nitazoxanide without reducing the immunosuppression. There possibly is only one earlier report of sapovirus diarrhea successfully treated with nitazoxanide without reducing immunosuppression.[5] The chronic norovirus and subsequent sapovirus diarrhea reported by Wright *et al.*[6] required prolonged treatment with nitazoxanide and reduction of immunosuppression leading to graft rejection. That patient as well as the one managed by Ghusson and Vasquez,[1,6] had substantial unplanned weight loss before the PCR-based diagnosis.

Stool PCR, if available, should be done for all SOT patients presenting with diarrhea. Though it is more expensive than conventional tests and cannot differentiate active and asymptomatic carriers, in transplant patients where risks are higher, delays in diagnosis should be avoided. We also suggest adding nitazoxanide to the treatment regimen without reducing immunosuppression.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Conflicts of interest

There are no conflicts of interest.

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NELL-1 as a Target Antigen in Asbestosis Associated Membranous Nephropathy — A Case Report

Abstract

An 80-year-old male with a history of prolonged asbestos exposure presented with 24-hour urine protein of 8 gm, and serum albumin of 1.7 gm/dl. Renal biopsy disclosed features of membranous nephropathy. Immunohistochemistry showed positivity for neural epidermal-like growth factor- like 1 (NELL1) (2+/3+). Further assessment uncovered an incidental finding of asbestos-related pleural plaques and left hemithorax volume loss on computed tomography (CT) chest, leading to a diagnosis of asbestosis. This case highlights the rare association between asbestosis and NELL-1 positive membranous nephropathy.

Keywords: *Membranous nephropathy, Asbestosis, NELL-1, Secondary membranous*

Introduction

NELL-1 positive membranous nephropathy has been seen various causes like malignancy, infections like hepatitis B, autoimmune disorders, indigenous medicines (containing mercury).[1,2] Exposure to various toxic environmental substances like asbestos, lead, mercury, have been linked with membranous nephropathy.[3] Here we describe NELL-1 positive membranous nephropathy in an individual with asbestosis.

Case Report

An 80-year-old male presented with lower limb swelling and periorbital edema for 10 days. He worked as military personnel for 35–40 years; and he stayed in a house with asbestos roofing for over 30 years. On evaluation, he was found to have urine albumin 4+ without any active urinary sediments, a 24-hr urine protein 8 gm, serum albumin 1.7 gm/dl, total cholesterol 340 mg/dl, serum LDL 263 mg/dl, triglycerides 166 mg/dl, and serum creatinine 0.9 mg/dl. A

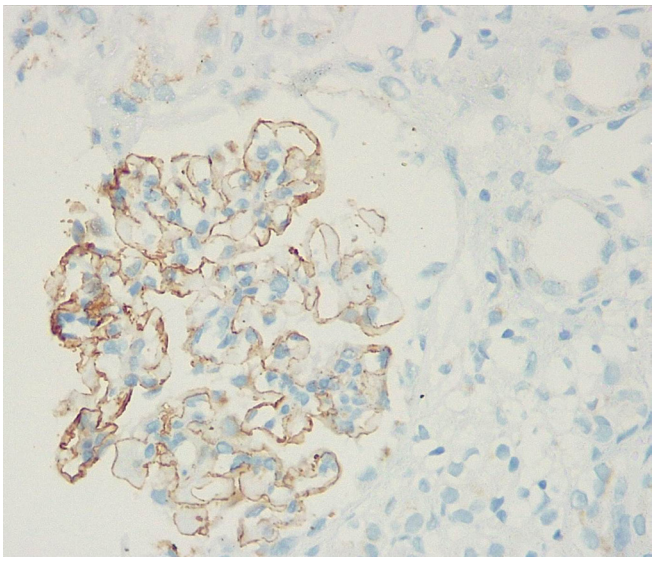

Figure 1: Immunohistochemistry showing diffuse NELL1 positivity (2+/3+) along the glomerular capillaries (NELL1 immunostain ×400) left hemithorax. NELL-1: Neural epidermal-like growth factor-like 1.

kidney biopsy revealed thickening of glomerular basement and stiffening of glomerular capillaries in all glomeruli. The periodic Schiff-methenamine stain revealed holes and spikes in occasional glomeruli. Immunofluorescence showed IgG 3+, IgM 3+, IgA negative, C3 2+, C1q negative, kappa light chain 3+, and lambda light chain 3+. Immunohistochemistry on paraffin block of renal tissue was done for phospholipase A2 receptor (PLA2R), thrombospondin (THSD7A), neural epidermal-like growth factor like 1 (NELL-1), semaphorin 3b, exostosin 1, and exostosin 2, which showed diffuse NELL-1 positivity (2+/3+) along the glomerular capillaries [Figure 1].

CT scan of the chest was done as a part of work up to exclude malignancies, revealed calcified pleural plaques and loss of volume in left hemithorax [Figure 2]. In view of significant asbestos exposure with the above finding in computed tomography (CT) chest and exposure to asbestos roofing for almost 35–40 years, diagnosis of asbestosis was made. However, this patient doesn't offer any respiratory complaints. In view of no response to 1mg/kg steriod, he was started on tacrolimus 2mg twice daily (0.05mg/kg) in two divided doses with 0.5mg/kg of prednisolone. He attained complete remission after 6 weeks of therapy following which steriod tapering has been started.

Discussion

Asbestos exposure has been associated with autoimmune disorders and the production of autoantibodies, potentially leading to MN.[3–5] There is no data on target antigen in Membranous Nephropathy related to asbestosis. NELL-1 positive membranous nephropathy is in association with carcinoma lung, carcinoma prostate, carcinoma breast, and so on; nonsteroidal anti-inflammatory drugs (NSAID), indigenous medication (containing mercury); autoimmune

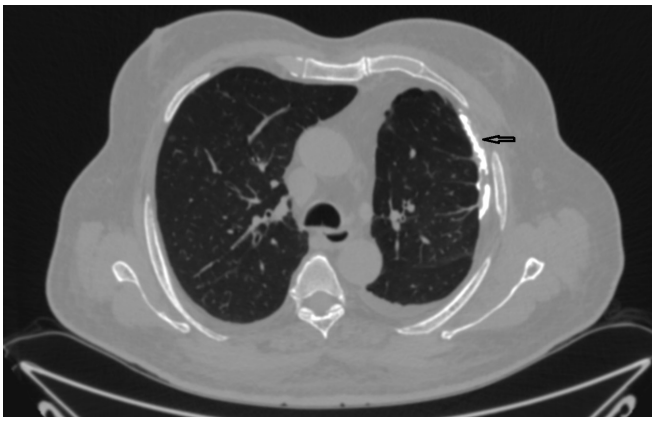

Figure 2: Black arrow indicates the calcified pleural plaques and loss of volume in left hemithorax.

disorders—Hashimoto thyroiditis, Sjogren syndrome, sarcoidosis; Hematopoetic stem cell transplantation; infection—Hepatitis B.[1,2,6]

NELL-1, primarily expressed in osteoblasts and renal tubules, is a novel target antigen implicated in various secondary causes of MN. Experimental evidence suggests a role for NELL-1 in bone regeneration and osteogenic differentiation, raising the possibility of its involvement in extraosseous calcification observed in asbestosis. To the best of our knowledge, this is the first report of NELL-1 positive membranous nephropathy associated with asbestosis and this association warrants further investigation into its pathophysiological significance and potential therapeutic implications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Conflicts of interest

There are no conflicts of interest.

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Concomitant Histological Features of Membranous Nephropathy and Anti-Neutrophil Cytoplasmic Antibody Associated Vasculitis

Abstract

The simultaneous occurrence of vasculitic glomerulonephritis and membranous nephropathy is unusual. We report two cases that presented to our outpatient department with rapidly progressive renal failure. On evaluation, in one patient, anti-myeloperoxidase (MPO) titers were high, and renal biopsy was suggestive of concurrent necrotizing and diffuse crescentic anti-MPO anti-neutrophil cytoplasmic antigen-associated glomerulonephritis with the circumferential cellular crescent formation and membranous glomerulopathy. He responded to plasmapheresis followed by maintenance immunosuppression with oral cyclophosphomide. Another patient was treated with Methylprednisolone and two doses of rituximab. Both the patients showed marked symptomatic improvement and became dialysis independent with stable creatinine at 3 months.

Keywords: *Anti-neutrophil cytoplasmic antibody associated Vasculitis, Crescentic glomerulonephritis, Membranous nephropathy, Plasmapheresis, Rapidly progressing renal failure*

Introduction

Membranous nephropathy (MN) is histologically characterized by subepithelial immunoglobulins deposits and complement.[1] Vasculitic or crescentic glomerulonephritis is rarely seen in MN except in systemic lupus erythematosus.[2,3] There are only a few cases with Wegener's granulomatosis that combine MN and crescentic glomerulonephritis.[4] Our knowledge of the immunopathogenesis, clinical features, treatment and outcomes of this unusual combination of membranous nephropathy and vasculitic or crescentic glomerulonephritis is limited. We report two patients who had concomitant necrotizing crescentic anti-MPO (Myeloperoxidase) associated glomerulonephritis and MN.

Case Reports

Case 1

A 58-year-old man with no known comorbidities presented with nonspecific pain abdomen. On evaluation, he was found to have hypertension, Serum creatinine - 3.4 mg/dl) and hematoproteinuria. At 12 days, his serum creatinine worsened to 10 mg/dl, and his anti MPO tires were >200 RIU/ml. Renal biopsy [Figure 1] suggested crescentic glomerulonephritis with IgG deposits. He was treated with a methylprednisolone pulse and four sessions of plasmapheresis. He required three sessions of hemodialysis, and was started on prednisolone and oral cyclophosphamide. At 3 months, he became dialysis independent.

Case 2

A 51-year-old lady with no known comorbidities presented with acute febrile illness decreased urine output, and generalized swelling of the body. On evaluation, she was found to have hypertension and serum creatinine of 1.4 mg/dl. Over two weeks, she had rapidly worsening creatinine to 10 mg/dl and required hemodialysis. Her anti MPO titre were >200 RIU/ml. Renal biopsy suggested crescentic glomerulonephritis [Figure 2] with IgG deposits. She was given a methylprednisolone pulse and two doses of rituximab. At 3 months, she became dialysis independent. The clinical and renal biopsy findings and treatment details of both patients are mentioned in Table 1.

Discussion

Immunoglobulin deposits are usually absent in the glomeruli of patients with anti neutrophil cytoplasmic antibody (ANCA)-associated glomerulonephritis. It is proposed that ANCA does not damage the glomerulus directly. Still, neutrophils activated by ANCA integrate into capillary walls and release several protein-degrading enzymes, and, finally, these pathological changes may cause necrosis to glomerular capillary walls.[5] Membranous glomerulopathy has subepithelial