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 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 [details in 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

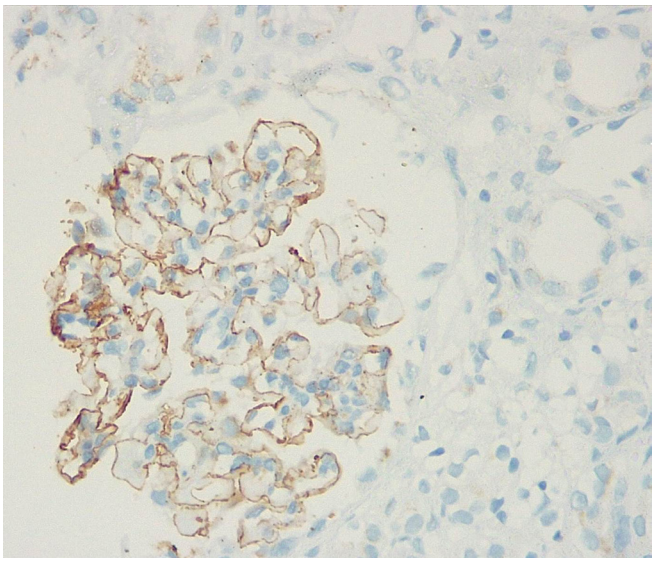

Figure 1: Immunohistochemistry showing diffuse NELL1 positivity (2+/3+) along the glomerular capillaries (NELL1 immunostain ×400) left hemithorax.

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

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 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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