Annals of Nuclear Medicine Vol. 14, No. 2, 131–134, 2000

Protein-loss into retroperitoneal lymphangioma: Demonstration by lymphoscintigraphy and blood-pool scintigraphy with Tc-99m-human serum albumin

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A rare, benign congenital lymphangioma has been reported to occur frequently in the neck and axilla, but rarely in the retroperitoneal space. We report a case of a retroperitoneal lymphangioma associated with hypoproteinemia caused by protein-loss into the tumor. In this case, lymphoscintigraphy with subcutaneously injected Tc-99m-human serum albumin (HSA) disclosed the communication between the tumor and the lymphatic system, and sequential abdominal scintigraphy with intravenously injected Tc-99m-HSA revealed the protein loss into the tumor. Abdominal scintigraphy with Tc-99m-HSA injected intravenously or subcutaneously is occasionally useful for determining the etiology of hypoproteinemia.

Key words: retroperitoneal lymphangioma, Tc-99m-HSA, lymphoscintigraphy, hypoproteinemia

CASE REPORT

A 14-year-old Japanese boy, who had a one-month history of bloody and watery diarrhea, was admitted to our hospital. The symptoms were more obvious in the morning and exacerbated by exercise. On physical examination, low blood pressure (systolic/diastolic, 90/50 mmHg), anemic palpebral conjunctiva, slight abdominal distention and pitting edema in the anterior lower legs were noted. No abdominal mass was palpable. Laboratory tests revealed anemia and hypoproteinemia; red blood cell count, 371 × $10^4/\mu l$; hemoglobin concentration, 9.9 g/d*l*; hematocrit, 32.3%; serum total protein and albumin concentrations, 3.9 g/d*l* and 1.96 g/d*l*, respectively.

Abdominal ultrasonography revealed a large cavernous or cystic mass, and ascites. Abdominal computed tomography (CT) showed a well-circumscribed cystic mass spreading over the whole abdomen. The inside of the mass showed water density on the CT (Fig. 1). The border between the mass and pancreas was indistinct, and a part of the mass seemed to infiltrate into the bowel wall. After an injection of contrast material, normal abdominal vasculature was delineated but no abnormal enhancement was demonstrated in the mass. The bowel was compressed by the mass. In particular, jejunum and ileum were displaced to the anterior space of the abdomen.

Since the borders of the mass with the pancreas and the colon were unclear on the CT, endoscopic retrograde cholangiopancreatography (ERCP) and barium enema were performed. On ERCP, there was no obvious abnormal finding. On barium enema, multiple submucosal tumors were suspected in the left transverse to the sigmoidal colon. The lesions ranged from 3 mm to 15 mm in diameter.

Angiography showed no obvious anatomical abnormality, but demonstrated stretched vasculature around the splenic flexure, descending colon and pancreas, indicating the presence of a hypovascular tumor extending to these organs. No apparent vascular proliferation was observed in the tumor.

Based on these findings, a diagnosis of lymphangioma was strongly suspected. To investigate the relationship between the tumor and the lymphatic system, lymphoscintigraphy with Tc-99m-human serum albumin (Tc-99m-HSA) was performed. Seventy-four MBq of Tc-99m-HSA was injected subcutaneously into the webbing

Received October 18, 1999, revision accepted December 16, 1999.

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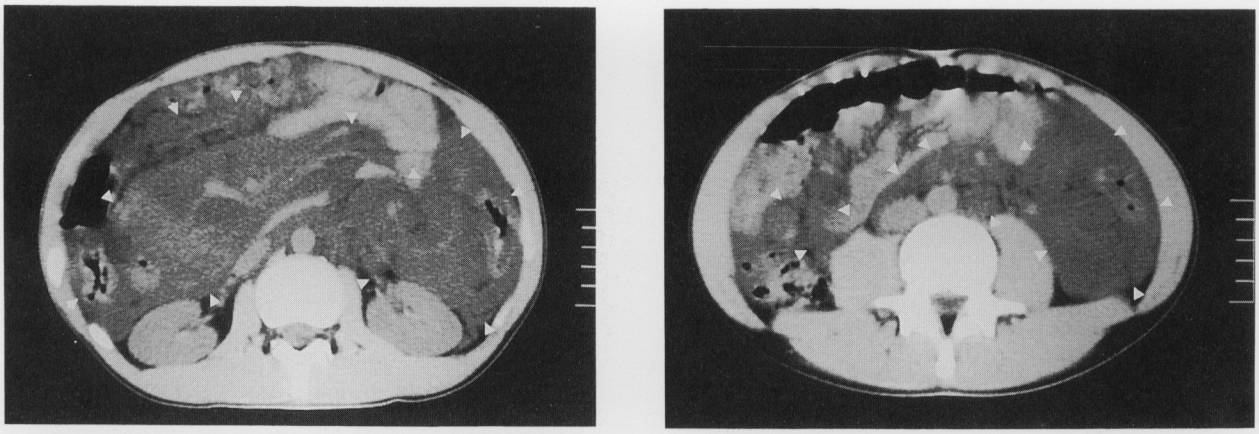

A B

Fig. 1 Plain abdominal CT at about the level of the first (A) and of the third lumber vertebra (B) demonstrate a well-circumscribed cystic mass of water density extending over the whole abdomen (arrow heads). The bowel is compressed to the right lower side by the mass.

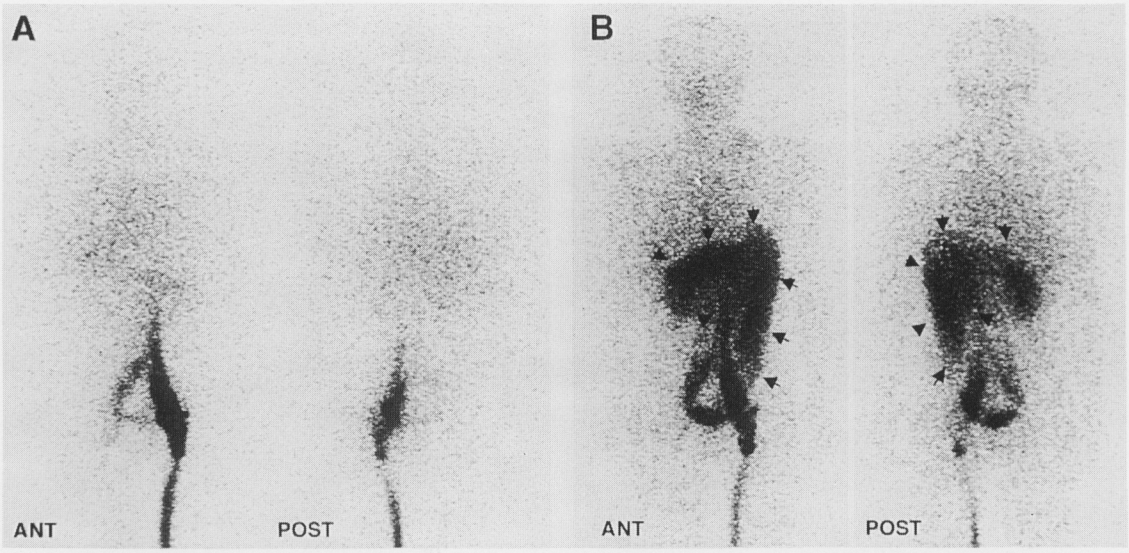

Fig. 2 Anterior and posterior whole body images obtained 30 minutes (A) and 3 hours (B) after the subcutaneous injection of Tc-99m HSA. On the images at 30 minutes, there is no apparent abnormal activity in the region of the tumor. The abnormal activity extending from mid to left abdomen, which corresponds to the cystic tumor on CT, becomes apparent on the images at 3 hours after the injection (arrow heads).

between the first and second toes, and whole body imaging was done 30 minutes, one hour, two and three hours after the injection. The lymphoscintigrams showed abnormal activity, which increased with time, in the abdomen (Fig. 2). The activity was localized to the region of the tumor. This finding proved the communication between the tumor and the lymphatic system, an important clue for diagnosing lymphangioma.

To clarify the etiology of the hypoproteinemia in this patient, blood pool scintigraphy with Tc-99m-diethylene triamine pentaacetic acid-human serum albumin (Tc-99m-DTPA-HSA) was performed. Seven hundred and forty MBq of Tc-99m-DTPA-HSA was intravenously injected as a bolus, and sequential images of the abdomen were taken 2.5, 5.5 and 24 hours after the injection. The obtained images showed abnormal activity increasing gradually with time. The location of the abnormal activity was not in the bowel, but in the tumor as seen on the lymphoscintigraphy (Fig. 3). This finding indicated that protein loss did not occur into the bowel, but into the tumor.

Based on these findings, a diagnosis of protein loss into the reteroperitoneal lymphangioma was made. The patient underwent surgery for sclerotherapy of the tumor with OK-432 as a sclerosing agent. The abdominal surgery revealed a multilocular cystic mass spreading over

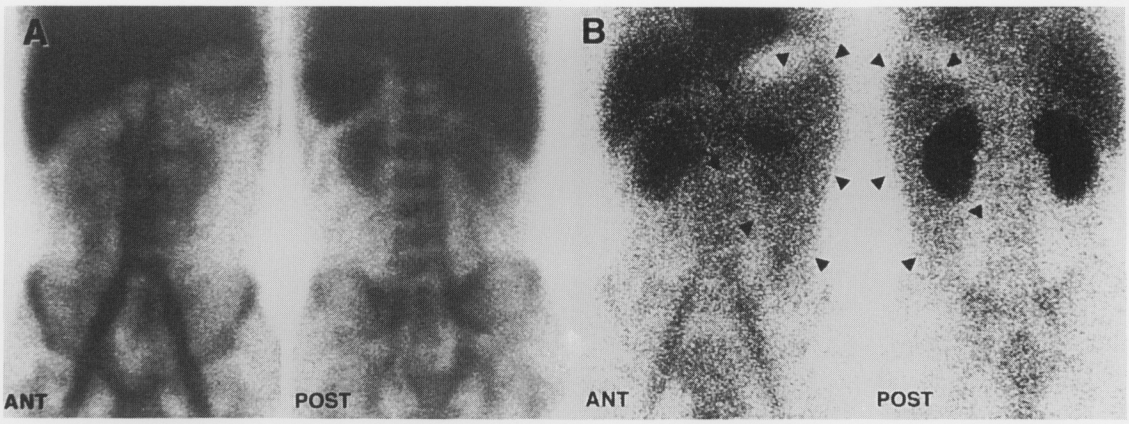

Fig. 3 Anterior and posterior abdominal images 5 minutes (A) and 24 hours (B) after the intravenous injection of Tc-99m-DTPA-HSA. Abnormal abdominal activity (arrow heads), which is not appreciable on the blood pool image at 5 min, is seen on the image taken at 24 hours after the injection. The extent of the abnormal activity is the same as seen on the lymphoscintigram, corresponding to the location of the tumor.

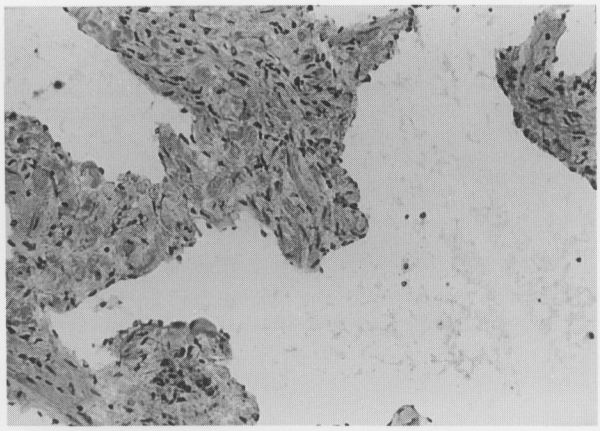

Fig. 4 Microscopically, the tumor section shows the presence of lacunae, which were lined with endothelial cells, without any blood cells inside them. These findings are compatible with lymphangioma.

the retroperitoneal space. Pathology of the tumor revealed the presence of lacunae, which were lined with endothelial cells, without any blood cells inside them (Fig. 4). Dilated lymph vessels and lymphocytes forming follicles were also observed in the tumor stroma consisting of connective, adipose and a little muscular tissue. Pathologically, the tumor consisted chiefly of a capillary lymphangioma, but small parts of cystic, cavernous lymphangioma and lymphangiomyoma were also seen.

The sclerotherapy of the tumor was effective for the protein loss. After treatment, the serum protein level returned to the normal range.

DISCUSSION

Cystic retroperitoneal lymphangioma is a rare, benign congenital tumor usually detected in childhood.[1–4] The incidence has been estimated to be less than one per 100,000 in-patients.[3] Half of the tumors are present at birth and up to 90 percent become evident within the first 2 years of life.[1] Gender distribution is equal,[2] although some reports have described male predominance.[3] Preferred sites of involvement are the neck and axilla,[5,6] consisting of approximately 95 percent of all lymphangiomas.[5] The rest include the mediastinum,[5,6] retroperitoneum,[5–7] mesentery,[1,5] omentum,[1,6] and many other organs.[5,6] Although the etiology of the tumor is still unknown, several hypotheses have been proposed. Some authors believe that the tumor is a hamartomatous growth from ectopic or malformed lymphatic tissue, others believe that the tumor occurs secondarily to a hyperplastic reaction to inflammation, trauma or localized degeneration of a lymph node.[3]

Pathologically, lymphangiomas consist of three groups: 1) capillary lymphangiomas composed of small lymphatics, 2) cavernous lymphangiomas composed of larger and spongy lymphatics, and 3) cystic lymphangiomas composed of large macroscopic lymphatic spaces containing collagen and smooth muscle.[3,6] Generally, typical findings are the presence of a tumor lined with flat endothelial cells and small lymphatic spaces in the tumor as seen in our case.[5–7]

Clinical symptoms of retroperitoneal lymphangioma are nonspecific, such as abdominal pain, abdominal distention and diarrhea.[5–7] Anemia, gastrointestinal bleeding and hypoproteinemia, which are seen in our case, are also described.[7] Imaging studies are important in diagnosing lymphangioma. CT or magnetic resonance imaging (MRI) can localize the tumor and demonstrate its cystic structure, suggesting the possibility of lymphangioma,[7,8] but non-tumorous cystic lesions such as abscesses and tumorous cystic lesions such as mesothelioma should be differ-

entiated.[8] It is often difficult to differentiate lymphangioma from other cystic tumors by the CT or MRI findings. To further characterize the tumor and to investigate the tumor-related pathophysiology, scintigraphic studies could be useful. In particular, lymphoscintigraphy is useful for the diagnosis of lymphangioma, being able to demonstrate the communication between the tumor and the lymphatic system.[9] If the patient had hypoproteinemia, abdominal scintigraphy with Tc-99m-DTPA-HSA could be quite useful to determine the location of protein loss. In the literature, several authors have reported protein loss enteropathy as a cause of hypoproteinemia in lymphangioma,[10] but there is no report of protein loss into the tumor. To the best of our knowledge, our case may be the first documented one of protein-loss into a lymphangioma confirmed by Tc-99m-HSA abdominal scintigraphy.

The fate of the serum protein leaked into the tumor is of great interest. Several possibilities could be considered, including intratumoral metabolism, reabsorption into the systemic circulation and gradual leakage into the bowel. Although we do not have enough clinical data to answer this question, the third possibility would be most probable, considering the patient's symptoms of hypoproteinemia and anemia associated with bloody and waterly diarrhea.

As for the treatment, excision of the tumor is desirable, but when it invades neighboring vital organs, other treatments such as sclerotherapy may be chosen.[4]

In conclusion, scintigraphic studies with Tc-99m HSA may be useful in determining the strategy for treatment, and providing useful information regarding the pathophysiological relationship of the tumor to the lymphatic system and to plasma protein turnover.

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