

and high blood pressure. Haematuria is the most common complication¹⁰ and may cause obstructive renal dysfunction.

It is generally accepted that an AVF can be reliably diagnosed by Doppler ultrasound.⁴ In our case, renal angiography confirmed the AVF and pseudoaneurysm.

Treatment options for symptomatic AVF range from total or partial nephrectomy to selective embolisation of the affected vessels. Nephrectomy may be the only option in a case of severe and uncontrollable acute haemorrhage. Arterial embolisation by catheter has been carried out successfully in recent years and the success rates are around 88%.^{5,6}

Selective embolisation is an effective treatment for post-biopsy AVF.¹¹⁻¹³ Its interference with the renal parenchyma is limited and it is less aggressive than open surgery. As such, in our view, it should be considered as the first choice of treatment whenever the urgency of these cases permits.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

1. Bilge I, Rozanes I, Acunas B, Minareci O, Nayir A, Oktem F, et al. Endovascular treatment of arteriovenous fistulas complicating percutaneous renal biopsy in three paediatric cases. *Nephrol Dial Transplant* 1999;14:2726-30.
2. Wenzel U, Helmchen U, Stahl RA, Nolte-Ernsting C. Massive bleeding after biopsy of a renal allograft. *Kidney Int* 2006;69:1101.
3. Kopečna L, Mach V, Procházka J. Arteriovenous fistula as a complication of renal biopsy. *Bratisl Lek Listy* 2005;106:218-20.
4. Yang CY, Lai MY, Lu CL, Tseng HS, Chiou HJ, Yang WC, et al. Timing of Doppler examination for the detection of arteriovenous fistula after percutaneous renal biopsy. *J Clin Ultrasound* 2008;36:377-80.
5. Maleux G, Messiaen T, Stockx L, Vanrenterghem Y, Wilms G. Transcatheter embolization of biopsy-related vascular injuries in renal allografts. Long-term technical, clinical and biochemical results. *Acta Radiol* 2003;44:13-7.
6. He HW, Jiang CH, Wu ZX, Li YX, Lu XL, Wang ZC. Transvenous embolization with a combination of detachable coils and Onyx for a complicated cavernous dural arteriovenous fistula. *Chin Med J* 2008;121:1651-5.
7. Ruth EM, Dittrich K, Jungert J, Uder M, Rascher W, Dotsch J. Successful interventional treatment of arteriovenous fistula after kidney biopsy in pediatric patients — a report of three cases. *Nephrol Dial Transplant* 2008;23:3215-8.
8. Martínez T, Palomares M, Bravo JA, Alvarez G, Galindo P, Entrena AG, et al. Biopsy-induced arteriovenous fistula and venous aneurysm in a renal transplant. *Nephrol Dial Transplant* 1998;13:2937-9.
9. Omoloja AA, Racadio JM, McEnery PT. Post-biopsy renal arteriovenous fistula. *Pediatr Transplant* 2002;6:82-5.
10. Lawen JG, Buren CT van, Lewis RM, Kahan BD. Arteriovenous fistulas after renal allograft biopsy: a serious complication in patients beyond one year. *Clin Transplantation* 1990;4:357-69.
11. Loffroy R, Guiu B, Lambert A, Mousson C, Tanter Y, Martin L, et al. Management of post-biopsy renal allograft arteriovenous fistulas with selective arterial embolization: immediate and long-term outcomes. *Clin Radiol* 2008;63:657-65.
12. Jiang WX, Wang HF, Ma J, Han HJ. Arteriovenous fistula and pseudoaneurysm as complications of renal biopsy treated with percutaneous intervention. *Chin Med J (Engl)* 2010;123(19):2736-8.
13. Lorenzen J, Schneider A, Körner K, Regier M, Adam G, Nolte-Ernsting C. Post-biopsy arteriovenous fistula in transplant kidney: treatment with superselective transcatheter embolisation. *Eur J Radiol* 2012;81(5):e721-6.
14. Breza J Jr, Javorka V Jr, Mizickova M, Goncalves FM, Breza J Sr. Arterio-venous fistula with pseudoaneurysm of renal artery. *Bratisl Lek Listy* 2012;113(5):289-92.

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Membranous glomerulonephritis in a patient with Hodgkin's lymphoma in remission

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To the Editor:

The association between membranous nephropathy and solid organ tumours is well known. In the case of Hodgkin's lymphoma (HL), the most common histological type of renal involvement is minimal change glomerulonephritis followed by focal segmental glomerulosclerosis.¹ We report the case of a patient with membranous glomerulonephritis (MG) who had been diagnosed five years earlier with HL and was in complete remission.

Our patient is a 50-year-old male with no relevant medical history, who was diagnosed, by biopsy of retroperitoneal adenopathy, with stage IV lymphocyte predominance HL with bone marrow involvement in October 2005. He was treated with polychemotherapy, eight ABVD cycles with increased partial response and consolidation ra-

diotherapy on the retroperitoneal mass. In October 2006, a complete response was observed by positron emission tomography (PET) and computerised tomography (CT). The patient remained asymptomatic until March 2010, when he developed complete clinical and biochemical nephrotic syndrome with proteinuria of 12g/day and normal renal function. His immunological profile was negative (antinuclear antibodies [ANA], anti-DNA, c and p anti-neutrophil cytoplasmic antibodies [ANCA], anti-GBM Ab, C3-C4, hepatotropic virus and human immunodeficiency virus serologies negative, cryoglobulins negative, immunoglobulins, blood and urine electrophoresis). Renal biopsy showed 13 glomeruli with slight mesangial matrix expansion, without interstitial or vascular abnormalities, with immunofluorescence positive for IgG with a granular pattern and weakly positive for C3; the electron microscope study displayed subepithelial electron dense deposits, consistent with stage 1 MG. Given this diagnosis, secondary causes of MG and HL recurrence were ruled out by additional studies (CT of the chest, abdomen and pelvis, PET-CT and bone marrow biopsy). After treatment with oral chlorambucil and steroids for 18 weeks, there was partial remission (proteinuria 3.5g/day in November 2010). During the following three months, the patient was treated with tacrolimus (4mg/day) and low-dose prednisone, with complete remission being achieved in February 2011, which was maintained after discontinuation of immunosuppressive therapy. The nephrotic syndrome currently remains in complete remission with normal renal function and no evidence of recurrence of HL 22 months later.

On reviewing the literature, we found more than 150 cases of HL associated glomerulonephritis, while only 5% of these were MG.² In most patients, MG manifests simultane-

ously with HL or its recurrence, but it may do so even a year before the latter is detectable.³ In the present case, HL was inactive at the time of diagnosis, despite which we assumed the existence of an aetiopathogenic relationship between the nephrotic syndrome MG and HL. Cervera et al. and Gomez-Campderá et al. described similar cases in which MG appeared 30 to 18 months after HL was in complete remission without evidence of recurrence.⁴

The HL-MG association aetiopathogenesis is not well defined, and abnormalities in T lymphocytes function and the overexpression of proto-oncogenes in HL appear to play an important role in the formation of immune complexes. These abnormalities in the immune system last for a long time despite HL being cured,^{1,5} which may predispose these patients to diseases mediated by T lymphocytes abnormalities.

MG treatment, when associated with active or recurrent HL, is based on combination chemotherapy of the underlying disease (ABVD or ABVD combined with COPP), with a high cure rate in both processes, as stated by Lien et al. in their review of paraneoplastic glomerulopathies.¹ Since our case involved HL that was in complete remission, the patient was treated with conventional therapy used in primary MG, with a good response and complete remission of symptoms.

In summary, MG is not only associated with solid organ tumours, but also with haematological diseases, although it is not the most common form of renal involvement. The immunity of patients who have suffered HL continues to be abnormal for some time after its cure. In all patients with a history of HL and nephrotic syndrome, we should rule out HL recurrence. This situation will determine the treatment and progression of the renal pathology.

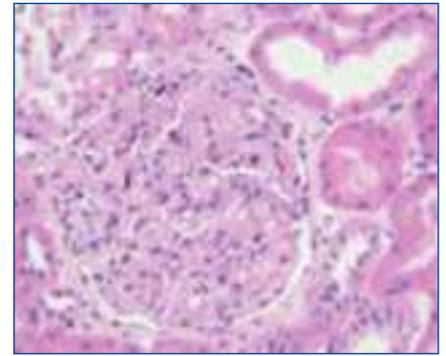


Figure 1. Glomerulus with mesangial matrix expansion.

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1. Lien YH, Lai W. Pathogenesis, diagnosis and management of paraneoplastic glomerulonephritis. *Nat Rev Nephrol* 2011;7:85-95.
2. Kayatas M, Yildiz G, Timuçin M, Candan F, Yildiz E, Sencan M. A case of acute renal failure caused by Hodgkin's lymphoma: concurrent membranous glomerulonephritis and interstitial HL-CD 20 Lymphoid Infiltration. *Ren Fail* 2011;33(3):363-6.
3. Mallouk A, Pham PT, Pham PC. Concurrent FSGS and Hodgkin's lymphoma: case report and literature review on the link between nephritic glomerulopathies and hematological malignancies. *Clin Exp Nephrol* 2006;10:284-9.
4. Gómez-Campderá FJ, López-Gómez JM, Jofre R, Flores E. Membranous nephropathy in Hodgkin's disease in complete remission. *Nephron* 1994;68:392.
5. Hotta O, Taguma Y, Kurosawa K, Sudo K, Takahashi H. Membranous nephropathy associated with nodular sclerosing Hodgkin's disease. *Nephron* 1993;63:347-50.

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Novel *NPHS1* Gene Mutation in an Iranian Patient with Congenital Nephrotic Syndrome of the Finnish Type

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Dear Editor,

Congenital nephrotic syndrome of the Finnish type (CNF; OMIM#256300) is a rare autosomal recessive genetic kidney disease that develops in utero and is usually diagnosed before the age of 3 months of postnatal life.¹⁻³ This disease is defined by massive proteinuria, consecutive hypoproteinemic edema and dyslipidemia from birth. Renal protein loss is furthermore accompanied by hypogammaglobulinemia predisposing these infants to bacterial infections such as peritonitis and respiratory infections, as well as thromboembolic complications that have repeatedly been observed.^{2,4} Kidney histology in this condition shows progressive mesangial sclerosis and capillary obliteration, and tubulointerstitial fibrosis. Many affected infants are prematurely, have low birth weight, and show poor statural growth and nutritional status.⁴

The gene that is causative for this condition, *NPHS1* (OMIM*602716),

encodes a trans-membrane cellular adhesion molecule named nephrin which is a crucial component of the glomerular slit diaphragm to maintain the size-selective filtration barrier.^{1,4}

CNF is a progressive kidney disease and typically leads to end stage renal disease (ESRD) between 3 to 8 years of age. Renal transplants have a considerable risk of recurrence of the glomerular disease due to anti-nephrin antibodies observed in most of affected patients.^{3,4}

Herein, an Iranian boy with CNF is presented who carries a novel mutation in the *NPHS1* gene.

A 45-day-old infant was admitted to the Children' Medical Center Hospital, the Pediatrics Center of Excellence in Iran, with chief complaint of generalized edema. There was a family history of edema and proteinuria in his sibling who died in 2nd month of life without a clear diagnosis. Parents are first cousins consanguine.

At physical examination, the patient had a weight of 4,750g, a body length of 52cm, and his blood pressure was 80/60mmHg. Laboratory data showed blood urea nitrogen (BUN) of 7mg/dL, creatinine (Cr) of 0.39mg/dL, total protein of 5g/dL, and albumin of 2.36g/dL. Other laboratory tests revealed the following values: cholesterol: 152mg/dL, triglyceridemia: 111 mg/dL, calcium: 7.5mg/dL, P: 5.6mg/dL, alkaline phosphatase: 2600IU/L, random protein/Cr: 525/44 mg/mg and 3+ protein in urinalysis. TORCH study was negative and immunologic investigations were normal. Thyroid tests showed hypothyroidism (TSH: 38 ng/dL, FT4: 0.4 ng/L). By echocardiography, valvular pulmonary stenosis was seen. Kidney biopsy showed mesangial proliferation in glomeruli and proliferative changes in smooth muscle layer in the artery, suggestive for nephrotic syndrome (Figure 1). Therefore albumin infusions, levothyroxin, and enalapril (0.1mg/kg/d) and other supportive care were started for the patient.

He developed end-stage renal failure at the age of 6 years and received a renal allograft from an unrelated living donor.

Four years later, he was hospitalized again with an abdominal mass. Burkitt's lymphoma was diagnosed and he was put on chemotherapy. However, unfortunately, he died because of cancer progression 7 months later.

Genetic studies on DNA samples of the patient and his parents were performed to analyze the *NPHS1* gene for suspected congenital nephrotic syndrome, Finnish type. Exons and flanking intronic regions of the gene (*NPHS1* Exon 1-29, NM_004646) were amplified by PCR. PCR amplicons were purified and subjected to direct sequencing using an automated capillary sequencer. Sequences were compared to the reference sequences deposited in the public database (NCBI). In the patient, homozygosity for a 1 bp duplication near the splice acceptor site of exon 17 of the *NPHS1* gene was detected (intron 16: c.2213-2dupA homozygous mutation). In both parents the heterozygous carrier status for the

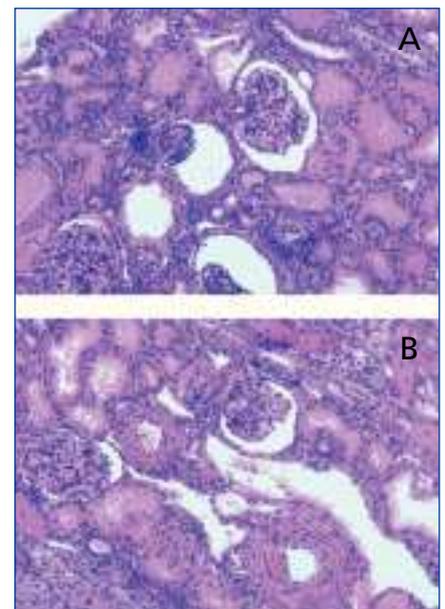


Figure 1. Histopathological findings in renal biopsy.

A. Mesangial proliferation in immature (fetal type) glomeruli with crowded podocytes (Hematoxylin and eosin, 200X). B. Mesangial proliferation in glomeruli and proliferative changes in smooth muscle layer in the artery causing vascular medial hypertrophy (Hematoxylin and eosin, 200X).