

# A Systemic Lupus Erythematosus Patient with Protein Losing Enteropathy

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Protein-losing enteropathy (PLE) is a rare manifestation of systemic lupus erythematosus (SLE), and it is an uncommon cause of hypoalbuminemia without proteinuria. We describe a case of an 11 year-old girl who had diarrhea and periorbital edema as the initial symptoms of SLE. PLE was diagnosed by 24-hour stool alpha-1 antitrypsin clearance and <sup>99m</sup>Tc-human serum albumin scintigraphy.

**Key Words:** 24-hour stool alpha-1 antitrypsin clearance, <sup>99m</sup>Tc-human serum albumin scintigraphy

## INTRODUCTION

Protein-losing enteropathy (PLE) is a disease characterized by a leakage of protein from the gastrointestinal tract that results in hypoalbuminemia and generalized edema. PLE may be considered a clinical syndrome related to many pathological conditions that leads to excessive intestinal protein loss. Although there have been several reports of PLE with SLE in adults, this association is relatively rare for children. We report here on the case of a previously healthy 11 year-old girl who presented with diarrhea and severe periorbital edema without apparent proteinuria. She was diagnosed with SLE and PLE.

## CASE REPORT

An 11-year old Korean girl was admitted to another hospital for periorbital edema that had started 2 weeks previous. She had been otherwise healthy and there was no remarkable family history. Laboratory studies were as following: white blood cell (WBC) count 3800/mm<sup>3</sup>, hemoglobin (Hb) 11.4 g/dL, and platelet count 139,000/mm<sup>3</sup>. Her urinalysis and serum electrolytes were normal. Blood urea nitrogen (BUN) was 29 mg/dL and the creatinine (Cr) level was 0.7 mg/dL. Her serum protein was 7.8 g/dL, serum albumin 2.9 g/dL and the serum cholesterol was 218 mg/dL. After 3 days, she was discharged without an explanation for the periorbital edema. After 4 months, she was admitted to our hospital with abdominal pain, diarrhea and fever that had lasted for 3 days. She also complained of knee joint pain. She continued to have severe periorbital edema, and she showed oral ulcers. The breath sounds were decreased at both lung bases. She had a weight loss of 4 kg during the last 4 months. Laboratory studies revealed WBC count 12,910/mm<sup>3</sup>, Hb 8.5 g/dL, and a platelet count of 90,000/mm<sup>3</sup>. The serum albumin was 2.3 g/dL. Serum electrolytes were as following: Na 130 mEq/L, K 4.6 mEq/L, and Cl 106 mEq/L. Her PT/PTT was 100%/51.1sec. Urinalysis showed 3-5 red blood cells under high power field microscopy and no proteinuria. BUN/Cr had increased to 29/1.3 mg/dL and the serum cholesterol was 208 mg/dL. Fractional excretion of sodium (FeNa) and the renal failure index (RFI) was 0.03 and 0.06, respectively, showing a prerenal type acute renal failure. Chest radiographs showed bilateral

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pleural effusion and an echocardiogram revealed pericardial effusion.

Antinuclear antibodies (ANA) were positive at a titer of 1:640 with a homogeneous pattern. Anti-ds DNA was positive with a titer of 1:160 and anti-SS-A/Ro, anti-SS-B/La were positive. Anticardiolipin antibodies were positive and lupus anticoagulant was negative. Her C3/C4 were 20.3/1.5 mg/dL. She fulfilled 6 of the 11 criteria of the American Rheumatology Association and was diagnosed with SLE (arthralgia, oral ulcer, serositis, hematologic abnormality, immunologic abnormality and positive ANA). However, the patient continued to have periorbital edema and hypoalbuminemia with no proteinuria. We were obliged to consider the extrarenal loss of protein. Twenty-four h stool alpha-1 antitrypsin (AAT) was measured and fecal AAT, serum AAT and AAT clearance was 315 mg/dL (normal  $\leq$  54 mg/dL/24 hours), 117 mg/dL ( $\leq$  110-200 mg/dL) and 215 mL, respectively, (normal  $\leq$  27 mL/24 hours), and this was consistent with PLE.  $^{99m}\text{Tc}$ -human serum albumin scintigraphy showed the protein loss was from the distal ileum (Fig. 1).

After establishing the diagnosis of SLE and PLE, we started treatment with prednisone 2 mg/kg,

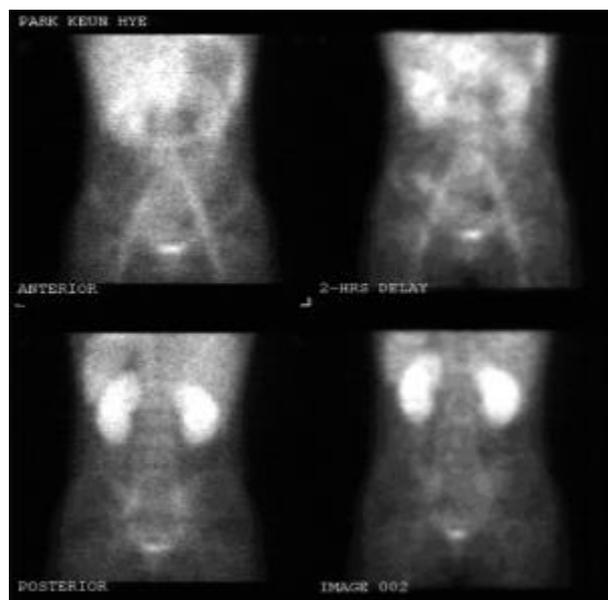


Fig. 1.  $^{99m}\text{Tc}$ -human serum albumin scintigraphy shows protein loss from small bowel (distal ileum). Serum albumin was shown to leak into distal ileum in 2-hour delay film.

and the periorbital edema and hypoalbuminemia dramatically improved within 2 days. Renal biopsy showed lupus nephritis class IV. The activity index and chronicity index were 5/24 and 2/12, respectively. Endoscopic biopsy of her duodenum showed a mild, chronic inflammation. Treatment was started with monthly pulse intravenous (i.v.) cyclophosphamide (750 mg/m<sup>2</sup>). Two weeks after treatment, the follow-up 24 h fecal AAT, serum AAT and AAT clearance were 22.4 mg/dL (normal  $\leq$  54 mg/dL/24 hours), 125 mg/dL (normal  $\leq$  110-200 mg/dL) and 21.5 mL (normal  $\leq$  27 mL/24 hours), respectively. Her C3/C4 had increased to 36.2/5.7 mg/dL and an echocardiogram showed no pericardial effusion. Total of five infusions of pulse i.v. cyclophosphamide were given. After 5 months, her C3/C4 had increased to 116/9.6 mg/dL, and the serum albumin was 4.1 g/dL.

## DISCUSSION

While PLE is associated with a variety of disorders, it is rarely associated with systemic lupus erythematosus (SLE). So far, almost 35 cases of lupus associated PLE have been reported,<sup>1,4</sup> but only 5 have been seen in children (Table 1).<sup>5-9</sup> Specific serological features appear to be present in the patients having PLE with SLE, including positive ANA (speckled pattern), negative anti-ds DNA, positive anti-RNP and low serum complement levels.<sup>10,11</sup> Our patient showed decreases in serum complement levels; however, ANA testing showed a homogenous pattern, and anti-ds DNA was positive at a titer of 1:640. ANA was measured a total of ten times after diagnosis, and except for the first time when the ANA showed a homogenous pattern, the rest of the tests showed a speckled pattern.

Several mechanisms may underlie the pathogenesis of PLE with SLE.<sup>4</sup> Intravascular activation and the conversion of complement has been proposed. Activated complement can cause increased capillary permeability and may lead to PLE. Our patient had a severe decrease in complement levels (C3/C4 20.3/1.5 mg/dL), and the previously reported pediatric patients also showed a decrease in complement levels, however, there

**Table 1.** Reported Cases of PLE with SLE in Children

Age/Sex	Albumin(g/dL)	Treatment	Diagnostic test
12/female 1	1.3	Steroids	Cr51
15/female 2	1.2	Steroids	Cr51
13/female 3	2.4	Steroids CTX	Alpha-1 antitrypsin
12/male 4	0.7	Steroids AZA	Alpha-1 antitrypsin
6/female 5	1.2	Steroids CTX	Alpha-1 antitrypsin
Present case 11/female	2.6	Steroids CTX	Alpha-1 antitrypsin <sup>99m</sup> Tc-human serum albumin scintigraphy

have also been reports of normal complement levels in some adult patients.<sup>4</sup> The lack of the parent's permission did not allow us to perform small bowel biopsy or colonoscopy; therefore, we could not confirm lymphangiectasia. The previously reported 5 pediatric patients with SLE<sup>9</sup> had lymphangiectasia, pericarditis, congestive heart failure, and intestinal venulitis as the presumptive causes. Our patient also had pericarditis, but it was not severe enough to be the cause of PLE. Table 1 lists all the cases of PLE associated with edema. Hypoalbuminemia was the most characteristic finding in these patients. Cr51 or stool alpha-1 antitrypsin testing has been used to diagnose PLE. We not only measured stool alpha-1 antitrypsin, but we also used <sup>99m</sup>Tc-human serum albumin scintigraphy, which until now has not been reported to be used to diagnose PLE in children.

Our patient had no generalized edema, but rather, she had periorbital edema. This may be due to the increase in the 24 h stool alpha-1 antitrypsin level that was not severe, and thus, the mild hypoalbuminemia resulted. Therefore, our patient showed PLE as the initial manifestation of SLE and fortunately, she showed a good response to steroids. Recently, there has been a report of a severe case of PLE with SLE in which steroids and other immunosuppressants had little effect, yet the patient showed a good response to octreotide and medium chain triglyceride (MCT).<sup>1</sup> This treatment may be beneficial for children who show

little response to steroids and cyclophosphamide.

Since SLE is a multi-system disease, one must always consider other diseases that may be involved. PLE is rarely associated with SLE, but as in our case, it may be the cause of hypoalbuminemia and so this must always be kept in mind.

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