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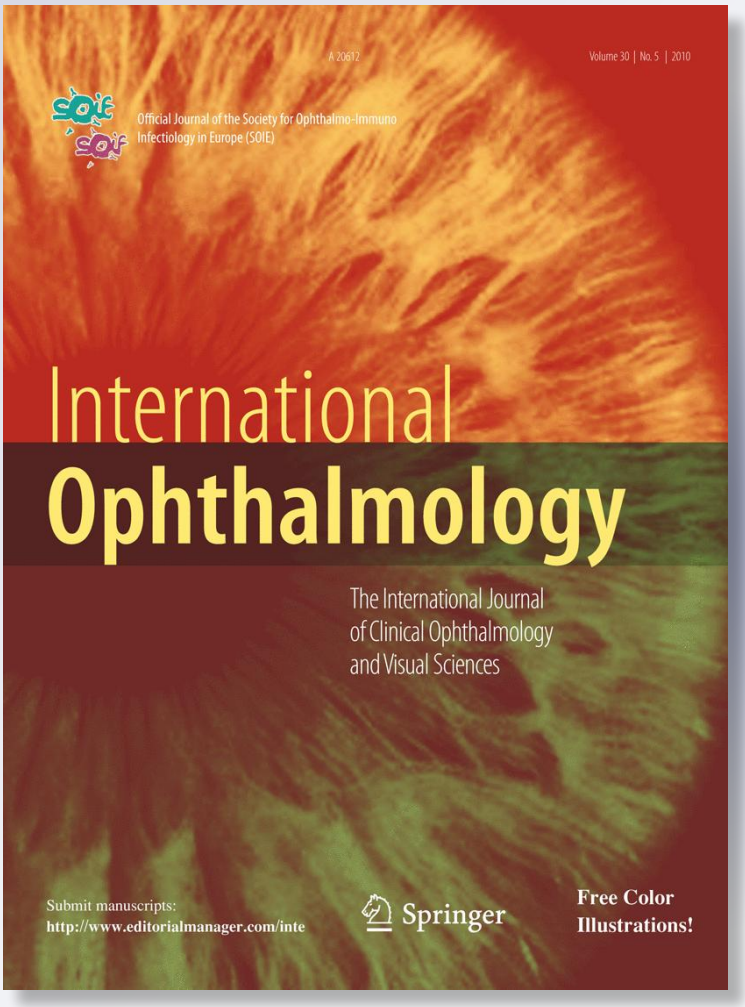

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CASE REPORT

Vogt–Koyanagi–Harada disease occurring during interferon-alpha and ribavirin therapy for chronic hepatitis C virus infection

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Abstract We report a case of Vogt–Koyanagi–Harada (VKH) disease in a 30-year-old patient who was receiving interferon-alpha and ribavirin therapy for chronic hepatitis C virus infection. The intraocular inflammation responded to systemic corticosteroid and mycophenolate mofetil treatment. Physicians should be aware of the association between interferon-alpha and ribavirin therapy for hepatitis C virus infection and the development of VKH disease.

Keywords Vogt–Koyanagi–Harada Disease · Interferon · Hepatitis C

Introduction

Vogt–Koyanagi–Harada (VKH) disease is a rare disease that usually manifests as bilateral panuveitis associated with involvement of the central nervous system, auditory system and skin, at variable levels [1]. The exact cause of the disease is still unknown, but evidence suggests that VKH disease is a systemic autoimmune disease with T-helper type 1 cells mediated immune process directed against one or more antigens found on or associated with melanocytes. Several studies demonstrated that tyrosinase family proteins are the antigens specific to VKH disease [2].

We report a rare case of VKH disease in a patient who was receiving interferon-alpha and ribavirin therapy for chronic hepatitis C virus infection.

Case report

A 30-year-old man known to have hepatitis C virus infection was on treatment with interferon-alpha-2b and ribavirin. Three months after the start of treatment, the patient presented to the emergency room with decreased vision in both eyes. Examination revealed that the visual acuity was 20/40 in the right eye and 20/50 in the left eye. The intraocular pressure was 12 mmHg in both eyes. Slit-lamp examination revealed quite conjunctiva, clear cornea and 3+ cells in the anterior chamber bilaterally. Fundus examination revealed exudative retinal detachment involving the macula and optic disc hyperaemia in both eyes (Fig. 1). Optical coherence tomography (OCT) showed macular detachment bilaterally (Fig. 2). Posterior segment ultrasound confirmed the presence

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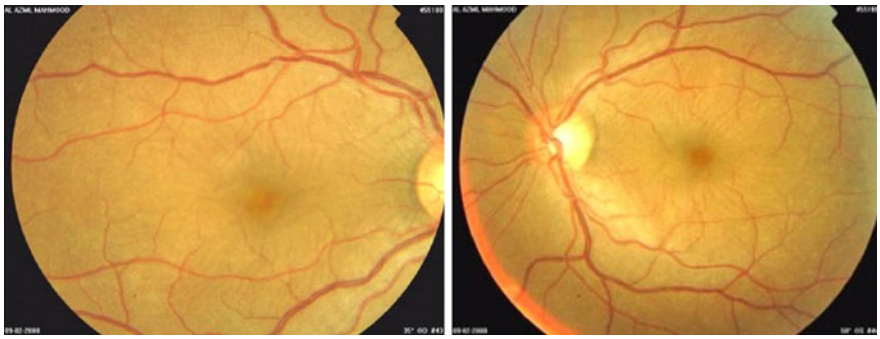

Fig. 1 Fundus photographs showing bilateral disc hyperaemia and exudative macular detachment

of bilateral exudative retinal detachment. Fundus fluorescein angiography showed early multiple pin-point hyperfluorescence at the level of the retinal pigment epithelium and late pooling of dye in the areas of exudative retinal detachment, in addition to optic disc leakage and staining (Fig. 3). Indocyanine green angiography showed multiple hypofluorescent spots in the early and late frames, in addition to fuzzy choroidal vessels. The patient was diagnosed to have VKH disease. Uveitis work-up including: complete blood count with differential, erythrocyte sedimentation rate, electrolytes, blood sugar, blood chemistry, liver function tests, Venereal Disease Research Laboratory test, fluorescent treponemal antibody absorption test, tuberculin test and chest X-ray were negative. The patient was treated with intravenous methylprednisolone 1 g for 3 days, prednisolone acetate drops 1% hourly and atropine drops 1% three times a day. Mycophenolate mofetil 1 g twice a day was added. Oral prednisone 1 mg/kg body weight was started on the fourth day. The patient discontinued interferon-alpha-2b and ribavirin therapy. Six months later, the patient was on prednisolone 10 mg/day and mycophenolate mofetil 500 mg twice a day, and his visual acuity was 20/20 in both eyes. Slit-lamp examination revealed quite conjunctiva, clear cornea, deep and quite anterior chamber bilaterally. Fundus examination showed mild retinal pigment epithelial changes in the macula and flat retina in both eyes.

Discussion

The most common ophthalmologic side effects of interferon-alpha therapy in patients with chronic hepatitis C virus infection are retinal haemorrhages and cotton-wool spots. These complications are benign and show early in the course of interferon therapy, within the first 8 weeks, in approximately 90% of patients [3, 4]. The mechanism of these retinal changes is not known. Sight-threatening ocular complications during interferon and ribavirin therapy is extremely rare. Sène et al. [5] reported two cases of central retinal vein occlusion, one case of central retinal artery occlusion, one case of acute anterior ischemic optic neuropathy and one case of severe hypertensive retinopathy.

To the best of our knowledge, there are only six reported cases of VKH disease in patients using interferon-alpha/ribavirin therapy for chronic hepatitis C virus infection [4, 6–8]. All cases presented with a decrease in visual acuity 3–4 months after starting interferon/ribavirin therapy and the diagnosis was made based on the ocular examination and fluorescein angiography findings. Patients were managed by

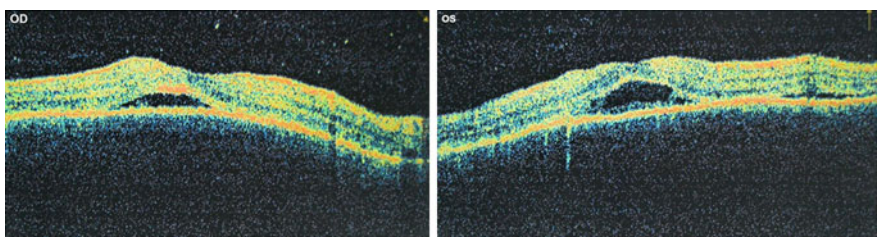

Fig. 2 Optical coherence tomography (OCT) showing bilateral exudative retinal detachment

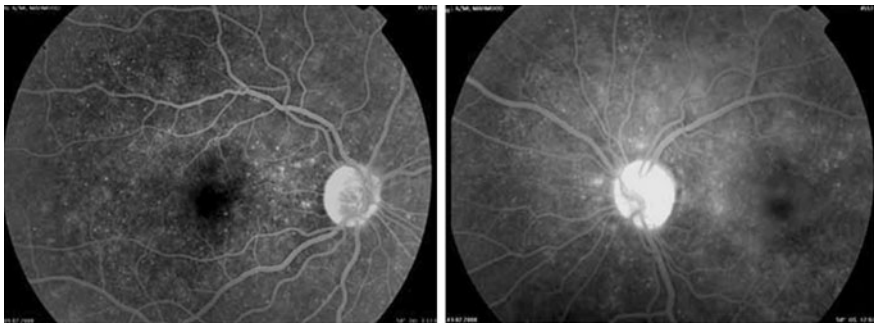

Fig. 3 Fundus fluorescein angiography showing bilateral multiple pinpoint hyperfluorescence at the level of the retinal pigment epithelium and pooling of dye in the areas of exudative retinal detachment. The optic nerve heads show leakage and staining

intravenous methylprednisolone followed by oral steroids and discontinuation of interferon/ribavirin therapy with very good visual outcome. Two cases were steroid-dependent [8]. Our report describes a similar entity to previous reports in terms of presentation, management and outcome.

The aetiology of VKH disease after interferon-alpha and ribavirin therapy in patients with chronic hepatitis C virus infection is unknown. Interferon-alpha and ribavirin therapy seems to exacerbate pre-existing autoimmune conditions, such as rheumatoid arthritis and psoriasis, and can trigger the de novo development of various autoimmune diseases, such as thyroiditis, hepatitis, diabetes, Mooren's ulcer, sarcoidosis, systemic lupus erythematous, haemolytic anaemia, immune-mediated thrombocytopaenia and vitiligo [9, 10]. Interferon-related VKH disease and other autoimmune diseases in patients with hepatitis C virus infection can be due to the immunomodulatory effect of interferon therapy, including enhanced lymphocyte cytotoxicity, increased expression of major histocompatibility class I antigens, production of proinflammatory cytokines and differentiation of antigen-presenting cells which might make individuals susceptible for autoimmune diseases in the presence of triggering factors such as hepatitis C virus infection [4].

In conclusion, there are an increasing number of reports linking interferon-alpha/ribavirin therapy in patients with hepatitis C virus infection and autoimmune diseases, including VKH disease. The possibility that interferon-alpha and ribavirin therapy in patients with hepatitis C virus infection can exacerbate or trigger autoimmune conditions necessitates close follow-up of hepatitis C virus infected patients under interferon-alpha and ribavirin treatment with ophthalmological monitoring.

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