Mammary-type myofibroblastoma with the nephrotic syndrome

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We describe a 23-year-old white man who presented with anasarca and a new periumbilical mass. He had preserved kidney function and laboratory findings consistent with nephrotic syndrome, including 9.7 g/day albuminuria. Serum serologies were positive for anti-SSa and anti-SSb and low complements but were negative for antinuclear antibody. Pathologic findings of the abdominal mass showed a mammary-type myofibroblastoma. A kidney biopsy revealed a diffuse proliferative and membranous immune-mediated glomerulonephritis with 10% interstitial fibrosis. This is a novel case of mammary-type myofibroblastoma associated with nephrotic syndrome mimicking a proliferative lupus pattern.

Nephrotic syndrome (NS) involves a constellation of physical and laboratory findings, including urinary albumin excretion >3.5 g/day, hypoalbuminemia, hyperlipidemia, and peripheral edema (1). Paraneoplastic glomerulopathy has previously been described as a common cause of NS, with most glomerular lesions having a membranous pattern (2). A minority of patients have proliferative lesions that can mimic lupus nephritis. We describe a young man who did not have systemic lupus erythematosus (SLE) but had glomerular findings of SLE-like lesions after a new diagnosis of a rare abdominal myofibroblastoma.

CASE DESCRIPTION

A 23-year-old white railroad conductor presented with dyspnea and progressive edema spreading from his feet to his abdomen over several days. He noted having fatigue, night sweats, headache, dyspnea, cough, and a 60-pound weight loss over 6 months. Two months earlier, he was seen in the emergency department with abdominal pain. Computed tomography (CT) revealed diffuse lymphadenopathy and an edematous process in the extraperitoneal region of the pelvis anterior to the bladder. He was started on prednisone 20 mg daily for 4 weeks and told to follow up with oncology.

On exam his vital signs were stable, except for a blood pressure of 160/95 mm Hg. He had mild crackles at both lung bases and a tender 4 cm palpable periumbilical mass. He had +4 pedal edema and no rash. Pertinent laboratory results included a white blood cell count of 6400/uL; hemoglobin, 8.3 g/dL; hematocrit, 26.1%; mean corpuscular volume, 77.7 fL; albumin, 1.3 g/dL; triglycerides, 263 mg/dL; low-density lipoprotein cholesterol, 121 mg/dL; and brain natriuretic peptide, 16 pg/mL. Urinalysis revealed a specific gravity of 1.027, pH of 6.0, 4+ protein, 3+ blood, 50 to 100 red blood cells per high-power field, 10 to 15 white blood cells per high-power field, and 9.7 g/day of albuminuria. Serum serologies returned low C3, 51.9 mg/dL; low C4, 8.9 mg/dL; positive anti-SS-A/Ro, anti-SS-B/La. Urine protein electrophoresis was 1144 mg/dL without M-spike. His entire serologic workup was negative including antinuclear antibody twice and anti-DNA. An abdominal CT scan revealed a mass *(Figure 1)*. Colonoscopy and esophagogastroduodenoscopy were unremarkable.

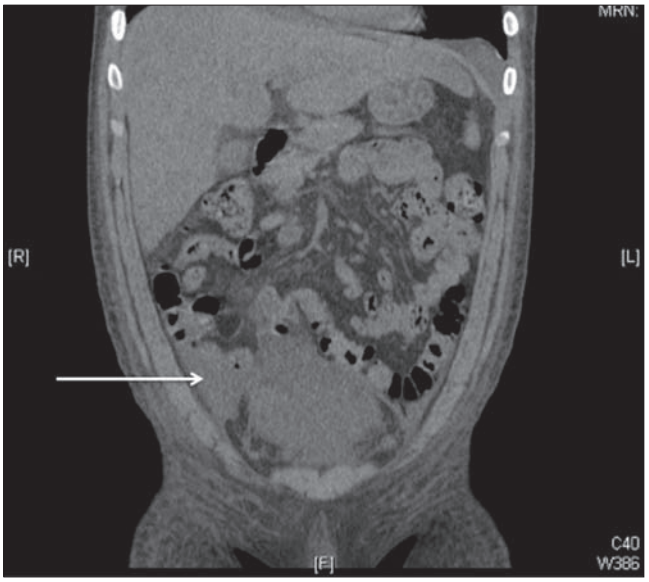

Figure 1. CT showing a focal hypodensity extending from the anterior aspect of the pelvis into the lower anterior abdomen, with the largest low-density lobular region just deep to the abdominal wall in the lower anterior abdomen measuring up to 9 × 4.7 cm (arrow).

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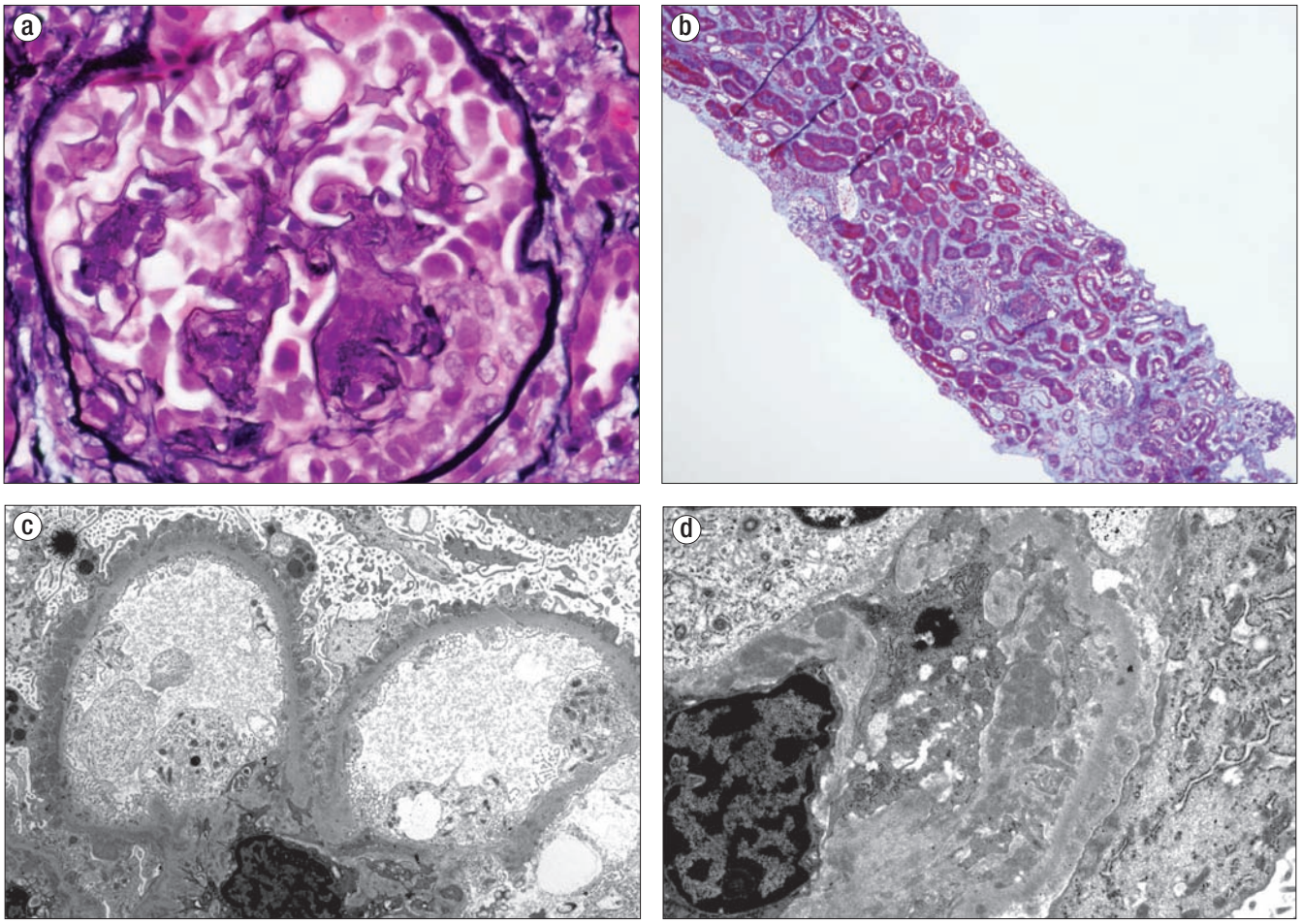

Figure 2. Kidney biopsy results. **(a)** A normal-sized glomerulus with a segmental cellular crescent and no definitive "spikes" or "holes" (Silver ×400). **(b)** Mild tubular atrophy and interstitial fibrosis (10%) (Trichrome ×40). **(c)** Electron microscopy showing numerous subepithelial deposits in a membranous pattern and **(d)** numerous mesangial deposits.

A kidney biopsy revealed diffuse proliferative and membranous immune-mediated glomerulonephritis with 10% interstitial fibrosis and cellular crescents but no vascular disease. Immunofluorescence staining revealed a diffuse fine granular pattern in the capillary loops and mesangium for IgG (2 to 3+), IgM (1 to 2+), kappa (2 to 3+), and lambda light chains (2 to 3+), but was negative for IgA *(Figure 2)*. An excisional biopsy of the pelvic mass revealed a lipomatous neoplasm with prominent myxoid areas. Molecular testing with fluorescence in situ hybridization was negative for DDIT3, which did not support myxoid liposarcoma.

The patient was treated for possible renal-limited lupus nephritis given his proliferative lesions with crescents. He was diuresed with furosemide and started on the Aspreva Lupus Management Study Group trial induction regimen in order to avoid gonadotoxicity with cyclophosphamide (3). The patient returned 2 weeks later with a continued complaint of dyspnea. His labs showed preserved renal function with persistent hypoalbuminemia. Serum C3 and C4 labs had increased to 89 mg/dL and 25.2 mg/dL, respectively, and 24-hour urine albumin was higher at 26 g/day. Because of his worsening albuminuria, he was given rituximab based on the LUNAR study protocol (4). The abdominal mass was surgically removed, and pathology revealed a cellular spindle cell neoplasm suggestive of mammary-type myofibroblastoma. One month later, his 24-hour urine albumin had fallen markedly to 1.5 g/day.

DISCUSSION

NS is caused by primary glomerular disease or is a consequence of a systemic disease or pathologic condition. Paraneoplastic glomerulopathy attributes the manifestations of glomerulonephritis not to tumor invasion or metastasis, but to unknown hormones, cytokines, or tumor antigens from the malignancy (2). NS is usually treated with guideline-based therapy for malignancy eradication (5, 6).

Our patient was diagnosed with a relatively rare tumor, mammary-type myofibroblastoma. This tumor is considered benign and does well even when the margins of resection are positive. It usually comprises bland spindle cells intermixed with collagen bundles and adipocytes. About 90% of these tumors express CD34 and desmin. Genetically, 92% of patients have a deletion or rearrangement of 13q14 resulting in a loss of the retinoblastoma gene. Originally, mammary-type myofibroblastoma was described in the male breast (7), but subsequently it has been described in other anatomic sites. In their 2015 review, Howitt and Fletcher described 143 cases, and only one

case had spread (8). There are no reports of this tumor being associated with NS.

The patient presented at the unusually young age of 23, while most malignancies associated with NS are in older patients (2). The kidney biopsy was consistent with a membranous pattern with subepithelial deposits on electron microscopy, but also with a proliferative pattern including crescents, which appeared lupus like. The patient did not have classic SLE clinicopathologic symptoms, with two negative antinuclear antibody tests and a negative anti-DNA test. Some patients present with histologic findings of SLE nephritis on biopsy, but without extrarenal symptoms, as described in a case series by Huerta et al (9). Without specific guidelines for treatment, patients with this presentation are treated as if they have true SLE nephritis, because most will eventually develop extrarenal SLE (9).

We surmised that this patient had a benign mammary-type myofibroblastoma that caused the proliferative glomerulopathy, and the NS resolved either by removal of this tumor or rituximab infusion. This case describes the first published association of mammary-type myofibroblastoma and NS.

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