

syndrome. *Neuroradiology* 2004;46(12): 978-83.

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## Peripheral nervous system involvement in a haemodialysis patient treated with pegylated interferon

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### To the Editor:

The prevalence of hepatitis C virus infection among patients on haemodialysis is estimated at 3%-23% in developed countries. Some of the adverse effects described in treating patients on haemodialysis with interferon as a monotherapy include<sup>1</sup>: flu-like symptoms, anaemia, immunological graft intolerance, depression, leukopenia, confusion, diarrhoea, bone pain, thyroid alterations, thrombocytopenia, and convulsions. To a lesser degree, there have also been descriptions in the medical literature of autoimmune diseases and neurological alterations in relation to this type of treatment in patients on haemodialysis. Pegylated interferon improves drug absorption and extends the half-life of this medication.

**Table 1.** Laboratory analysis results.

	Pre-treatment	Month 3. Suspension	Month 3-4. Evolution			Month 5
Hb (g/dl)	11.8	9.6	8.8	7.2	9.9	10.2
Leukocytes	5280	3380	12430	10910	7170	6750
Platelets	111000	51000	92000	151000	155000	121000
AST (U/l)	16	21	33		31	22
ALT (U/l)	8	11	15		9	6
GGT (U/l)	18					29
CPK (U/l)	61			27	68	
Albumin (g/dl)	3.5					2.5
CRP (mg/dl)	1.3		20.5		4.6	2.7
TSH (µU/ml)				9.62		7.42

Results from laboratory analyses arranged by treatment with pegylated interferon. Before treatment, at the moment treatment was suspended (month 3), after suspension of treatment (months 3-4), and 5 months after start of treatment (month 5). ALT: alanine-aminotransferase; AST: aspartate-transaminase; CPK: creatinine phosphokinase; GGT: gamma-glutamyl-transferase; CRP: C-reactive protein; TSH: thyrotropin-stimulating hormone.

Here we describe the case of a 47-year old male on haemodialysis with no known allergies, a history of smoking and social drinking, and a previous addiction to parenteral drugs. The patient suffered from stage 5 chronic kidney disease of an unknown origin. The patient had received a transplant but had to return to haemodialysis after 8 years. The patient also had arterial hypertension, positive serology for hepatitis C virus (HCV), positive CRP (genotype 3a), positive cryoglobulins, chronic gastritis, bronchiectasis, and had prob-

lems with his vascular access in the form of a permanent right jugular catheter.

The patient had no alterations in transaminase levels or clotting factors, and in the absence of ultrasound indications of portal hypertension, we started him on treatment with alpha-2-a pegylated interferon as a monotherapy, considering the patient to be a candidate for a second kidney transplant. During the first three months of treatment, the patient suffered only mild adverse side ef-

**Table 2.** Autoimmune state following suspension of interferon.

	Results
<b>Thyroid peroxidase antibodies</b>	Negative
<b>Thyroglobulin antibodies</b>	Negative
<b>Anti-TSH receptor antibodies</b>	Negative
<b>ANA</b>	Negative
<b>Anti dsDNA</b>	Negative
<b>Anti-Sm</b>	Negative
<b>Anti-Ro</b>	Negative
<b>Anti-La</b>	Negative
<b>Anti-RNP-70</b>	Negative
<b>Rheumatoid factor</b>	49IU/ml (0-14)
<b>Protein electrophoresis</b>	Polyclonal increase in gamma fraction
<b>C3 and C4</b>	Normal

ANA: anti-nuclear antibodies; TSH: thyrotropin-stimulating hormone.

fects related to treatment, in the form of mild thrombocytopenia and nausea.

After this initial period, a series of complications began to arise:

- Right basal pneumonia with haemoptysis, pleural effusion, and marked thrombocytopenia. At this point we suspended treatment with interferon.
- Epigastric pain with irradiation into the hypochondria and lumbar area that intensified during haemodialysis and that did not recede with analgesia, prompting several incomplete haemodialysis sessions.
- Deterioration in general state of health, including weight loss, anaemia despite increased doses of darbepoetin, and weakness in the legs, prompting hospitalisation. We performed a gastroscopy, observing antral and ectatic gastropathy with no signs of acute bleeding. A computed axial tomography (CAT scan) of the chest detected a solid hilar tumour in the lower right quadrant that was producing a total obstruction of the bronchus in the right lower lobule. We performed a bronchoscopy, extracting the blood clot from the aforementioned location. A bronchial swab and biopsy revealed negative test results. We diagnosed the patient with hypothyroidism.
- Diplopia, inability to close the left eye, and inability to walk, three weeks after suspending interferon and in an outpatient setting. A cranial CAT scan revealed no signs of acute damage, but signs of vascular leukoencephalopathy were observed, which were later confirmed by nuclear magnetic resonance (NMR). A CAT scan of the eye sockets revealed a symmetrical increase in the size of the extra-ocular muscles and the inferior, medial, and superior rectus muscles of both eyes, suggesting thyroid orbitopathy. The patient refused transferral to the neurology department. After an initial neurological examination including electroneurography and NMR, the diagnostic conclusion

was that of peripheral nervous system involvement with symptoms of thick fibre sensory neuropathy (deep sensitivity), including paralysis of the left sixth cranial nerve, in relation to treatment with interferon, with spontaneous recovery 3 months after suspending treatment.

We started treating the patient with hormone replacement therapy using levothyroxine. We also considered administering corticosteroids to treat the 6<sup>th</sup> cranial nerve paralysis, as well as the possibility of an autoimmune component. However, we decided against this strategy in order to avoid the potential for viral replication (viral RNA had become negative after three months of treatment) and in light of the clinical deterioration of the patient, maintaining a conservative approach. The patient's symptoms progressively improved after treatment was suspended.

Autoimmune and neurological involvement in patients on haemodialysis treated with pegylated interferon is an uncommon complication.<sup>1-3</sup> Measurements of auto-antibodies prior to treatment with interferon is a fundamental step for the differential diagnosis of autoimmune complications. Some authors have described an increase in endogenous interferon-alpha during haemodialysis sessions in patients with positive HCV serology (without treatment), which could explain the decrease in viral load produced during treatment.<sup>4</sup> However, this supposed increase in interferon could produce a paradoxical effect, as in our case, and activate the complement system, which could in turn be related to the intra-dialytic lumbar pain.

Paralysis of the 6<sup>th</sup> cranial nerve is not a common occurrence in the context of thyroid orbitopathy.<sup>5</sup> In our case, involvement of the peripheral nervous system and the normal aspect of the external extra-ocular rectus muscle leads us to believe that the peripheral nervous system involvement was the cause of the squinting. Several cases have been published of patients not on haemodialysis who were treated with pegylated

interferon and suffered paralysis of the 6<sup>th</sup> cranial nerve. The induction mechanism for the involvement of the 6<sup>th</sup> cranial nerve stemming from treatment with interferon is still not understood. The treatment option for many of these cases described was corticosteroids.<sup>6-8</sup>

Our objective in presenting this case was not to alarm the medical community regarding the complications inherent to the treatment of patients on haemodialysis with interferon, but rather to alert the readership as to the less common and late adverse effects that the nephrologist might be the first to notice.

### Conflicts of interest

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

1. Gordon CE, Uhlig K, Lau J, Schmid CH, Levey AS, Wong JB. Interferon treatment in hemodialysis patients with chronic hepatitis C virus infection: A systematic review of the literature and meta-analysis of treatment efficacy and harms. *Am J Kidney Dis* 2008;51(2):263-277.
2. Wilson LE, Widman D, Dikman SH, Gorevic PDI. Autoimmune disease complicating antiviral therapy for hepatitis C virus infection. *Semin Arthritis Rheum* 2002;32(3):163-73.
3. Pouthier D, Theissen F, Humbel RL. Lupus syndrome, hypothyroidism and bullous skin lesions after interferon alfa therapy for hepatitis C in a hemodialysis patient. *Nephrol Dial Transplant* 2002;17(1):174.
4. Badalamenti S, Catania A, Lunghi G, Covini G, Bredi E, Brancaccio D, et al. Changes in viremia and circulating interferon- $\alpha$  during hemodialysis in hepatitis C virus-positive patients: only coincidental phenomena? *Am J Kidney Dis* 2003;42(1):143-50.
5. Daumerie Ch, Duprez Th, Boschi A. Long-term multidisciplinary follow-up of unilateral thyroid-associated orbitopathy. *Eur J Intern Med* 2008;19(7):531-6.
6. Oishi A, Miyamoto K, Kashii S, Yoshimura N. Abducens palsy and Sjögren's syndrome induced by pegylated interferon therapy. *Br J Ophthalmol* 2007;91(6):843-4.
7. Fukumoto Y, Shigemitsu T, Kajii N, Omura R, Harada T, Okita K. Abducent nerve

paralysis during interferon alpha 2a in a case of chronic active hepatitis C. *Intern Med* 1994;33(10):637-40.

8. Hosogi M, Hasebe S, Matsuo T, Ohtsuki H. Abducens nerve palsy in a case under treatment with systemic interferon. *Rinsho Ganka* 1997;51(7):1357-60.

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## Renal amyloidosis due to hyper-IgD syndrome

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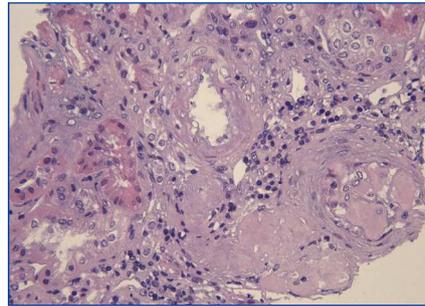
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### Dear Editor,

Amyloidoses are a group of life-threatening diseases characterized by deposition of fibrillar misfolded proteins with an antiparallel beta-sheet structure.<sup>1</sup> Renal Amyloidosis is determined by extracellular deposition of amyloid fibrils within kidney compartments. Clinically evident renal involvement is presented as proteinuria or nephrotic syndrome.<sup>2</sup> Systemic reactive (AA) amyloidosis, leading to renal failure, is a severe complication of most hereditary periodic fever syndromes. We report the occurrence of renal AA amyloidosis causing severe nephrotic syndrome in a young Italian man affected with Hyper-IgD Syndrome (HIDS).

### CASE REPORT

A 29-year-old man of southern Italian ancestry, was admitted to the hospital. Since the first months of life he had experienced characteristic febrile attacks associated with sore throat, myalgias, vomiting and

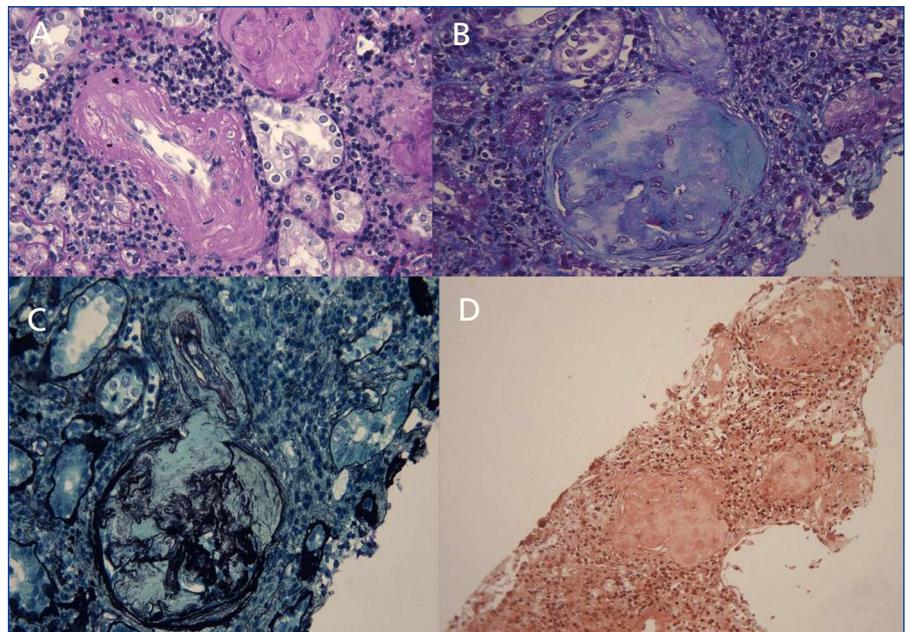


**Figure 1.** Kidney biopsy.

Extensive glomerular deposition of amorphous and pale acidophilic material with involvement of the capillary walls and mesangium and obliteration of some capillary lumens. There is also a deposition of this material in tubular basement membranes, in interstitium and in vessel walls (Hematoxylin and Eosin [H&E], 20x).

diarrhoea. Later the attacks of fever reduced their frequency but in the last year there was an increased frequency of febrile episodes with proteinuria in nephrotic range. On admission his blood pressure was 150/80mmHg and temperature 36.5°C. Heart sounds were clear with regular sinus rhythm and pulse rate was 88

beats/min. Physical examination showed normal findings and no symptoms suggestive of respiratory, abdominal or urinary infection were apparent. Chest radiography and abdominal ultrasonography scan revealed no abnormalities. Laboratory investigations showed proteinuria 9.17g/day, a raised erythrocyte sedimentation rate, a normal C-reactive protein, a total leukocyte count of 12,500/mm<sup>3</sup>, serum amyloid 3.67mg/L, serum IgD 233UI/ml (normal range 0-100), creatinine 1.09mg/dl. Immunological tests and other laboratory parameters resulted negative or within normal limits. Kidney biopsy: among 28 glomeruli, 18 showed a weakly eosinophilic amorphous material infiltrating the mesangium (Figures 1 and 2). After positive Congo red staining, the deposits revealed apple-green birefringence under polarized light, consistent with the presence of amyloid. On immunocytochemistry, the amyloid deposits were negative for antibodies against kappa and lambda chains (Figure 3). Clinical and laboratory findings suggested diagnosis of systemic reactive amyloidosis. The research for MEFV, for Familial Mediterranean Fever (FMF) and TNFRSF1A, for Tumor



**Figure 2.** Kidney biopsy.

This material is only weakly positive for Periodic Acid-Schiff (PAS) (Fig. 2A, 20x), paler than collagen with Goldner Trichrome stain (Fig. 2B, 20x) and appears as negative defect (loss of argyrophilia) with Jones Methenamine Silver (JMS) stain (Fig. 2C, 20x); the glomeruli, tubules, interstitium and vessels stain with Congo red (Fig. 2 D, 10x).