

# Acute Urticaria Induced by Interferon in a Patient with Chronic Hepatitis B Virus: A Case Report

## KRONİK HEPATİT B'Lİ BİR HASTADA İNTERFERON İLE İNDÜKLENEN AKUT ÜRTİKER: OLGU SUNUMU

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### Summary

Interferons (IFN) are cytokines produced by cells in response to stimulation by certain antigens and infectious agents with antiviral, antiproliferative, and immunomodulatory functions. Here we present a case of acute urticaria developed after first injection of IFN alpha 2a for the treatment of chronic hepatitis B infection. The patient was given, after 15 days of washout period, IFN alpha-2b, and experienced the same reaction more seriously. This is the first report showing that IFN, a drug used for treatment of urticaria, could cause such a reaction.

**Key Words:** Interferon, Urticaria, Chronic hepatitis B

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### Özet

İnferonlar (IFN) bazı antijenler ve enfeksiyöz ajanlarla stimülasyona karşı hücreler tarafından üretilen, antiviral, antiproliferatif ve immünomodülatör etkileri olan sitokinlerdir. Burada kronik hepatit B enfeksiyonu tedavisi için verilen ilk IFN alfa 2a enjeksiyonundan sonra gelişen bir akut ürtiker olgusunu bildiriyoruz. Hastaya 15 günlük "washout" periyodu sonrasında IFN alfa 2b verildi ve aynı reaksiyon daha şiddetli olarak ortaya çıktı. Bu, ürtiker tedavisinde kullanılan bir ilaç olan IFN'un ürtikere neden olduğunu bildiren ilk olgu sunumudur.

**Anahtar Kelimeler:** İnterferon, Ürtiker, Kronik hepatit B

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Interferons (IFN) are cytokines produced by cells in response to stimulation by certain antigens and infectious agents. IFNs have antiviral, antiproliferative, and immunomodulatory functions (1). Here we present a case of acute urticaria developed after injection of IFN alpha 2a and after fifteen days of washout period, IFN alpha-2b.

### Patient Report

A forty year old male patient admitted to our outpatient clinic with fatigue. His hepatic transaminases were high (ALT:185 and AST:86). HBs Ag and HBe Ag were positive. HBV DNA was detect-

ed by polymerase chain reaction in the sera. Liver biopsy was compatible with the features of chronic active hepatitis B. We decided to put him on an IFN (alpha-2a) treatment. The first injection of 9 million units was made under close observation of the physician. Five to six hours later, patient developed a severe itching, and wide spread hyperaemic, urticarial plaques with raised edges (Figure 1). The patient improved with IV antihistaminic and IV prednisolon treatment. IFN alpha 2 treatment was stopped. Two weeks later, we tried other type of IFN hoping that the allergic reactions would not occur. This time we prescribed interferon alpha-2b. But the molecular difference between 2a and 2b did not make any difference. Patient experienced angioedema with severe itching plus significant faintness. After 24 hours of hospitalization he improved again with IV steroid and antihistaminic administration. As the reaction was more serious this sec-

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**Figure 1.** The urticarial plaques were prominent on the anterior surface of the trunk.

ond time, we decided to treat the patient with agents other than IFN, and gave him colchicine and vitamin preparations. He is under follow up now.

### Discussion

Interferon, up to date, has been used for various disorders; especially for some malignancies and chronic hepatitis (2). This is the first case reported in the literature (Medline 1966-1999) that IFN caused acute angioedema necessitating permanent discontinuation of the drug. It is also interesting that IFN alpha 2b, when applied after a washout period, caused the same reaction more severely than the first injection. This implicates a cross allergic reaction between two different types.

Although IFNs have been used for 20 years, skin lesions directly attributed to IFN were seldom. Skin necrosis after a latent period was reported in

various studies with IFN beta for the treatment of multiple sclerosis (3,4). Such an event was not reported for IFN alpha. Among a few well-known skin reactions about IFN alpha are the exacerbation of psoriasis and lichen planus (5,6). On the other hand, the benefit of IFN over histamine mediated events was investigated in studies done for systemic mastocytosis. In one study, six patients with documented systemic mast cell disease were enrolled to determine the possible benefits of interferon alpha-2b and was concluded that treatment with IFN-alpha was associated with a decline in bone marrow mastocytosis and reduced excretion of histamine metabolites (7, 8). Furthermore IFN was tried as a therapeutic agent in some studies for chronic urticaria with a remarkable success (8, 9). Mattesen EL, reported that a 68-year-old woman with a 5 year history of chronic recurrent urticarial vasculitis with angioedema, refractory to conventional treatment including glucocorticosteroids, H1 and H2 blockers, nonsteroidal antiinflammatory agents, methotrexate, hydroxychloroquine, dapsone, azathioprine, intravenous gamma globulin, and plasma exchange, was successfully treated with interferon alpha 2a (9). Kolde et al administered interferon alpha to six patients with urticaria pigmentosa for up to 12 months. Eventually, they stated that although IFN-alpha was highly effective in the control of symptoms, it did not influence the cutaneous lesions of urticaria pigmentosa (10). Considering these data, one could not expect to see an acute angioedema due to IFN alpha-2a. We hoped not to see the same urticarial reaction with IFN alpha-2b and administered it to the patient. But this did not make any difference in the clinical outcome.

Eventually we had to admit that the response to interferon alpha therapy in skin diseases is unpredictable with amelioration in some patients and deteriorating others. A similar contradictory effect of IFN could be seen for cases of colitis. Some reports declared IFNs' benefit in ulcerative colitis, some accused of being causative for it (11,12). This findings indicate that, there is need for further and deeper understanding of all relationships of IFN at molecular level in vivo, in order to predict accurately the clinical outcomes after IFN.

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