Annals of Nuclear Medicine Vol. 19, No. 7, 597–601, 2005

Localization of chyle leakage site in postoperative chylothorax by oral administration of I-123 BMIPP

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The authors present a 71-year-old woman who had a right chylothorax after right upper lobectomy for lung cancer. As the chylothorax was considered to be due to thoracic duct injury at the time of operation, lymphoscintigraphy was performed by oral administration of I-123 beta-methyl-iodophenyl pentadecanoic acid (BMIPP). After visualization of the stomach and intestine, abnormal accumulation of the radiotracer was found initially around the right pulmonary hilum and then spread laterally in the upper pleural cavity, indicating chyle leakage in the region of the right pulmonary hilum. Scintigraphic finding was well correlated with the subsequent thoracoscopic observation, showing chyle leakage from a lymphatic tributary near its confluence to the thoracic duct at the level of the azygos continuation. The disruption site was ligated by video-assisted-thoracoscopic-surgery procedure with successful termination of the chyle leakage. Lymphoscintigraphy by oral administration of I-123 BMIPP is thought to be a useful method for localization of chyle leakage in patients with chylothorax induced by thoracic surgery.

Key words: chylothorax, lymphoscintigraphy, I-123 BMIPP, oral administration

INTRODUCTION

CHYLOTHORAX is an uncommon but well-known complication following thoracic surgery. Since chronic loss of chyle leads to anemia, hypoproteinemia, hypocalcemia, and malnutrition, this disease necessitates early and adequate treatment. Chylothorax is usually treated conservatively, but a surgical procedure is sometimes needed for persistent chyle leakage.[1,2] When surgical intervention for chylothorax is considered, preoperative estimation of the chyle leakage site is of help for the planning and management of the surgery but this is not always easy. The authors performed lymphoscintigraphy by oral administration of I-123 beta-methyl-iodophenyl pentadecanoic acid (BMIPP) in a patient with right chylothorax that developed after surgery for right lung cancer. The scintigraphy revealed chyle leakage site and was helpful in the management of surgery.

Received March 14, 2005, revision accepted June 8, 2005.

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CASE REPORT

A 71-year-old woman was hospitalized for further examination of an abnormal shadow seen on a chest radiograph. A tumor with notch and spiculation (30 × 27 mm) was revealed on chest CT (Fig. 1) and was histologically diagnosed as adenocarcinoma from the specimen obtained by CT-guided biopsy. Right upper lobectomy by video-assisted-thoracoscopic-surgery (VATS) was performed together with the right hilar and mediastinal lymph node dissection. From the first postoperative day, milky white fluid was observed to drain from the tube inserted into the right upper pleural cavity, and right chylothorax was diagnosed. The patient was initially treated conservatively with complete oral intake cessation and total parental nutrition. However, the daily volume of chylous discharge continued to be 100 m*l* to 500 m*l* and did not decrease significantly up to the 5th postoperative day. In addition, as the remaining right lung did not fully inflate and an air space was found to persist at the upper thorax on a chest radiograph (Fig. 2), surgical intervention of chylothorax by VATS procedure was scheduled. To identify the leakage site of chyle preoperatively, lymphoscintigraphy with oral administration of

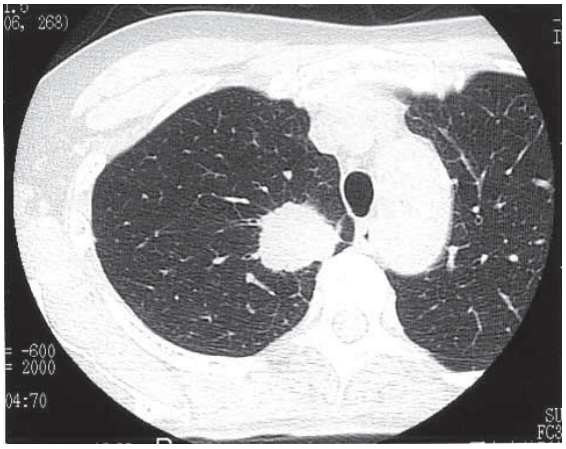

Fig. 1 CT revealed a tumor with notch and spiculation (30 × 27 mm) in the upper lobe of the right lung.

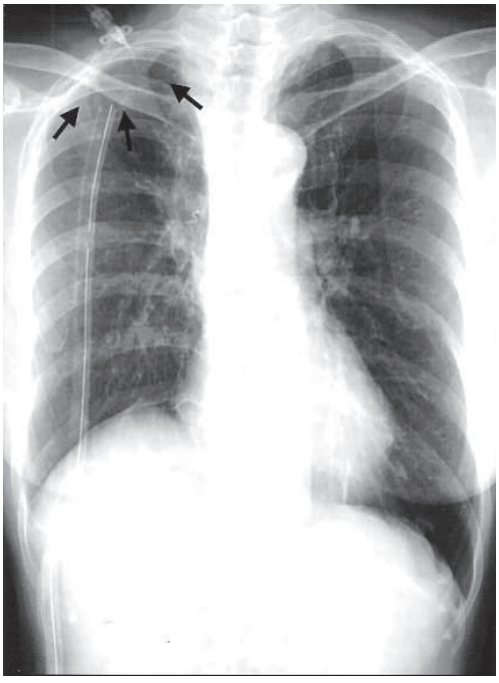

Fig. 2 The chest radiograph after right upper lobectomy shows that the remaining right lung does not show sufficient inflation, and an air space is seen at the upper thorax (*arrows*). A drainage tube is inserted with the tip in the upper pleural cavity.

I-123 BMIPP was preformed. She gave informed consent for the study in advance. A slice of bread with 111 MBq of I-123 BMIPP and peanut butter spread on the surface was given orally with reference to the previously reported method.[3] After oral intake of the radiotracer, serial images including chest and upper abdomen were obtained at 60, 120, 180, 270 minutes with 300 seconds acquisition time. Intense uptake of the stomach and the small intestine was observed on the image at 60 minutes (Fig. 3-A). Thereafter, at 120 minutes, curvilinear radiotracer accumulation was found upward from the right pulmonary hilum in the medial side of the right pleural cavity (Fig. 3-B), and the thoracic duct was detectable as a strip-shaped faint activity in the mediastinum. With lateral extension of the radioactivity in the right thorax, radioactivity in the drainage tube and consequently in the drainage bag was found at 180 minutes (Fig. 3-C). Scan at 180 minutes also showed subtle mediastinal accumulation of the radiotracer consistent with the cardiac silhouette. The liver began to appear on the image obtained at 180 minutes and was better visualized at 270 minutes (Fig. 3-D). Judging from these findings, it was assumed that the thoracic duct or its lymphatic tributary had been damaged around the right pulmonary hilum, causing chyle leakage into the right upper pleural cavity. Two hours after the lymphoscintigraphy, VATS was performed and disruption of a lymphatic tributary near its confluence to the thoracic duct at the level of the azygos continuation was revealed, which was well consistent with the preoperative consideration based on the I-123 BMIPP study. The chyle leakage was ligated and the postoperative course was uneventful. The patient was discharged without recurrent chylothorax 17 days after the reoperation.

DISCUSSION

The prevalence of chylothorax complicating pulmonary resection has been reported to range from 0.5% to 2.4%.[4–6] The present patient underwent right upper lobectomy for adenocarcinoma using VATS procedure and complicated chylothorax. During recent years, VATS has been described for resection of pulmonary nodules, since this procedure lacks the drawbacks of thoracotomy as a minimally invasive surgical technique.[7] Although the prevalence of chylothorax induced by VATS has not been well investigated, Jancovici et al. experienced 3 out of 102 patients (0.3%) with chylothorax after VATS.[8]

There are two treatment options, conservative management or surgical intervention, for postoperative chylothorax. The basic principle of conservative treatment of chylothorax after pulmonary resection is to inflate the lung to decrease the dead space in the pleural cavity.[4] After pulmonary resection, the remaining lung comes to adhere to the chest wall and mediastinum thus plugging the chyle leak, diminishing its flow, and facilitating closure of the injured thoracic duct or its tributaries.[9] In addition, the patients with chylothorax are given either medium chain triglycerides orally or prescribed total parental nutrition with complete cessation of oral feeding to reduce the chyle flow though the thoracic duct, which allows time for the fistula to seal off and collateral lymphatic vessels to open up.[10] While postoperative chylothorax is generally treated conservatively, surgical therapy is limited to patients who do not respond well to conservative therapy. However, methods and timing of surgery are still controversial. Because of its easy man-

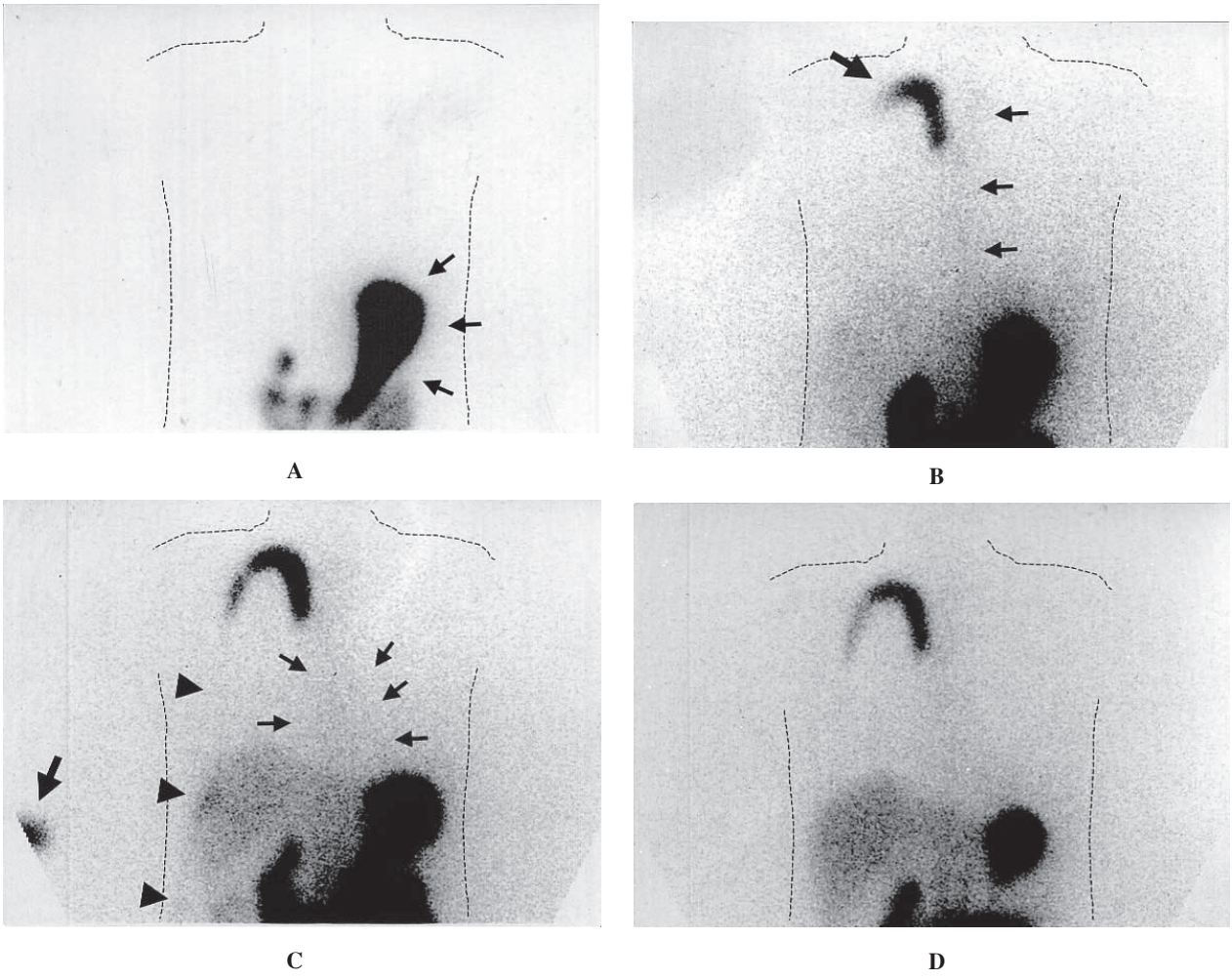

Fig. 3 Sequential I-123 BMIPP lymphoscintigraphy of the chest and upper abdomen. Images were obtained at 60 (A), 120 (B), 180 (C), and 270 (D) minutes after oral administration of 111 MBq I-123 BMIPP. A: Intense radioactivity is visible in the stomach (*arrows*) and the small intestine. B: Curvilinear radiotracer concentration spreading upward from the right pulmonary hilum is observed in the right upper pleural cavity (*large arrow*). The thoracic duct is demonstrated as a strip-shaped faint activity in the mediastinum (*small arrows*). C: The radioactivity in the right pleural cavity extends laterally just like following the fringe of the remaining right lung and also found in the drainage tube (*arrow heads*). As a result of outflowing of I-123 BMIPP from the pleural cavity through the tube, the drainage bag is partially visualized at the edge of the field of view (*large arrow*). Faint activity corresponding to the heart is observed in the mediastinum (*small arrows*) and the liver begins to appear. D: The radioactivity in the right pleural cavity is apparently unchanged, and the liver is visualized more clearly.

ageability and low morbidity, VATS is recently becoming the method of choice in the management of postoperative chylothorax, as well as one of the options of the initial surgical procedures for intrathoracic disease.[1,4,8] Peillon et al. advocate early reoperation by VATS, particularly when the chyle leaks are more than 300 m*l* per day during 5 days or when oral recovery intake induces a chyle loss relapse.[11] As to the present patient, since the chyle drainage from the chest tube persisted for 5 days after the operation with no tendency to reduce the volume, and moreover, there was a dead space due to insufficient inflation of the remaining lung, it was assumed that the chyle leak would not easily disappear, and early surgical intervention using VATS was taken into consideration.

It is clinically helpful to know the chyle leakage site in chylothorax preoperatively. To date various diagnostic imagings have been introduced for this purpose. Lymphangiography, being performed after invasive cannulation of an afferent lymph vessel on the dorsum of a foot, is one of the well investigated techniques for diagnosing chylothorax.[10,12] However this procedure compels patients to rest for a long time, and may have the risk for fat embolism and adverse reactions to the contrast material. In nuclear medicine, which can evaluate the lymph flow in the thoracic duct under near physiological condition, some radiopharmaceuticals and techniques have been

employed. There have been reports concerning the usefulness of lymphoscintigraphy by interdigital subcutaneous injection of radiotracers such as Tc-99m human serum albumin or Tc-99m sulfur colloids.[13,14] However, there are reports as well that such lymphoscintigraphies failed to demonstrate chyle leak into the pleural space in patients with chylothorax.[15] On the other hand there have been attempts to demonstrate chylothorax by concentrating radioactive triglyceride or long-chain fatty acid via thoracic duct after oral administration. Woolfenden et al. reported a case of chylothorax confirmed by orally administered I-131 Triolein.[15] Thoracic duct was also demonstrated by oral administration of I-123 heptadecanoic acid or I-123 iodophenyl pentadecanoic acid.[16,17] However, these radiotracers are unavailable in the recent clinical setting in Japan. I-123 BMIPP is commercially available and has been clinically used for the evaluation of fatty acid metabolism in the heart. Qureshy et al. first described the clinical usefulness of I-123 BMIPP by oral administration for thoracic duct imaging and also reported a case showing accumulation of I-123 BMIPP in chylothorax.[3] The lymphoscintigraphy using I-123 BMIPP for the present patient was performed with reference to their method.

The mechanisms of intestinal absorption of long-chain fatty acid are as follows. In small intestine, long-chain fatty acids become dissolved in the central lipid portion of the bile acid micelles together with monoglycerides and are carried to the surface of the microvilli in the brush border of the small intestinal enterocytes. After entering the enterocyte, the fatty acids and monoglycerides are combined to form triglycerides, which aggregate into chylomicrons together with cholesterol and phospholipids. Chylomicrons are excreted by cellular exocytosis into the basolateral spaces around the cell and from there, they pass into the lymph in the central lacteal of the villus and then enter the thoracic duct, which merges into the venous system at the left jugular subclavian junction.[18] When orally administered, I-123 BMIPP, acting as a long-chain fatty acid, is absorbed into lymph channels in a similar manner as mentioned above. After entering the general circulation through the thoracic duct, I-123 BMIPP is distributed mainly to heart and liver, which was already documented in the initial clinical study performed for evaluating myocardial fatty acid metabolism.[19] Chiba et al. described increased triglyceride radioactivity in chyle in the thoracic duct after enteral feeding of I-123 BMIPP in an experimental study using rats.[20] They also pointed out the possible usefulness of I-123 BMIPP for the diagnosis of chylothorax.

Giving I-123 BMIPP spread on a slice of bread with peanut butter is a well-conceived way. Peanut butter, containing much fat, has a role to release cholecystokinin in duodenum, which contracts the gall bladder and consequently increases bile salts in the small intestine. In addition, solid meal can slow down the small intestinal emptying in itself allowing for sufficient time for absorption of the included I-123 BMIPP. Therefore I-123 BMIPP, when orally administered in this manner, is easier to form bile acid micelles and be absorbed in the small intestine.

Chyle leakage in the patient was identified in the region of the right pulmonary hilum in I-123 BMIPP lymphoscintigraphy, which was well correlated with the subsequent thoracoscopic observation. In contrast, the thoracic duct of the patient was only faintly demonstrated in the I-123 BMIPP study. However, this indicates that the thoracic duct remained patent, not completely disrupted even with a lesser internal lymph flow. The thoracic duct patency is also given proof by the finding that the liver and heart appeared after the identification of the radioactivity in the pleural cavity. That is, they were visualized by distribution of I-123 BMIPP after it entered the general circulation through the thoracic duct. The poor visualization of the thoracic duct is related to the active chyle leak into the pleural cavity and conservative therapy for more than 5 days, reducing the chyle flow in the thoracic duct.

In conclusion, lymphoscintigraphy by oral administration of I-123 BMIPP can evaluate the lymph flow from the small intestine to the thoracic duct and is thought to be a useful method for localization of chyle leakage in patients with chylothorax induced by thoracic surgery.

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