Case Report

Minimal change disease with interferon-beta therapy for relapsing remitting multiple sclerosis

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Abstract

Interferon beta is widely used for the treatment of relapsing and remitting multiple sclerosis. Renal side effects including nephrotic syndrome have been increasingly described with interferon beta treatment. We describe an illustrative case of a patient who developed severe nephrotic syndrome due to minimal change disease in association with interferon beta therapy and showed partial remission following cessation of interferon beta and treatment with corticosteroids.

Keywords: interferon beta; minimal change disease; nephrotic syndrome; relapsing remitting multiple sclerosis

Introduction

Interferon beta (IFN-β) is well established as a standard treatment for relapsing remitting multiple sclerosis (RRMS). The drug is usually well tolerated, but constitutional side effects and autoimmune adverse effects have been reported. Proteinuria has also been reported but is a rare side effect. We report a case of nephrotic syndrome following interferon beta-1a (IFN-β-1a) therapy, for RRMS, and partial remission following drug withdrawal and steroid therapy.

Case

A 44-year-old female with a 4-year history of RRMS was admitted for evaluation of pedal oedema of 3-month duration. She had spasticity involving both lower limbs and required intermittent self-catheterization for bladder spasticity. She fulfilled the diagnostic criteria for RRMS, defined by more than two attacks within 18 months. Subcutaneous IFN-β-1a treatment of 44 mcg thrice weekly was commenced 20 months prior to this admission. Twelve months previously, she also received a course of methylprednisolone for severe disease exacerbation. She had a 6-month history of type 2 diabetes mellitus with no microvascular complications and was on metformin and gliclazide.

There was no past or family history of renal disease. Her blood pressure was 140/90 mmHg. Initial investigations showed creatinine 82 μmol/L, HbA1C 7.0%, serum albumin 24 g/L, total cholesterol 4.9 mmol/L and triglycerides 6.5 mmol/L. Urine examination revealed 10–100 erythrocytes/high power field. No dysmorphic red cells or casts were found. Proteinuria was quantified at 42 g/24 h. ENA, ANA, ANCA and ds-DNA were negative and C3 and C4 levels were normal. Electrophoresis and immunofluorescence for IgG, IgA, IgM, C1q, C3, kappa and lambda light chains was negative. Electron microscopy revealed the extensive foot process effacement characteristic of minimal change disease (MCD) (Figures 1 and 2).

Discussion

IFNs are widely used for the treatment of various malignancies, hepatitis C and multiple sclerosis. INF-β is postulated to act in multiple sclerosis by inhibiting proliferation and activation of T cells. INF-β also inhibits T-cell migration across the blood–brain barrier [1]. Although considered safe, interferon therapy is associated with side effects, especially flu-like symptoms, fatigue and anorexia.
Renal side effects are uncommon, mild and are more frequently described with INF-α. Rare severe manifestations include acute renal failure secondary to acute tubular necrosis or acute interstitial nephritis [2], haemolytic uraemic syndrome [3], focal segmental glomerulosclerosis (FSGS) [4] and MCD. Induction of autoimmunity and autoantibody production resulting in glomerular immune deposition is thought to be the mechanism of renal side effects of INF.

The incidence of transient proteinuria during IFN-β therapy is ~20%. To our knowledge, only four cases of nephrotic syndrome associated with IFN-β treatment have been previously reported. Gotsman et al. [5] described a 52-year-old female who developed nephrotic syndrome 4 months after IFN-β treatment for multiple sclerosis. Proteinuria was found to be 4.6 g/24 h and a biopsy revealed FSGS. Proteinuria resolved with withdrawal of INF alone. Nephrotic syndrome was described in a 39-year-old man with RRMS 22 months after commencing IFN-β.

Renal complications have not been ascribed directly to multiple sclerosis. There exists one case report describing a case of membranous glomerulonephritis and thrombocytopenia in a patient with progressive multiple sclerosis [10]. However, this is likely to be a de novo, sporadic renal condition unrelated to multiple sclerosis. The temporal association with IFN drug therapy in our patient suggests that the severe nephrotic syndrome was most likely due to drug therapy rather than a direct complication of multiple sclerosis.

In conclusion, our case illustrates an uncommon renal complication of IFN-β therapy, and we alert others to be mindful that long-term treatment with IFN-β may cause proteinuria and nephrotic syndrome. Periodic urine analysis for proteinuria should be performed in patients receiving long-term IFN-β therapy for RRMS. Heavy or persisting proteinuria and nephrotic syndrome may warrant a renal biopsy to exclude an underlying primary glomerular disease.

Conflict of interest statement. None declared.

References


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