von Recklinghausen's neurofibromatosis associated with membranous glomerulonephritis

Muzafar M. Wani, MD, DM, *Abdul R. Reshi,* MD, *Khursheed A. Banday,* MD, *Mohd S. Najar,* MD.

ABSTRACT

A 70-year old woman, known case of von Recklinghausen's neurofibromatosis presented with nephrotic syndrome and mild azotemia. Renal biopsy revealed membranous nephropathy. After ruling out secondary causes of membranous nephropathy, a possible coexistence of von Recklinghausen's neurofibromatosis and membranous nephropathy were thought of. This association has rarely been reported.

Saudi Med J 2006; Vol. 27 (4): 534-535

Von Recklinghausen's neurofibromatosis is a genetic disorder characterized by a variety of developmental abnormalities of skin along with increased risk of nervous system tumors.[1,2] Co-existent renal involvement has been described rarely.[3-7] We report a case of neurofibromatosis associated with membranous glomerulonephritis (MGN). Review of the literature shows this association to be very rare.

Case Report. A 70-year old Kashmiri lady was admitted to our hospital with generalized edema and ascites. She had multiple pigmented spots and subcutaneous swellings over abdomen and trunk since her childhood. Physical examination revealed multiple subcutaneous neurofibromas covering the entire skin surface and multiple *café au lait* spots on face, neck and chest (**Figure 1**). She had short stature (height 150cms), thoracodorsal scoliosis and anasarca. She was afebrile and her blood pressure was 160/100 mm Hg, with normal cardiovascular, respiratory and neurological examination. Abdominal examination revealed ascites and mild hepatomegaly. The laboratory findings revealed, hemoglobin 10 gm/dl, white blood cell count 4300, platelet count 322000, glutamic-oxaloacetic transaminase 35 IU, serum glutamic pyruvic transaminase 40 IU, C-reactive protein 100 mg/dl, urinary proteins 2+, no red blood cells or casts, 24 hour urinary protein was 5 grams, serum albumin 26 g/L and total protein 45 g/L, total cholesterol 300 mg/ dl, blood urea 38 mg/dl, serum creatinine 1.7 mg/dl, C3 148 mg%, IgA 2.3 g/L, IgG 3.9 gm /L, IgM 2.3 g/L. The results of the serological tests for HbS ag, hepatitis C virus, antinuclear antibody, rheumatoid arthritis, venereal disease research laboratory test, human immunodeficiency virus and ASO titres were within normal limits. The x-ray chest revealed mild cardiomegaly, electrocardiogram was normal. The ultrasonographic scan of abdomen revealed ascites with rest of the abdominal viscera normal. The CT head was normal and a coagulogram was within normal limits. Upper gastrointestinal endoscopy and colonoscopy were normal. Renal biopsy under ultrasound guidance was performed. Multiple sections stained with hematoxylin and eosin, para-aminohippuric acid, methenamine silver stain showed 12 glomeruli, most of the glomeruli

From the Department of Nephrology, Sheri-Kashmir Institute of Medical Sciences, Soura, *India*.

Received 26th July 2005. Accepted for publication in final form 15th January 2006.

Address correspondence and reprint request to: Dr. Muzafar M. Wani, 6/2, Polo View, Srinagar, Kashmir, J&K 19001, *India*. Tel. +194 2454558. Fax. +194 2458756. E-mail: mmmwani@rediffmail.com

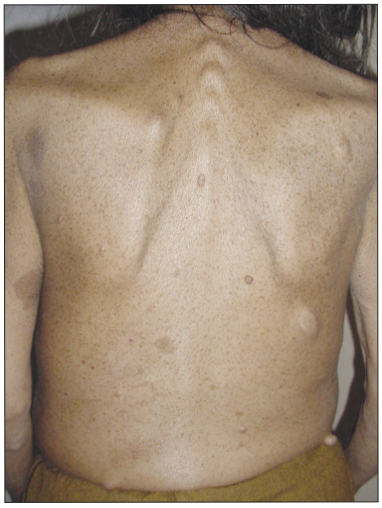

Figure 1 - Neurofibromas and *café au lait* spots on trunk.

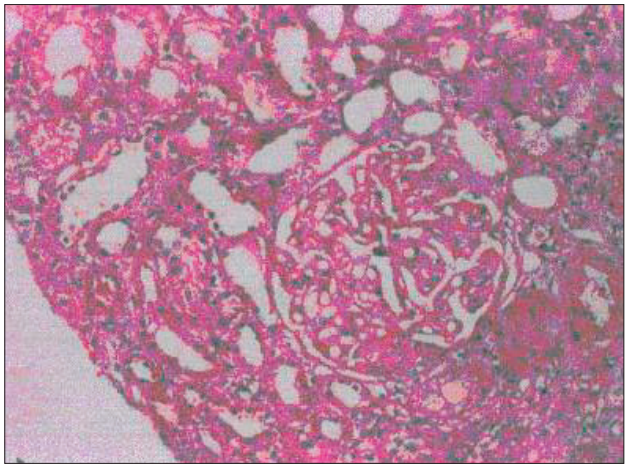

Figure 2 - Light microscopy showing features of membranous glomerulonephritis.

showed diffuse thickening of the glomerular basement membrane with large lucent holes in enface sections of the GBM on silver stain. Arterioles and small arteries show moderate to marked hyaline arteriosclerosis. These findings were suggestive of membranous glomerulopathy (**Figure 2**). Immunofluorescence revealed the presence of granular immune deposits which stained positive for IgG, IgM and C3 on the epithelial aspect of the GBM.

Discussion. von Recklinghausen's neurofibromatosis is a genetic disorder characterized by cutaneous neurofibromas, café au lait spots, axillary freckling, and hematomas of the iris and pseudoarthrosis of the tibia.[2] Neurofibromas are benign peripheral nerve tumors, present as multiple, palpable, rubbery cutaneous swellings. They are generally asymptomatic, but if they grow in an intervertebral foramen, they may produce a compressive radiculopathy or neuropathy. Aqueductal stenosis with hydrocephalus, scoliosis, short stature, hypertension, epilepsy and mental retardation may also occur.[2] These patients are at increased risk of developing nervous system tumors. Glomerular lesions associated with von Recklinghausen's neurofibromatosis have been reported rarely.[1-7] Medline search revealed 6 cases of von Recklinghausen's neurofibromatosis associated with glomerular lesions, these are minimal change disease,[3] membranous nephropathy[1,2,6] and mesangial-proliferative glomerulonephritis.[5,7] Membranous glomerulonephritis is a common cause of nephrotic syndrome in adults. Though usually idiopathic it may be secondary to underlying malignancy in 10-15% of the cases.[8] In this case, MGN manifested as nephrotic syndrome and mild azotemia. Secondary causes of membranous nephropathy were ruled out at the time of presentation. Whether this was a simultaneous occurrence of MGN in von Recklinghausen's neurofibromatosis or, a chance association cannot be excluded. The review of the literature and our case report illustrates that von Recklinghausen's neurofibromatosis may be associated with MGN but raises the question as to why this association is not seen more often. However, considering the possible mechanism of the occurrence of MGN in malignancies, the occurrence of glomerular lesions may be related with von Recklinghausen's neurofibromatosis, although it cannot be ruled out that the diseases occurred independently.

References

1. Kakubo T, Hiki K, Horii A, Kobayashi Y. Recklinghausen's neurofibromatosis associated with membranous nephropathy. ***Nephron*** 1993; 65: 486.
2. Toth T, Trinn C, Simon L, Nagy J. A case of membranous glomerulonephritis associated with Recklinghausen's neurofibromatosis. ***Clin Nephrol*** 1996; 45: 271-272.
3. Fujiwara R, Kunitachi H, Sabe H. A case of von Recklinghausen's disease associated with nephritic syndrome (in Japanese). ***Naika*** 1985; 56: 1176-1178.
4. Shibata T, Kudoh K, Ishii T, et al. A case of membranous nephropathy associated with von Recklinghausen's disease (in Japanese). ***Kidney Dial*** 1990; 29: 145-148.
5. Fujishiro N, Ohta H, Kawashima S, Kawada Y, Machida M. A case of neurofibromatosis associated with aortitis syndrome (in Japanese). ***Jpn J Med*** 1970; 59: 44-48
6. Kokubo T, Hiki Y, Horii A, Kobayashi Y. A case of Recklinghausen's associated with membranous nephropathy. ***Nippon Jinzo Gakkai Shi*** 1994; 36: 951-954.
7. Taniguchi Y, Yorioka N, Kanbe M, Okushin S, Oda H, Nishida Y et al. Parent and child cases of IgA nephropathy associated with von- Recklinghausen's disease. ***Nephron*** 1997; 75: 113-114.
8. Ponticelli C, Passeriae P. Membranous glomerulonephritis. In: Massry SG. Glassock RJ, editors, Text book of Nephrology. 4th ed. Philadelphia (PA): Lippincot Williams; 2001. p. 707-713.