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Relapse of Vogt-Koyanagi-Harada Disease during Interferon- α and Ribavirin Therapy in a Case of Chronic Viral Hepatitis C

Miho Soma Akira Hirata Takamitsu Takahashi
Satoshi Okinami

Department of Ophthalmology, Saga University Faculty of Medicine, Saga, Japan

Key Words

Vogt-Koyanagi-Harada disease · Interferon- α · Chronic hepatitis C virus

Abstract

A 60-year-old woman, who had been diagnosed with and treated for Vogt-Koyanagi-Harada (VKH) disease 17 years before, was receiving pegylated interferon- α and ribavirin therapy for chronic hepatitis C virus. Three weeks after the start of therapy, she complained of visual blurring, eye pain, and an increased hearing loss. Based on a slit lamp and fundus examination, she was diagnosed with a relapse of VKH disease. After discontinuation of the pegylated interferon- α and ribavirin therapy and administration of corticosteroid therapy, her visual acuity returned to 1.0 in both eyes without ocular inflammation, and remained stable thereafter. When interferon therapy is administered to hepatitis C virus patients, those who also have a history of VKH disease must be closely monitored for ophthalmologic complications.

Introduction

Starting in 2000, pegylated interferon- α (PEG-IFN) has been the treatment of choice for chronic hepatitis C virus (HCV) infections. Typical ocular adverse effects related to this treatment include retinopathy. Visual loss is usually absent or limited, and reversible after cessation of therapy. However, severe ocular complications have been reported in a few cases. Here, we report for the first time a patient who experienced a relapse of Vogt-Koyanagi-Harada (VKH) disease during treatment with PEG-IFN and ribavirin therapy for HCV infection.

Case Report

A 60-year-old woman was referred to our department for fundus examination on June 25, 2008, and was scheduled to begin PEG-IFN and ribavirin therapy for chronic HCV infection. She had been diagnosed with VKH disease in 1991 and had been treated for 15 months with both injection and oral steroid therapies (fig. 1a, b). After the initial treatment, no further symptoms or evidence of the disease were observed over the next 17 years. At the time of the examination, she had no symptoms, and her visual acuity was 1.2 in her right eye and 1.0 in her left eye. The fundus of both eyes showed a sunset appearance, but slit lamp and fundus examinations showed no active inflammation. Based on our findings, treatment with PEG-IFN and ribavirin was started.

At 3 weeks after the start of the therapeutic intervention, the patient complained of visual blurring, eye pain, and an increased hearing loss. Her visual acuity was reduced to 0.2 in her right eye and remained at 1.0 in her left. A slit lamp examination disclosed bilateral granulomatous uveitis. A fundus examination revealed bilateral serous retinal detachment without retinal vasculitis (fig. 2a, b). Fluorescein angiography showed multiple leakage of fluorescein dye from the choroid into the subretinal space (fig. 2c, d). Auditory acuity was mildly diminished in both ears. As we diagnosed a relapse of the patient's VKH disease, PEG-IFN and ribavirin therapy was discontinued. We began administration of intravenous pulses of methylprednisolone (1,000 mg/day for 3 days), followed by daily oral corticosteroids, which were then tapered off over time. Two months after the symptoms first appeared, her visual acuity returned to 1.0 in both eyes without ocular inflammation and remained stable thereafter for more than 15 months.

Discussion

Over the last decade, PEG-IFN and ribavirin therapy has become the standard treatment for HCV. IFN- α belongs to the type 1 interferon family, which is involved in the host's natural defense against viruses, bacteria, and neoplasia. IFN- α -treated rats with experimental autoimmune uveitis have been shown to exhibit only minimal disease [1]. Recent publications have emphasized the effects of IFN- α on refractory uveitis, including VKH disease [2]. Although the mechanisms of its efficacy are believed to be multifactorial, they have not yet been well elucidated.

In contrast, several autoimmune disorders, such as sarcoidosis, Mooren's ulcer, Graefe's disease, systemic lupus erythematosus, type I diabetes or rheumatoid arthritis, have been observed during IFN- α and ribavirin therapy. These cases have been attributed to immunomodulatory actions related to the therapy [3, 4]. There have been some reports stating that VKH disease occurs after IFN therapy for HCV. In these reports, the disease was indicated to have emerged 3 months to 2 years after the start of IFN therapy [5–7]. In the current case, however, we identified the relapse of VKH disease at only 3 weeks after starting IFN therapy, even though the disease had been dormant for 17 years.

The immunological activities of IFN, including enhanced lymphocyte cytotoxicity, increased expression of major histocompatibility class I antigens, production of proinflammatory cytokines, and differentiation of antigen-presenting cells, may predispose susceptible individuals to the development of an autoimmune disorder [3–5]. Moreover, IFN- α can cause an immune response shift to T-helper-1-type predominance and alter the expression of histocompatibility class I and II antigens, possibly leading to the development of VKH disease [5, 8]. In addition, administration of IFN- α may lead to the development of VKH disease via an increase in the production of endogenous IFN- γ , and it has been reported that serum endogenous IFN- γ titers are significantly elevated in VKH disease patients [9, 10]. These possible mechanisms may explain how IFN

exacerbates preexisting autoimmune conditions and leads quickly to the relapse of VKH disease, as shown in this case.

In conclusion, when IFN therapy is administered to HCV patients, especially those who have a history of VKH disease must be closely monitored for ophthalmologic complications due to immediate relapse of VKH disease.

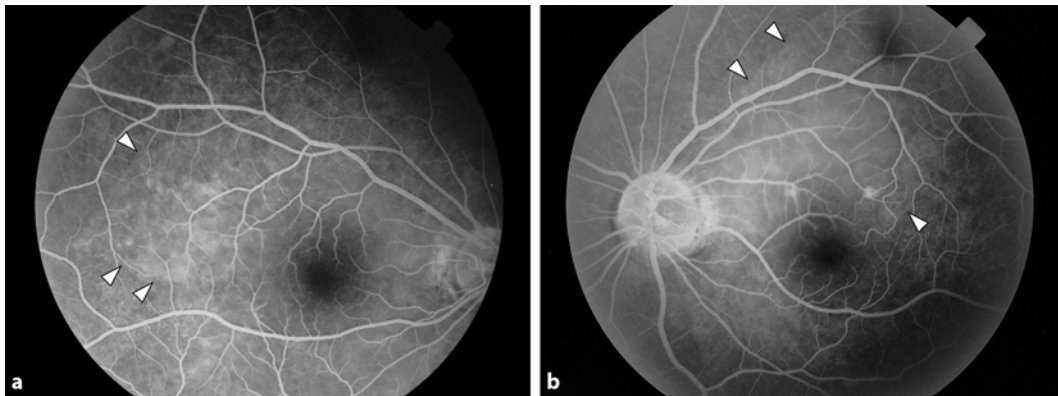


Fig. 1. Fluorescein angiographic features of the patient at the initial onset of VKH disease in April 1991. Fluorescein angiography shows multiple locations of pinpoint subretinal leakage and serous retinal detachment. **a** Right eye. **b** Left eye.

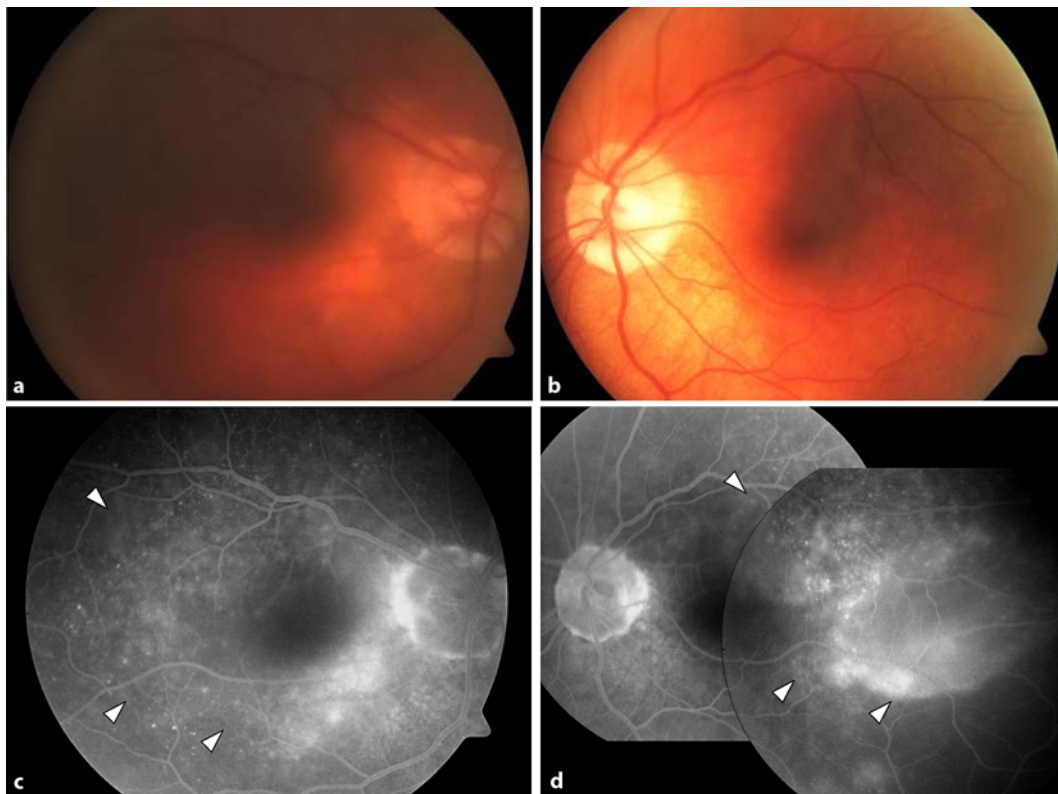


Fig. 2. Fundus photographs of the patient at the second onset of VKH disease in June 2008 after the start of PEG-IFN and ribavirin therapy. Both eyes show a sunset appearance with serous detachment (**a**, **b**). Fluorescein angiography shows multiple locations of pinpoint subretinal leakage corresponding to serous retinal detachment (**c**, **d**). **a**, **c** Right eye. **b**, **d** Left eye.

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