Case Report

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Journal of Clinical & Experimental Nephrology
ISSN 2472-5056

2018
Vol.3 No.4:18

DOI: 10.21767/2472-5056.100069

Retinal Lesions and Renal Impairment Associated with Interferon β1α Therapy for Multiple Sclerosis: A Case Report

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Received date: September 26, 2018; **Accepted date:** October 22, 2018; **Published date:** October 25, 2018

Citation: Chelioti E, Theodoropoulou E (2018) Retinal Lesions and Renal Impairment Associated With Interferon β1α Therapy for Multiple Sclerosis: a Case Report. J Clin Exp Nephrol Vol.3 No.4: 18. DOI: 10.21767/2472-5056.100069

Abstract

Background: Recombinant interferon β is now the mainstay of maintenance therapy for multiple sclerosis in many countries. Retinal lesions are rarely related with subcutaneous interferon β1α in multiple sclerosis. Interferon nephrotoxicity is also an extremely rare side effect. We report a case of interferon-associated retinopathy and nephropathy in a patient with multiple sclerosis receiving subcutaneous interferon β1α.

Case report: A 42 years old Caucasian female with a history of multiple sclerosis on continuous treatment with interferon β1α, presented with anemia, thrombocytopenia, albuminouria, mild elevation of liver enzymes, renal impairment and sudden hypertension without visual disorders. Ocular fundus exam showed several retinal cotton wool spots indicating interferon-retinopathy and the drug was discontinued. Biochemical and immunological analyses were negative for autoimmune renal diseases. The retinopathy disappeared without specific therapy 2 months after discontinuing interferon β1α and kidney function restored. Interferon β1α resumed 16 weeks after stopping treatment due to multiple sclerosis relapse. On an iterative fundus exam 3 months after resumption of interferon β1α, no further cotton wool spots have recurred. 6 and 12 months later, with the patient on interferon β1α treatment, the ocular fundus was free of lesions and kidney function was within normal range.

Conclusions: In our patient, both complications resolved after drug cessation and the diagnosis of interferon β1α retinopathy and nephropathy was retained due to the lack of any other etiology.

Keywords: Retinal cotton wool spots; Subcutaneous interferon β1α; Multiple sclerosis; Interferon-associated nephropathy

Background

Recombinant Interferon (IFN) β is considered the mainstay of maintenance therapy for Multiple Sclerosis (MS) in many countries. A variety of side effects has been described among which flu-like symptoms; inflamed injection sites and depression are the most frequent. Retinopathy is a well-known adverse effect of interferon-α (IFNα) in patients treated for hepatitis C. On the other hand, retinal lesions are rarely related with subcutaneous interferon β1α in MS. IFNβ1α nephrotoxicity is also an extremely rare side effect. There are only eight reports on multiple sclerosis related IFNβ1α retinopathy. Likewise there is only one case of IFNβ1α associated retinopathy and nephropathy. We present a case of IFNβ1α associated retinopathy and nephropathy and review the literature and clinical properties of these extremely rare adverse effects.

Case Report

A 42 years old Caucasian female with a history of MS (diagnosed 15 years ago), on continuous treatment with subcutaneous IFNβ1α on final dose (44 mcg, 3 times/week) with no relapse for the last 8 years, no previous history of hypertension, heart and renal disease presented dyspnoeic (SO_2=89%), hypertensive (160/100 mmHg), with tachycardia (HR=93/min) and without peripheral oedemas. She suffered of anaemia (HCT=28.7%), thrombocytopenia (PLT=94000), hyponatremia (Na=122 meq/l), hypokalemia (K=3.1 meq/l), mild elevation of liver enzymes (SGOT=49, SGPT=41) and mild renal impairment (Creatinine=2 mg/dl or 176.8 μmol/L, Urea nitrogen=32 mg/dl or 11 mmol/L). The chest CT revealed small pleural effusions with no signs of pulmonary embolism. The echocardiogram was positive for concentric left ventricular hypertrophy and impaired systolic and diastolic function (ejection fraction=45%-50%). Subsequent imaging exploration revealed two kidneys of normal size. After diuretic and antihypertensive treatment the patient's clinical status and laboratory testing was improved except kidney function tests that kept deteriorating (creatinine=3.2 mg/dl or 282.88 μmol/L, urea nitrogen=63 mg/dl or 22.5 mmol/L). The urine analysis revealed albuminouria (total protein=2000 mg/d, 24-h

excretion) and the immunological work up was negative for autoimmune disorders affecting the kidney. An ocular fundus exam was conducted that showed several retinal cotton wool spots. Without any evidence of other possible causes, the administration of IFNβ1α was suspended, since the retinal lesions were suspected to represent IFN-retinopathy. Due to good clinical status and improved kidney function (creatinine=1.7 mg/dl or 150 μmol/L, urea nitrogen=25 mg/dl or 9 mmol/L, total protein=338 mg/day, 24-h excretion) the patient was dismissed and embedded a nephrology and ocular follow up. Two months after drug cessation, with MS on remission, the retinal lesions were resolved and her renal function kept improving, reaching normal levels. IFNβ1α was initiated 16 weeks after cessation due to relapse with muscle weakness and sensory disturbance in the left leg, with a regimen of 50% of the final dose (22 mcg 3 times weekly) gradually titrated to a full dose in a period of one month. 3 months after resumption of IFNβ1α the fundus exam showed no retinal lesions. 6 and 12 months later, with the patient on IFNβ1α treatment, the ocular fundus was free of lesions and kidney function was within normal range.

Discussion

Interferon β treatment can have significant side-effects. Reactions at the injection site are common and can include necrosis. Flu-like symptoms and depression are also common but tend to diminish with time. There is a high prevalence of mainly asymptomatic liver dysfunction associated to INFβ therapy. Other possible side effects include partial reversible polyneuropathy, leukopenia, anemia and suicide [1].

Since the introduction of IFNα therapy for viral hepatitis, retinopathy has been identified as an important adverse effect of IFNα therapy for this disease. Typical ocular lesions include cotton wool spots and retinal haemorrhages at the posterior fundus. Cotton wool spots and retinal haemorrhages may occur alone or together. Two weeks to 3 months after the start of interferon therapy for viral hepatitis retinal haemorrhages and cotton wool spots develop. The incidence of retinopathy depends on the initial dose of interferon. The retinopathy disappears spontaneously during therapy or rapidly after stopping the therapy. Despite the retinopathy, most patients have had good visual acuity.

Sommer et al. [2] described the first case of IFNβ-1b associated retinopathy during treatment for MS. To our knowledge there are only eight cases reported in the international literature [2-10]. Consensus is lacking regarding treatment of IFN-retinopathy in a patient with MS due to its infrequency. In one case IFN-treatment was continued under strict monitoring of ophthalmologic condition, and showed no serious visual deterioration [3]. In contrast IFN was discontinued in other cases and retinopathy subsided without specific therapy [8,9]. In the case described by Sallansonnet-Froment et al. [7] IFNβ1α was discontinued due to serious visual disturbance. Visual disturbance gradually improved and retinal lesions had disappeared by 2 months after drug cessation. In the present case the patient lacked visual symptoms and the retinal lesions were an incidental finding. Cotton wool spots resolved after discontinuation of IFNβ1α within 2 months. Upon restarting IFN on full dose the lesions did not recur.

IFNβ1α associated renal disease has been reported as a rare adverse effect. There are several cases of nephrotic syndrome in patients who had undergone long-term IFNβ treatment for MS. In the ones that kidney biopsies were conducted the common histology diagnosis was membranous nephropathy [10]. There is only one case reported in the international literature with IFNβ associated nephropathy with concurrent retinopathy [9]. In our case the patient presented with renal impairment and albuminouria additionally to the retinal cotton wool spots. Cessation of IFNβ administration resulted in a gradual improvement of renal function that reached normal levels within 2 months.

Conclusions

IFNβ1α associated retinopathy in a patient treated for MS is an extremely rare adverse effect. Cotton wool spots on the fundus seem to be the prominent lesion with or without visual disturbance. Retinal lesions resolved rapidly after discontinuation of IFNβ when chosen in the reported cases. IFNβ1α associated nephropathy is an also rare adverse effect. To our knowledge this represents a rare case of INFβ1α associated cotton wool spots and renal impairment and the first in the English-language ophthalmic literature. Our case supports that both complications resolved after drug cessation and the diagnosis of INFβ1α retinopathy and nephropathy was retained due to the lack of any other etiology.

Conflict of Interest

The authors declare that they have no competing interests.

Source of Financial Support

The authors declare that they have no relevant financial interests.

Authors' Contributions

All authors participated in the review, drafting, and final approval of the manuscript.

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