

A Rare Complication of Morbid Obesity: Elephantiasis Nostras Verrucosa and Amyloidosis

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ABSTRACT

Elephantiasis nostras verrucosa (ENV) is a rare, chronic, and progressive disease. Recurrent leg ulcers and cellulitis are the major cause of morbidity and mortality for ENV. However, the coexistence of ENV with AA amyloidosis is extremely rare. Also, obesity is exceptionally responsible for the etiology of ENV. Herein, We present a morbid obese case of severe kidney failure and nephrotic syndrome due to AA amyloidosis associated with ENV.

Keywords: AA amyloidosis, Elephantiasis nostras verrucosa, Elephantiasis, Obesity, Nephrotic syndrome, Kidney disease

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INTRODUCTION

Elephantiasis, also known as lymphatic filariasis, is a rare, chronic, and progressive disease that is caused by infections of *Wuchereria bancrofti*.¹ However, Elephantiasis nostras verrucosa (ENV) (non-filarial Elephantiasis) is a disease characterized by chronic lymphedema causing progressive cutaneous hypertrophy.² Lymphedema increases the risk of infections.^{1,2} Therefore, recurrent leg ulcers/cellulitis related to infections are the major cause of morbidity and mortality.^{1,2} Systemic (AA) amyloidosis on account of proteins deposits extracellularly in tissues as insoluble fibrils. AA amyloidosis is related to chronic infectious, inflammatory diseases, or some cancers.^{2,3} Renal diseases are the important cause of morbidity and mortality for cases with AA amyloidosis.^{4,5} The coexistence of ENV with AA amyloidosis is extremely rare. Also, obesity is exceptionally responsible for the etiology of ENV. Herein, we present a 69-year-old morbid obese female patient with ENV admitted to hospital because of severe kidney failure and massive nephrotic syndrome due to AA amyloidosis.

CASE PRESENTATION

The patient had a history of ENV for 10 years and was hospitalized 5-6 times in the last 3 years for recurrent cellulitis on the legs. Lymphedema on Legs was presented. At the same time, there was redness and cutaneous hypertrophy on the back of the leg. The etiology of ENV has been reported to be associated with morbid obesity. Body mass index was 43.3 kg/m². She was admitted to our outpatient clinic with extensive generalized edema and shortness of breath that lasted for 1 month. She was hospitalized upon detection of severe kidney failure accompanied by severe nephrotic syndrome. The patient had no history of diabetes and hypertension. One year prior to admission, she was diagnosed to be bicytopenia (anemia and thrombocytopenia) accompanied by cellulitis and was diagnosed with AA amyloidosis via bone marrow biopsy. Her bone marrow biopsy demonstrated no abnormalities in erythroid, myeloid series, and megakaryocytes but Congo red staining was positive in blood vessel walls (Figure 1). Laboratory data and blood chemistry included albumin 1.9 g/dL, blood urea 98 mg/dL, creatinine 3.9 mg/dL,



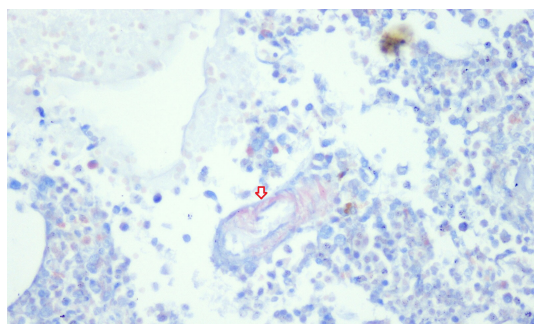


Figure 1. Congo red staining was positive on the vessel walls in the bone marrow (Congo red $\times 200$).

estimated glomerular filtration rate (eGFR) 11 mL/min/1.72 m², total cholesterol 480 mg/dL, triglyceride 510 mg/dL, quantitative proteinuria 9.5 g/day, C-reactive protein 75.0 mg/dL (normal range, 0-5.0 mg/dL), serum amyloid A (SAA) > 220 (normal range, 0--4). Urinalysis revealed 3+ proteinuria and no hematuria. A renal biopsy had not been performed due to morbid obesity and severe kidney failure. Monoclonal gammopathy was not detected in protein and immunofixation electrophoresis. *Wuchereria bancrofti* serological analysis was negative. There was no evidence to suggest collagen tissue disease ([ANA antinuclear antibody], anti-ds DNA [anti-double stranded DNA], and ANCA [antineutrophil cytoplasmic antibodies] were negative) and Familial Mediterranean Fever gene mutation was negative. The patient was diagnosed with AA amyloidosis due to ENV and recurrent cellulitis. At the same time, ENV was associated with obesity by excluding other possible causes. Acute hemodialysis was initiated due to severe kidney failure and diuretic-resistant hypervolemia.

DISCUSSION

Elephantiasis is a manifestation of a spectrum of different etiologies. Theoretically, beyond helminthic infection (Lymphatic Filariasis), many causes are responsible, such as inherent malfunction of lymphatic channels, a chronic lymphangitis, removal of the lymph nodes, trauma, mechanical obstruction, radiotherapy, venous insufficiency, malignancy, heart failure, and obesity.^{2,6} Obesity is an epidemic public health problem leading to many complications and results in both skin changes and different skin diseases. However, it is rarely associated with

ENV in the literature.⁶ In these patients, chronic venous stasis, venous insufficiency, and inflammation are the main causal factors of ENV. Both the fight against obesity and early diagnosis are vital conditions for the treatment and prevention of this complication.

Amyloidosis is a rare disease. AA is the most common type of amyloidosis in the Mediterranean region and the Middle East due to common chronic inflammatory diseases (i.e., familial Mediterranean fever).⁴ Also it may rarely be secondary to chronic infectious diseases. Recurrent infections are common in patients with Elephantiasis. On the contrary, AA amyloidosis secondary to recurrent bacterial infections such as cellulitis is very rare in these patients. Beloncle et al. presented two case reports on the association between primary lymphedema, chronic leg ulcers, and AA amyloidosis.⁵ At the same time, there are case reports documenting a secondary renal amyloidosis associated with chronic lymphatic filariasis caused by *Wuchereria bancrofti*.⁷ Our report is different from other cases due to the obesity as the most important contributor to the defined condition. Obesity can lead to serious kidney failure due to metabolic and hemodynamic reasons.⁸ It usually causes focal segmental glomerulosclerosis. At the same time, obesity is rarely a susceptibility factor for idiopathic AA amyloidosis in current studies.^{9,10} Although we could not perform a kidney biopsy, we considered the cause of kidney failure as amyloidosis due to bone marrow involvement.

In conclusion, AA amyloidosis should be considered as a possible complication in obese patients with ENV. This situation can cause serious organ involvement, especially kidney. Clinicians should be aware of the association of ENV and amyloidosis, particularly in obese patients.

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Main Points

Obesity is an epidemic public health problem leading to many skin diseases, such as Elephantiasis nostras verrucosa. AA amyloidosis should be considered as a possible complication in obese patients with Elephantiasis nostras verrucosa. Amyloidosis-related kidney disease should be considered in these patients.

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