Rare complication of interferon alpha therapy : retinal vein thrombosis

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Key words : interferon-alpha, thrombosis.

Abbreviations

Interferon (IFN), retinal vein thrombosis (RVT), underlying hypercoagulable state (UHS).

Introduction

Interferon (IFN)-alpha therapy is associated with an increased risk of diabetes mellitus and hypertriglyceridaemia and can be an additional risk factor for a hypercoagulable state (1). Diabetes mellitus is well recognized side effect of interferon therapy (2), but thrombosis was reported in some patients with hematological malignancies (3) and a few chronic hepatitis C patients (4-6) whom treated with interferon alpha. There is no reported case about retinal vein thrombosis in chronic hepatitis B patient treated with interferon alpha. We presented an interesting and rare complication of IFN-alpha treatment in this paper.

Case

K-O, 38-year-old male patient was admitted to the hospital with complaint of fatigue. On physical examination, there was no remarkable finding. Blood pressure was also in normal range. Laboratory results were as follow : hemoglobin 12.3 gr/dl, leucocyte 7800/mm^3, polymorphonuclear leukocyte 4600/mm^3, platelet 248000/mm^3, alanine aminotransferase 101 IU/L (5-45), aspartate aminotransferase 64 IU/L (5-42), alkaline phosphatase 240 IU/L (90-260), gamma-glutamyl transpeptidase 45 IU/L (5-85), glucose 100 mg/dl (70-110), cholesterol 250 mg/dl (130-200), triglyceride 190 mg/dl (40-170). Hepatitis B surface antigen, antibody to hepatitis B e antigen and hepatitis B virus DNA (38 pg/ml, by Digene) were positive. Hepatitis B e antigen was negative. Liver biopsy confirmed chronic B hepatitis (histologic activity index : 8, stage 2 according to the Knodell scoring system). IFN-alpha 2a (9 MU/tiw, sc) and lamivudine (100 mg/day, po) were started. At first month of the treatment, glucose level was increased to 251 mg/dl. The other laboratory results were as follows : Hemoglobin 12 gr/dl, leukocyte 4200/mm^3, polymorphonuclear leukocyte 1900/mm^3, platelet 186000/mm^3. Then diabetic diet and an oral antidiabetic drug (Glicilazide 80 mg/twice in a day) were given, and he controlled regularly.

After two months, the patient had blurred vision. Ophthalmic angiography revealed bilateral retinal vein thrombosis (RVT). Afterwards the IFN treatment was discontinued, and hyperbaric oxygen therapy was started. The patient was given 22 hyperbaric oxygen sessions. Oral antidiabetic drug was stopped and insulin was started. Blurred vision improved after treatment. The patient was investigated for underlying hypercoagulable state (UHS). Prothrombin gene mutation and factor V Leiden mutation were absent. Serum levels of protein C, S, antithrombin III and cardiolipin antibodies (Ig G and M) were found in normal range.

Discussion

Retinal vein thrombosis is a relatively common sight-threatening disease that occurs with increasing frequency in hypertensive, diabetic and hyperlipaemic individuals. It is common in patients with an UHS. But we did not detect any UHS in our case. Because of his hematological parameters and physical examination were normal. So, we did not think a myeloproliferative disease. Becker *et al.* (7) hypothesized that IFN-alpha, by changing the cytokine profile experienced by endothelial cells, leads to endothelial cell injury and vascular thrombosis. Also, experimental studies have demonstrated that IFN-alpha induces endothelial cell damage and basement membrane thickening (8). There is some literature that reported ophthalmologic complications with interferon therapy (4-6). Retinopathy is one of the reported side effects of interferon therapy and is characterized by retinal hemorrhages, cotton wool spots and macular edema (6). But retinal vein thrombosis is very rare (9).

In our case ; there was no hypercoagulable state. He had no diabetes mellitus and family history for diabetes mellitus before treatment. He had only hyperlipidemia, but diabetes mellitus manifested at first month of the IFN-alpha treatment. Development of diabetes mellitus during interferon treatment is well recognized complication (10, 11). Insulin dependent diabetes mellitus may

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develop during IFN-alpha treatment by direct cytolytic effect on beta cells or via immune activation of dendritic cells (2). But retinal vein thrombosis is not common during this therapy. So, we did not perform ophthalmologic examination before IFN treatment, and when diabetes mellitus manifested. Also, Cuthbertson *et al.* (6)'s study did not support routine screening for retinopathy in patients treated with interferon. In our case, hyperlipidemia, secondary diabetes mellitus and endothelial damage caused by IFN-alpha, should be considered as facilitative factors for thrombosis. We did not test anti-islet autoantibodies to evaluate the risk of developing insulin dependent diabetes mellitus. We do not know the presence of infraclinical diabetes.

In the light of this knowledge, ophthalmologic examination should perform at least within the first three months of alpha interferon therapy in a patient with manifested diabetes mellitus.

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