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LETTERS AND CORRESPONDENCE

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Immediate or Delayed Therapy With 2-CdA for Hairy Cell Leukemia in a Jehova's Witness?

To the Editor: Couban and Wilson recently reported a Jehova's Witness with pneumonia of unknown ethiology and severe anemia due to hairy cell leukemia, who had immediate therapy with standard-dose-2-chlorodeoxyadenosine (cladribine, 2-CdA), and subsequently due to persistent cytopenia granulocyte colony-stimulating factor and erythropoietin. From my experience with 2-CdA treatment of more than 100 patients with advanced hairy cell leukemia, I find it unlikely that the recovery from cytopenia was accelerated by the addition of the growth factors. Despite the successful outcome of the presented case, I strongly discourage the management, since it is associated with an unacceptable risk of fatal complications, mainly opportunistic infections [1].

In the reported case, the leukocytes started to rise on the fourth week from start of 2-CdA, and the hemoglobin around the sixth week. This is identical to what we found in patients with febrile complications following 2-CdA with no growth factors [1]. In fact, we have also documented that granulocyte–macrophage colony-stimulating factor (GM-CSF) did not accelerate neutrophil recovery when given following 2-CdA in patients with hairy cell leukemia and advanced cytopenia (GM-CSF group n = 12, matched control group n = 15) [2].

More importantly, it is well documented that 2-CdA gives an early decrease in both hemoglobin and neutrophil counts [1,3], in addition to the dramatic fall of T-cell counts [4]. The early fatality rate from 2-CdA in hairy cell leukemia is 3% [2,3], with a much greater risk in patients with unresolved infection of unknown ethiology at the start of treatment [1]. Such patients, as well as patients with severe anemia who refuse transfusions should not be treated immediately with standard-dose 2-CdA. The safest way would be to start with interferon-α (IFN-α), which gives much less of early immune suppression and deterioration of anemia and await recovery from infection and some improvement from cytopenia. 2-CdA should be given as definitive therapy later. Another alternative would be to give low-dose CdA, i.e., 2 mg/m^2 daily for 7 days [5], or 5 mg/m^2 daily for 3 days (Juliusson et al., unpublished observations). This schedule gives the same time to recovery from cytopenia, with less immunosuppression, and probably less deterioration of anemia.

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Photosensitivity and Thrombocytopenia Due to Amitriptyline

To the Editor: A 68-year-old woman, with no familial or personal history, presented with a pruritic erythematous rash over the face, neck, and both hands (Fig. 1). She had received daily doses of 60 mg amitriptyline and 2 mg flunitrazepam for depression for approximately 4 months. Laboratory data revealed a platelet count of 31 × 10^9/l (normal, 110–340 × 10^9/l) and a prothrombin time of 10.6 sec (normal, 12–16 sec). A partial thromboplastin time and Lee-White clotting time were normal. Other blood and urine hematochemical values were within the normal range. Bone marrow aspiration showed megakaryocytic hyperplasia with many young megakaryocytes. Treatments with 40 mg of prednisone daily and fluocinonid cream were started. Within 3 days, the platelets increased to 110 × 10^9/l and the skin rash disappeared.

Patch and photopatch (UVA 5 J/cm^2) testings with amitriptyline (10 and 30% petrolatum) and flunitrazepam (10 and 30% pet.) were performed using Finn Chambers® (Epitest, Ltd., Helsinki, Finland) on Scanpor® tape (Norgesplaster A/S, Oslo, Norway) and were all negative. Ten milligrams of amitriptyline was orally given without sun protection and after 2 days an itchy erythematous rash appeared on the face and thrombocytopenia developed.

Amitriptyline is a widely used tricyclic antidepressant [1]. It is known to produce various cutaneous side effects such as dermatitis herpetiformis-like eruption, hyperpigmentation in synergism with minocycline, eczematous exanthema, vasculitis, or skin blisters [2–4]. Although amitriptyline can also induce thrombocytopenia and thrombocytopenic purpura [5], pho-

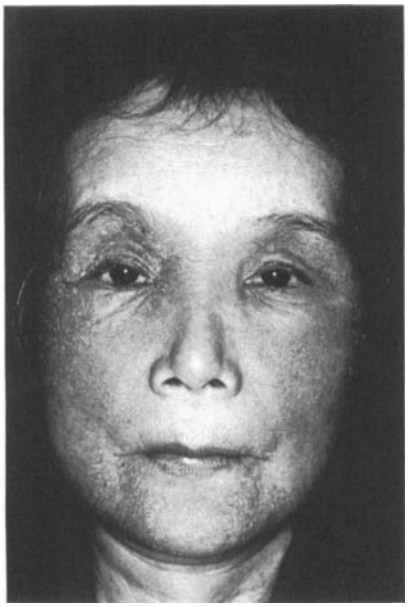

Fig. 1. Erythematous rash on the face and neck.

tosensitivity with thrombocytopenia has not been reported. The mechanism by which photosensitivity and thrombocytopenia are produced is unknown. The possibility that the fall in platelet count represented an idiopathic thrombocytopenia cannot be dismissed [5], however, the temporal relationship between the initiation of the drug and the onset of a skin rash and thrombocytopenia suggests more than a chance association.

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Growth of Eyebrow After Alpha Interferon Administration

To the Editor: Administration of alpha-interferon (α-IFN) is increasingly used in treatment of viral hepatitis and hematological malignancies including chronic myelogeneous leukemia, multiple myeloma, and hairy cell leukemia. Adverse effects of α-IFN include flu-like symptoms and gastrointestinal symptoms. We encountered the rare side effect of α-IFN in a patient with growth of the eyebrows.

A 57-year-old male was diagnosed with multiple myeloma in March 1933. Radiographic examination revealed punched-out lesions of the skull, tumor of the sternum, fracture of the ribs and throacic veretebrae. Hematological examination revealed: Hb 6.3 g/dl, platelet $8.3 \times 10^4/\mu l$, WBC 4,300/μl. Biochemistry revealed: total protein 14.7 g/dl, albumin 2.8 g/dl, IgA 10,980 mg/dl, κ. Bone marrow aspiration revealed 100% of myeloma cells. The patient was in stage III. He was treated with three courses of VAD (vincristine, adriamycin, and dexamethasone) chemotherapy with simultaneous administration of interferon alpha-2b, 300 MU/day. Radiation therapy was performed for the sternum tumor. Bone pain decreased, IgA level decreased to 1,360 mg/dl, and bone marrow plasma cells decreased to 7.6%. The patient was discharged and daily administration of α-IFN was continued. The patient was hospitalized again in September 1994 since IgA level increased to 5,000 mg/dl and bone marrow aspiration revealed 27.6% myeloma cells. Three more courses of VAD chemotherapy were administered and α-IFN was continued thereafter.

Growth of the eyebrows was noted approximately 3 months after administation of α-IFN was started. The eyebrow hair fell out soon after each course of chemotherapy, but grew again soon after administration of α-IFN, and maximum length was approximately 10 cm (Fig. 1).

This is the first reported case of eyebrow growth due to α-IFN. Pathogenesis of eyebrow growth due to α-IFN is unknown. There have been a few reports of the eye lash growth [1,2]. In a case, cimetidine, administered with α-IFN, was considered the causative agent [1]. However, in our case, no other drugs were co-administered with α-IFN. There is also a report of the growth of scalp hair [2]. In our case, only eyebrow growth was observed.

In a case of Crow-Fukas syndrome due to plasma cell dysclasia, manifestation of hirsutism was observed [3]. However, in our case, multiple myeloma was well controlled.

Androgens had been reported to have paradoxically different effects on human hair follicles depending on their body sites [4]. Androgens stimulate hair growth such as beard and pubis, have little effects on protective hair such as those of the eye lash, but can cause regression or balding of the scalp hair. Our case might not be related to androgen metabolism since the eyebrows grew.

The immune system of the hair follicle may play a role in hair growth. Alpha-IFN not only acts on T-cells, but also on antigen presenting cells such as macrophages, and these cells may regulate hair growth via the release of cytokines such as γ-IFN and tumor necrosis factor [5]. There is additional evidence that the alteration of the immune system of the hair follicle affects hair growth. Defective monocyte/macrophage function, which significantly diminishes production of tumor necrosis factor α by these cells, has been demonstrated in patients with alopecia universalis [6]. One of the well-established side effects of the immunosuppressive agent cyclosporin A is hirsutism [7], and the primary action of this drug is interference with the production of cytokines such as interleukin-2 and

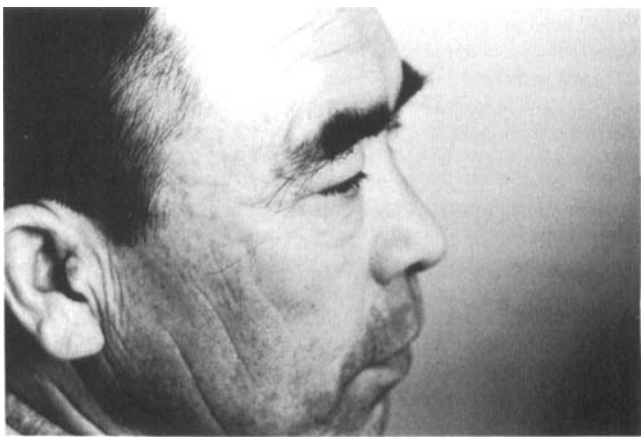

Fig. 1. Growth of eyebrow in a patient receiving alpha interferon.