Beneficial Effects of Interferon-alpha in a Case with Behçet’s Disease

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Abstract

At the age of 20 years, a Japanese man with recurrent oral aphthae, genital ulcers, folliculitis, erythema nodosum, episodic arthritis and epididymitis was diagnosed as having Behçet’s disease (BD) in 1966. He has had active ocular manifestations of BD since 1990. These symptoms have never abated for a long period of time. A right renal cell carcinoma developed and he underwent right nephrectomy in April 1996. Treatment with interferon-alpha was started from June 1996 as supplemental chemotherapy. No active phase developed during administration of IFN-alpha. We suggest that IFN-alpha may play a role as an immunomodulatory agent in BD.

Key words: renal cell carcinoma

Introduction

Behçet’s disease (BD) is a multisystemic disorder mainly characterised by recurrent oral and genital ulcerations, skin lesions and inflammatory eye diseases. We describe a patient who was successfully treated with interferon-alpha (IFN-alpha) over three years. During IFN-alpha administration no active phase was maintained.

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Case Report

A 53-year-old Japanese man had had recurrent oral aphthae, genital ulcers, folliculitis, erythema nodosum, episodic arthritis, and epididymitis since 1966, and was diagnosed as having Behçet’s disease by the Criteria for Diagnosis of Behçet’s disease proposed by the International Study Group for Behçet’s disease (1). Acute inflammatory attacks of recurrent oral aphthae lasting four or five days twice a month, episodic arthritis lasting three or four days once a week, folliculitis and erythema nodosum once a month, and genital ulcer once or twice a year recurred, indicating a long-term high activity of the disease, and the disease had not abated. At the first diagnosis, he was treated with nonsteroidal antiinflammatory drugs alone, and did not receive corticosteroids or other immunosuppressants. Around 1990, he developed biocular iridocyclitis, retinitis and uveitis, and received subconjunctival injection of dexamethasone (1 mg) at attack. Medication with colchicine (1 mg) was initiated in 1995, but the symptoms did not improve, and diminution of vision was progressive. Therefore, he was admitted to another hospital for the treatment of ophthalmic symptoms in April 1996. At physical examination on admission, vision of the right was at the level of light perception and vision on the left was 0.2. Cells were detected in the binocular anterior chambers on slit lamp examination. Oral aphthae, genital ulcer, folliculitis, nodular erythema, and joint pain were detected. Laboratory data showed an elevated erythrocyte sedimentation rate (ESR) of 63 mm/h, C-reactive protein (CRP) level of 5.5 mg/dl, and immunoglobulin A (IgA) level of 700 mg/dl. Ultrasonography examination on admission revealed a renal cell carcinoma of the right kidney, and he had radical right nephrectomy in May 1996. Because metastases were detected in the excised lymph nodes, intramuscular administration of five million units of IFN-alpha once a week was started as a postoperative supplemental therapy in June 1996. Active lesions of BD disappeared within five weeks after initiation of the IFN-alpha administration. He has had no active phase for three years during continuous IFN-alpha administration. Colchicine (1 mg) was discontinued in August 1997. Adverse effects of IFN, such as fever on the days of IFN administration, and slight variation of escaped hepatic enzymes were observed. Laboratory findings in May 1999 showed human leukocyte antigen (HLA) type was A2, 24; B35, 51; CW3 and ESR, CRP and IgA had returned to normal levels. Although there was no improvement...
Discussion

The cause of BD is still unknown, but it shares features with other autoimmune disorders. Generally immunosuppressants (corticosteroids, cyclophosphamide, azathioprine, cyclosporin A) are effective in the treatment of BD (2). Recently, IFN-alpha, having antiviral, antiproliferative and immunoregulatory properties, has been used in BD treatment. IFN-alpha has been increasingly tried in patients who have not eye disease and has been effective for mucocutaneous manifestations and arthritis (3–5). There have been case reports on five patients with severe refractory eye disease who were successfully treated with steroids, immunosuppressants and IFN-alpha in various combinations (6–8). Kött et al described a patient with retinitis resistant to systemic corticosteroid, in whom six million units of IFN-alpha daily improved the symptoms (6). Feron et al and Durand et al reported that patients with severe ocular involvement were successfully treated with three million units of IFN-alpha three times a week (7, 8). In the present case, treatment with five million units of IFN-alpha once a week has been effective for all symptoms of BD and disease activity was controlled on this regimen. Our observations suggest that IFN-alpha may be a beneficial alternative in BD with severe ocular involvement. On the other hand, Segawa et al reported a patient with chronic myelogeneous leukemia who developed several characteristic features of BD during treatment with the IFN-alpha (9). Studies with larger numbers of patients and a longer follow-up are needed to determine the exact effectiveness, the dose and the role of IFN-alpha. The reason for the effectiveness of IFN-alpha, an immunoactivator has not been clarified.

It is hypothesized that the addition of exogenous factors such as viruses and bacteria to hereditary predisposition to HLA-B51 is the cause of the development of BD. Increasing evidence indicates that cytokines (interleukin (IL)-2, IFN-gamma) produced by helper T cell type 1 (Th1) cells bring about the pathological state of BD (10). As a close involvement of cytokines in the pathology of BD is revealed, modification of the cytokine environment is expected to be specific therapy for BD. Hu et al reported that the development of heat shock protein-induced uveitis was significantly reduced in rats treated with IL-4, which is a cytokine produced by Th2 (11). There have been no reports that indicate the effect of IFN-alpha on the cytokine environment. Although antiviral or antiproliferative effects of the drug can be considered, we suggest that IFN-alpha may play a role as an immunomodulatory...
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agent in BD. We believe that elucidating the action mechanism of IFN-alpha may be a clue in the investigation of the pathogenesis of BD. The exact role of IFN-alpha in the treatment of BD, as well as its mechanism of action, await further study.

References