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CASE REPORT | SMALL BOWEL

Diagnosis of a Lymphoenteric Fistula by Single-Photon Emission Computed Tomography/Computed Tomography Lymphoscintigraphy

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ABSTRACT

Protein losing enteropathy can present as an immunodeficiency. This report describes a rare cause of protein losing enteropathy due to a lymphoenteric fistula and how a novel use of a pre-existing combined imaging technique of single-photon emission computed tomography/computed tomography lymphoscintigraphy helped in making the diagnosis.

INTRODUCTION

The clinical manifestation of protein losing enteropathy (PLE) is variable and determined by the underlying cause. PLE can present as an immunodeficiency. This is a case report of using single-photon emission computed tomography/computed tomography (SPECT/CT) lymphoscintigraphy in the diagnosis of a lymphoenteric fistula, a rare cause of PLE.

CASE REPORT

A 71-year-old woman was diagnosed with non-Hodgkin lymphoma in 1985. She was treated initially with chlorambucil monotherapy. Eleven years later, she was treated with a combination of chlorambucil, cyclophosphamide, hydroxydaunomycin, oncovin, and prednisolone chemotherapy for disease relapse, with minimal response. This was followed by rituximab and FMD (fludarabine, mitoxantrone, dexamethasone) with good response, culminating in BiCNU, etoposide, Ara-C, melphalan chemotherapy and an autograft. She then had a further relapse requiring cyclophosphamide, prednisolone, rituximab chemotherapy and local radiotherapy for nodules on her left temporal bone and scapula.

In 2010, the patient was commenced on antibody replacement because she developed recurrent sinopulmonary infections and was noted to be profoundly hypogammaglobulinaemic. She had a further relapse with widespread lymphadenopathy and skin nodules, which was treated with radiotherapy to the anterior chest wall and neck, followed by 6 cycles of rituximab and bendamustine with a very good response. Around this time, she developed lymphedema of her legs and left arm. She was subsequently put on rituximab maintenance which finished in January 2014. Unfortunately, she came off immunoglobulin replacement unintentionally from the end of 2013 till mid-2014. During this period, she developed recurrent lower respiratory tract infections and bacterial pneumonia secondary to H1N1 flu. A thoracic CT subsequent to her admission with pneumonia showed ground-glass changes with bronchial thickening suggestive of bronchiectasis. Her antibody levels checked off antibody replacement treatment, showed an immunoglobulin G of 0.84 g/L, an immunoglobulin A of 0.11 g/L and an immunoglobulin M of $<$0.04 g/L. Owing to her infection burden and structural lung disease, she was re-established on antibody replacement without test vaccinations being carried out. She was also noted to be lymphopenic at the time with a CD4 count of $<200 \times 10^6$ cells/L and was commenced on cotrimoxazole 960 mg 3 times a week as pneumocystis prophylaxis.

She continued to have suboptimal antibody trough levels despite adequate antibody replacement. Her chronic hypoalbuminaemia which was previously noted, with no evidence of proteinuria or liver disease, raised the possibility of a PLE. An echocardiogram was

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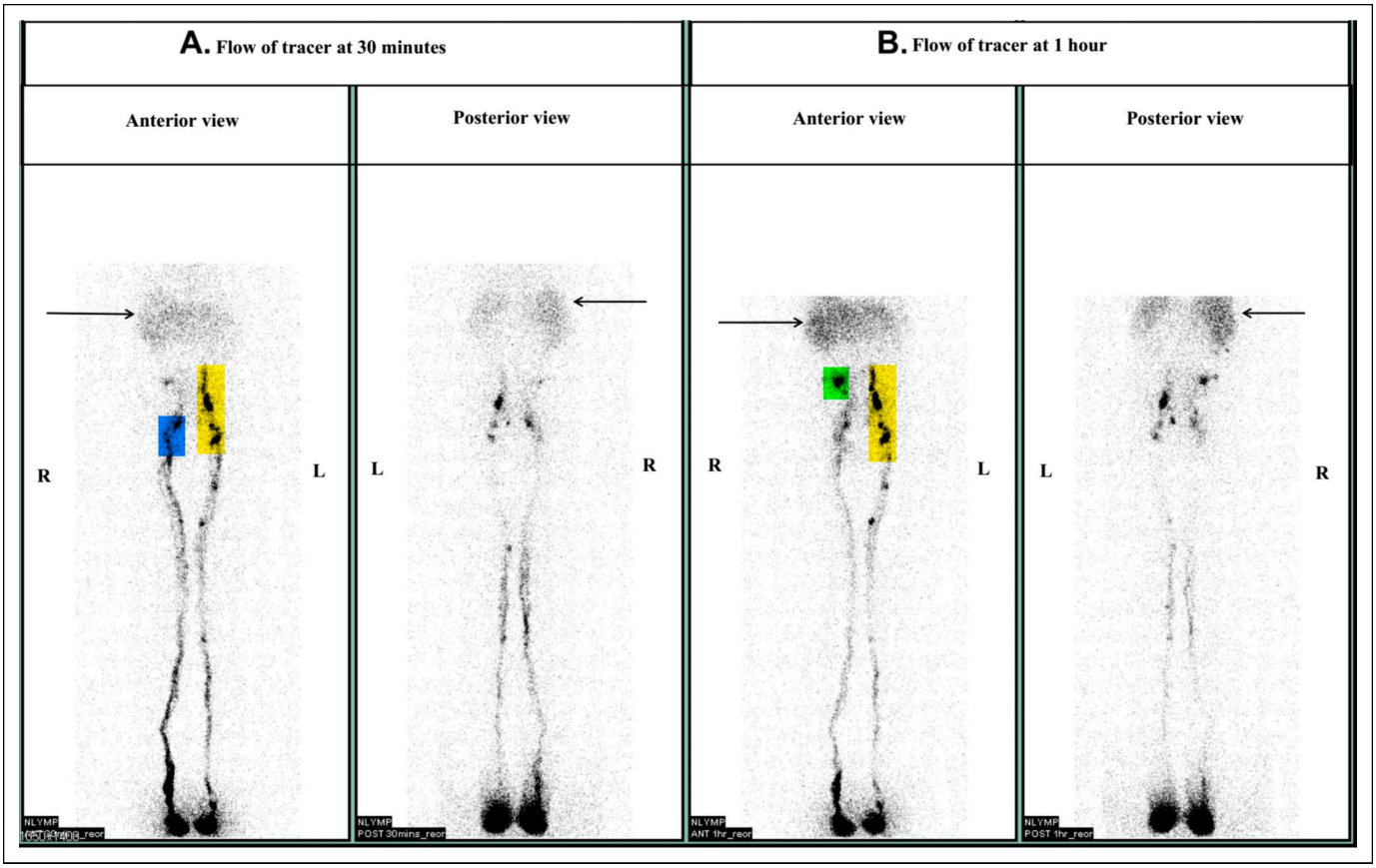

Figure 1. Lymphoscintigraphy showing (A) the flow of a tracer at 30 minutes anterior and posteriorly and (B) flow of a tracer at 1 hour anterior and posteriorly. Flow of the tracer is seen in the deep lymphatics, past the groin in (A and B). The yellow highlighted area shows good tracer flow in the left through the inguinal lymph nodes, pelvic lymph nodes, and para-aortic lymph nodes at 30 minutes and 1 hour. The blue highlighted area shows the flow of a tracer at 30 minutes in the right through inguinal and pelvic lymph nodes but no tracer activity in the para-aortic lymph nodes. The green highlighted area shows tracer activity in the mesenteric lymph nodes at 1 hour. Note clear visualization of the liver, shown by the arrow (→).

carried out, and this showed normal left ventricular size and function. A radio labeled albumin tracer study confirmed gastrointestinal protein loss, with increased albumin detected in her stools. She then had a colonoscopy, gastroscopy, and a video capsule endoscopy, which were all macroscopically normal. Histology from the gastroscopy and colonoscopy was microscopically normal. A whole body CT scan carried out to investigate her PLE was unremarkable. Finally, a SPECT/CT lymphoscintigram confirmed the presence of a lymphoenteric fistula.

DISCUSSION

Peripheral edema is the commonest cause of presentation in PLE.[1] The main laboratory findings are reduced serum concentrations of albumin, protein, γ-globulins, fibrinogen, transferrin, and ceruloplasmin[1].The primary causes of PLE can be divided into erosive gastrointestinal disorders, nonerosive gastrointestinal disorders, and disorders involving increased central venous pressure or mesenteric lymphatic obstruction. Radiolabeled albumin and faecal clearance of alpha 1-antitrypsin are used for the diagnosis of protein malabsorption and intestinal losses.[2]

In patients with lymphatic obstruction, loss of lymphocytes into the gastrointestinal tract can produce significant lymphopenia with detectable alterations in cellular immunity.[3,4] The cause of this patient's lymphopenia and hypogammaglobulinaemia is due to her chemotherapy for lymphoma compounded by her lymphoenteric fistula, likely secondary to disruption of normal lymphatic flow because of previous neoplasia. The treatment of PLE should be directed at the underlying condition.

This patient was not offered embolization of her lymphoenteric fistula. She continues to be supported with antibody replacement and antimicrobial prophylaxis and is doing well despite subtherapeutic trough immunoglobulin levels. The use of a SPECT/CT lymphoscintigraphy helped to ascertain the diagnosis and should be recognized as a useful tool in investigating patients with PLE. This imaging modality was carried out initially by injecting radiocolloid (Technetium-99m) into the subcutaneous tissue between the first and second toes of both feet in this patient. A flow study was performed, and the arrival of radionuclide delivery to the knees and groin was timed (Figure 1). At 30 minutes, there was a flow through the deep lymphatics past the groin. At 2 hours, a SPECT/CT was performed which showed good progression of a tracer on the left through the inguinal to

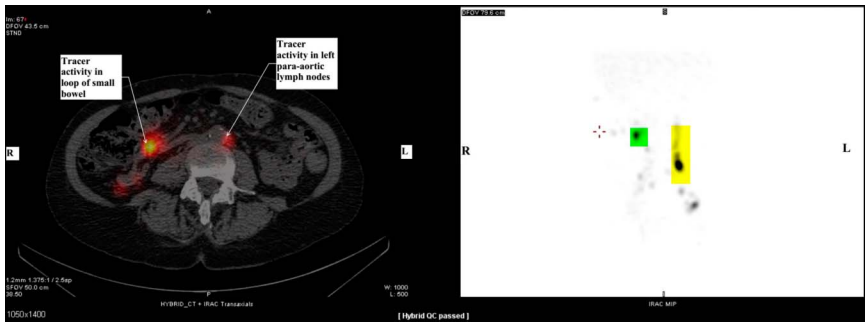

Figure 2. Photon emission computed tomography/computed tomography carried out at 2 hours on the left and correlating it with the lymphoscintigraphy on the right. This shows activity in the left inguinal, pelvic, and para-aortic lymph nodes (highlighted yellow) with no activity in the right para-aortic lymph nodes but instead flow into 2 right sided mesenteric nodes (highlighted green) with subsequent activity appearing in an adjacent loop of small bowel (seen on single-photon emission computed tomography/computed tomography as red in color). The appearance is consistent with a blocked lymphatic system above the mid-abdomen with retrograde flow into right mesenteric nodes and adjacent small bowel.

pelvic to para-aortic nodes (Figure 2). On the right, however, the flow of a tracer was reduced and there was no activity in the para-aortic lymph nodes but instead flow into 2 right sided mesenteric nodes with subsequent activity appearing in an adjacent loop of small bowel. The appearances were consistent with a blocked lymphatic system above the mid-abdomen with retrograde flow into mesenteric nodes and adjacent small bowel.

Lymphoscintigraphy has been described as a tool to detect abnormal lymphatics but lacks anatomical information. Lymphangiograms on the other hand is invasive. This is the first ever reported clinical case of SPECT/CT lymphoscintigraphy used in the diagnosis of a lymphoenteric fistula. There have been reports of using this modality of combined imaging for evaluating chylothorax.[5] Intraoperative correlation was not performed in our case. SPECT/CT lymphoscintigraphy can overcome the previously noted limitations of lymphoscintigraphy by adding more accurate anatomical information.

DISCLOSURES

Author contributions: A. Anantharachagan is the sole contributor and article guarantor for this manuscript.

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