Turk J Gastroenterol 2005; 16 (1): 41-43

Scintigraphic diagnosis of protein-losing enteropathy secondary to amyloidosis

Amiloidoza bağlı gelişen protein kaybettiren enteropatinin sintigrafik tanısı

Ayşegül AKGÜN[1], Ebru TANI ACAR[1], Memduh Sami TANER[1], Zehra ÖZCAN[1], Ercan OK[2]

Ege University School of Medicine, Departments of Nuclear Medicine[1], Department of Internal Medicine[2], İzmir

Protein-losing enteropathy is an uncommon syndrome of excessive loss of protein via the gastrointestinal mucosa. ^{99m}Tc-dextran scintigraphy was performed on a 42-year-old woman with Protein-losing enteropathy. She had secondary amyloidosis due to rheumatoid arthritis. Abnormal leakage of the radiotracer was observed in the mid-abdominal region suggesting the site of protein loss. It is concluded that ^{99m}Tc-dextran scintigraphy is useful as a noninvasive and simple test for the imaging and confirmation of diagnosis in protein-losing enteropathy.

Key words: Protein-losing enteropathy, amyloidosis, ^{99m}Tc-dextran, small bowel

Protein kaybettiren enteropati gastrointestinal mukoza yoluyla aşırı derecede protein kaybı ile giden sendromdur. 42 yaşında romatoid artirite sekonder amiloidozu bağlı Protein kaybettiren enteropati gelişen bayan hastaya ^{99m}Tc-dextran sintigrafisi uygulandı. Protein kaybını düşündüren orta abdominal bölgede anormal radyoaktivite tutuluşu izlendi. ^{99m}Tc-dextran sintigrafisinin protein kaybettiren enteropatinin görüntülenmesinde ve tanının doğrulanmasında basit ve non-invaziv bir test olarak yararlı olduğu kanısına varıldı.

Anahtar kelimeler: Protein kaybettiren enteropati, amilodoz, ^{99m}Tc-dextran, ince barsak

INTRODUCTION

Protein-losing enteropathy (PLE) has been associated with many disorders occurring at different anatomic sites in the gastrointestinal tract, including inflammatory bowel disease, cancer (e.g. lymphoma), a variety of clinical conditions that result in increased central venous pressure (e.g. cardiac failure, primary cardiomyopathy), amyloidosis and infections (e.g. tuberculosis, bacterial overgrowth) (1). Secondary amyloidosis is a common clinical problem associated with chronic diseases. While amyloidosis occurring with rheumatoid arthritis is not uncommon in the literature, only a few cases of PLE due to gastrointestinal amyloidosis secondary to early-stage rheumatoid arthritis have been reported previously (2, 3). Endoscopic biopsy, serum and stool levels of alpha-1-antitrypsin and radiolabeled macromolecules, either albumin or transferrin labeled with ^{125}I and ^{111}In, have been used to diagnose PLE (4). Radiolabeled macromolecules have been preferred because of their ability to quantify protein loss, ease of use, physiological methodology and opportunity for diagnostic imaging. Recently ^{99m}Tc-dextran scintigraphy has been found to be an ideal, inexpensive and noninvasive method for detecting PLE (5-8).

We recently had a patient with PLE and chronic renal failure caused by amyloidosis secondary to rheumatoid arthritis in which diagnosis of PLE was confirmed by ^{99m}Tc-dextran scintigraphy.

CASE REPORT

A 42-year-old woman with a known 10-year history of rheumatoid arthritis was referred to the Department of Internal Medicine because of chronic diarrhea, abdominal pain and loss of appetite. She also had known chronic renal failure and a routine hemodialysis program. She defined diarrhea 3 or 4 times per day, with normal color and bad smell, and no blood or mucus. In the clinical examination she was cachectic (BMI 14 kg/m^2), hypotensive (70/50 mmHg), had decreased turgor-tonus, bilateral pretibial edema, dry tongue, and general tenderness in the abdomen with no defense

Address for correspondence: Ayşegül AKGÜN
Ege University School of Medicine, Department of Nuclear Medicine
Bornova 35100, İzmir, Turkey
E-mail: aakgun@med.ege.edu.tr

Manuscript received: 19.07.2004 **Accepted:** 01.02.2005

or rebound; other systemic evaluations were normal. The laboratory tests revealed profound hypoalbuminemia (1.5 g/dl), hypoglobulinemia (3.2 g/dl), and relatively low blood urea and creatinine levels in a patient on chronic hemodialysis treatment (33 mg/dl and 2.08 mg/dl, respectively). No clinical or laboratory signs of liver disease were detected. Serum cortisol, ACTH, fT_3, fT_4 and TSH levels were normal. There was 1.5 g protein loss in 24-h urine analysis. Her echocardiography revealed left ventricular concentric hypertrophy, normal vena cava inferior index, bilateral minimal pleural effusion, normal wall motions and ejection fraction (>%50). Amyloidosis was thought to be responsible for her hypotensive state.

Double contrast colon X-ray and enteroclysis examinations were normal. Cultures of stool were negative for pathogens. Rectal biopsy was positive for amyloidosis. Abdominal ultrasonography revealed thickening of intestinal wall, especially jejunal side, and bilaterally atrophic grade 2 kidneys. No mass lesion or abdominal lymph node was seen. There was no local cause of intestinal protein loss. A clinical suspicion of malabsorption was indicated when the patient had a failed response to treatment. PLE was suspected as the reason for hypoproteinemia and further investigation was needed. She was referred for scintigraphy to locate the site of suspected protein loss.

Tc-99m dextran was prepared in our laboratory according to the method prescribed previously (9). The labeling efficiency was more than 95%. After slow intravenous administration of 10 mCi (370 MBq) ^{99m}Tc-dextran, serial anterior abdominal images were obtained using a large-field-of-view gamma camera equipped with low energy parallel hole collimator. Abdominal images of 1000 K-counts were taken in 30 minutes and 1, 2, 3 hours after injection of the radiotracer with a matrix size of 256x256. ^{99m}Tc-dextran scintigraphy showed normal distribution in the liver and spleen. Increased ^{99m}Tc-dextran accumulation was noted in the region of the small bowel suggesting the intestinal leakage of tracer at 1 h and the following images were obtained. Due to chronic renal failure, physiologic kidney uptake was not observed (Figure 1a, 1b).

The patient was maintained on parenteral nutrition with a frequent need for intravenous albumin. Prophylactic antibiotic was used for bacterial overgrowth. Her condition was unchanged and the patient was lost two months after presentation.

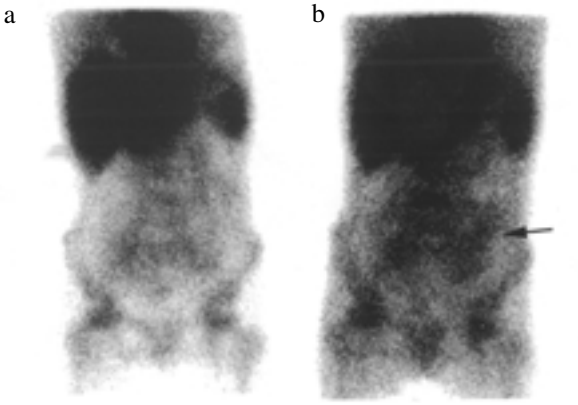

Figure 1. Anterior abdominal image at (a) 30 min and (b) 1 h after injection of ^{99m}Tc-dextran. While 30 min image shows no radiotracer leakage from the gastrointestinal tract, 1 h anterior abdominal image shows accumulation of tracer in mid-abdominal region, suggesting the intestinal leakage of the small bowel

DISCUSSION

Rheumatoid arthritis is the most common disease producing secondary amyloidosis in developed countries. The main target organ by far is the kidney. Gastrointestinal disturbances including diarrhea, constipation and malabsorption (22%) are the most common after kidney manifestations (10).

PLE is one of the major problems that may be associated with amyloidosis leading to protein loss from the gastrointestinal mucosa. Idiopathic change in permeability of mucosal capillaries and conductance of interstitium, resulting in 'weeping' of protein-rich fluid from the mucosal surface, is thought to be the responsible mechanism of PLE in amyloidosis (11).

PLE has been diagnosed by two main mechanisms. The first is measurement of fecal excretion of radiolabeled proteins (Cr51 and I131-albumin) after intravenous injection or that of alpha 1-antitrypsin. Fecal excretion of radiolabeled proteins is not widely used due to cumbersome methodology and limited availability. Although fecal clearance of alpha 1-antitrypsin seems to be an inexpensive and quite reliable test of protein-losing enteropathy, it is measured by determining stool volume and both stool and plasma alpha 1-antitrypsin concentrations. However, none of these methods is able to diagnose the site of the leak.

The second mechanism is to localize the site of protein loss using intravenously administered radionuclide agents such as ^{99m}Tc-dextran and ^{99m}Tc-

HSA. Although ^{99m}Tc is the ideal tracer for the imaging of PLE, it does not allow quantification of protein loss due to its short physical half-life. On the other hand, ^{99m}Tc-labeled agents cannot cross intestinal mucosa because of the impermeable barrier between the vascular endothelium and luminal contents. Thus they remain in the vascular compartment with a long intravascular half-life (7, 12), which is helpful in localizing the site of enteric protein loss.

It is noted that while interpreting the scintigraphic findings, false-positive accumulations of ^{99m}Tc-dextran due to active bleeding in the gastrointestinal tract, unsuspected intestinal worms and ulcerative colitis should also be considered (5); however, all these clinical conditions were excluded in our case.

While both of these agents have been frequently used, some authors have reported that ^{99m}Tc-dextran has a superior performance to ^{99m}Tc HSA in the diagnosis of PLE (7, 8). Lower radiation burden, faster background clearance and higher in-vitro and in-vivo stability than ^{99m}Tc HSA supports ^{99m}Tc-dextran as a more ideal agent for PLE imaging. ^{99m}Tc-dextran has a higher molecular weight (60 to 90 kd), and thus remains stable in the vascular compartment. Other advantages of ^{99m}Tc-dextran over ^{99m}Tc HSA include less hepatic uptake and its availability as a kit formulation, which is quite easy and inexpensive.

We conclude that ^{99m}Tc-dextran scintigraphy was useful, not only in diagnosing protein-losing enteropathy, but also in localizing the abnormal protein leakage in the gastrointestinal tract.

REFERENCES

1. Norton J, Greenberger JN, Isselbacher KJ. Disorders of absorption. Harrison's Principles of Internal Medicine (14th ed.). New York: McGraw-Hill; 1996: 1630-1.
2. Hashimoto T, Kawamura H. Amyloidosis in rheumatoid arthritis. Nippon Rinsho 1992; 50: 586-91.
3. Kurohori Y, Akama H, Takagi K, et al. Case of protein-losing enteropathies due to gastrointestinal amyloidosis secondary to early-stage rheumatoid arthritis. Nippon Naika Gakkai Zasshi 1998; 10: 2088-90.
4. Wilson JD, Braunwald E, Isselbacher KJ, et al. Harrison's Principles of Internal Medicine (12th ed.), International ed. New York: McGraw-Hill; 1991: 1267-8.
5. Bhatnagar A, Singh AK, Lahoti D, et al. ^{99m}Tc-dextran: a promising new protein- losing enteropathy imaging agent. Eur J Nucl Med 1996; 23: 575-8.
6. Lahoti D, Bhatnagar A, Singh AK, et al. ^{99m}Tc-dextran: a new and sensitive general purpose scintigraphic agent for diagnosing intestinal inflammation. Clin Nucl Med 1999; 24: 424-7.
7. Sivaratnam DA, Pitman AG, Giles E, et al. The utility of Tc99m-dextran in the diagnosis and identification of melanoma metastases responsible for protein-losing enteropathy. Clin Nucl Med 2002; 27: 243-5.
8. Bhatnagar A, Lahoti D, Singh AK, et al. Scintigraphic diagnosis of protein-losing enteropathy using ^{99m}Tc-dextran. Clin Nucl Med 1995; 20: 1070-3.
9. Dass RS, Singh AK, Chaub UPS. Development of a dextran kit for labeling with ^{99m}Tc and its evaluation for lymphoscintigraphy. Nucl Med Biol 1993; 20: 701-6.
10. Gertz MA, Kyle RA. Secondary systemic amyloidosis: response and survival in 64 patients. Medicine (Baltimore) 1991; 70: 246-56.
11. McQuaid KR. Alimentary Tract. Current Medical Diagnosis & Treatment (42nd ed.). New York: Lange Medical Books/McGraw-Hill; 2003: 597-8.
12. Chiu N, Lee B, Hwang S, et al. Protein-losing enteropathy: diagnosis with ^{99m}Tc labeled human serum albumin scintigraphy. Radiology 2001; 219: 86-90.