Genia Pig polyclonal anti-insulin | | 1:200 | Autoclave (pH 9.0) | Dako, Kyoto, Japan |

Table 2. Results of immunohistochemistry

| Marker | Nodule | | | | Islet cells in the pancreas | Ductal cells in the pancreas and liver | Hepatocytes in the liver |
|---|---|---|---|---|---|---|---|
| | Cuboidal endocrine cells (i) | Duct-forming columnar cells (ii) | Large polygonal cells (iii) | Pyramidal exocrine cells (iv) | | | |
| Human Hepatocyte | − | − | + | − | − | − | + |
| Chromogranin A | − | − | + | − | − | − | + |
| CK 7 | − | + | ± | − | − | + | ± |
| Synaptophysin | + | − | − | − | + | − | − |
| CK 19 | − | + | − | − | − | + | − |
| Glucagon | ± | − | − | − | ± | − | − |
| Somatostatin | ± | − | − | − | ± | − | − |
| Insulin | ± | − | − | − | ± | − | − |

+: Positive, ± : Partly positive, −: Negative.

patic progenitor cells in pigs (Table 2) as well as in humans [7]. The results indicate that the large polygonal cells in the nodule included hepatic progenitor cells. The liver and the pancreas are derived from a common embryonic structure in early development. A previous study on fate mapping in mice suggested that the ventral pancreas progenitors were located at the caudal verge of the liver bud during the 1–3 somite stages [1]. Ectopic hepatic tissue is not likely to be the present lesion, because both the hepatic and the pancreatic tissues were admixed and disarranged in the nodule. Therefore, the nodule was diagnosed as abdominal hamartoma that was probably derived from a fragment of the liver bud or from the even more primitive multipotent ventral foregut.

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