Dideoxyinosine-Associated Ofuji Papuloerythroderma in an HIV-Infected Patient

M. Just
J.M. Carrascosa
M. Ribera
I. Bielsa
C. Ferrándiz

Department of Dermatology, Hospital Universitari Germans Trias i Pujol, Universitat Autònoma de Barcelona, Badalona, Spain

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Ofuji papuloerythroderma (OPE) is characterized by a widespread pruritic eruption of fixed erythematous papules producing an erythro-derma appearance [1]. A relationship to malignancies and infections has been reported [2, 3]. We report a young patient with AIDS who developed – after starting treatment with dideoxyinosine (DDI) – a widespread cutaneous eruption consistent with the diagnosis of OPE.

A 31-year-old man presented with a 10-month history of an itching skin eruption. He had been seropositive for human immunodeficiency virus (HIV-1) and chronic hepatitis C virus 4 years before. Since then, the patient has been on dapsone, pyrimethamine and folinic acid treatment. One month before the onset of the rash, treatment with 2',3'-DDI, 200 mg/12 h, had been introduced. The rash began symmetrically with erythema and hyperkeratosis on the palms and soles. Five months later, an erythematous rash with pruritic red flat papules appeared on the trunk, which spread progressively over the entire skin surface sparing the head, flexures and body folds, giving to the skin a cobblestone appearance. The mucous membranes were uninvolved. There were some palpable axillar and inguinal lymph nodes. A routine full blood count was normal, except for a lymphopenia with 0.040 × 109 CD4/1, without eosinophilia or abnormal titers of IgE; liver and kidney function tests were also normal. Chest X-ray, total-body bone scanning and bone marrow biopsy showed no abnormalities. A computed tomography scan of the chest and abdomen showed enlarged axillar, inguinal, paraaortic and infrarenal lymph nodes, and hepatosplenomegaly. Histologic examination of a flat papule revealed granulomatous dermatitis with a perivascular and periadnexal lymphohistiocytic infiltrate (CDS) with eosinophils and occasional multi-nucleated giant cells and Langerhans cells. ß-TCR gene rearrangement studies did not show monoclonality proliferation. Histology of an inguinal lymph node showed dermatopathic lymphadenitis. Treatment with DDI was stopped, and after 2 months of PUVA...
therapy (cumulative dose of 69 J/cm²) complete clearing was obtained. Up to date, 2 years later, the patient is alive without cutaneous lesions suggesting OPE. Papuloerythroderma was first described by Ofuji in 1984 as a pruritic chronic dermatosis characterized by pruritic solid papules and erythroderma-like lesions resulting from their confluence, which characteristically spares the face and body folds [1]. Its histology is not specific and usually consists of a dense inflammatory cell infiltrate composed of lymphocytes, histiocytes, eosinophils and Langerhans cells around the blood vessels. Lymphadenopathy, eosinophilia, lymphopenia and elevated IgE levels may associate the eruption [4]. Its etiopathogenesis remains unknown. Lymphomas and visceral tumors, such as gastric and lung cancers as well as HIV-infection and tinea corporis have been found to be associated with OPE [2, 3, 5-9]. Characteristically, all reported cases occurred in elderly people. These facts led several authors [10-12] to the conclusion that OPE could be a peculiar pattern of expression of several inflammatory dermatoses in elderly people more than a disease per se. The present case, which started 1 month after the introduction of DDI therapy and occurred in a young man, raises new questions about the etiopathogenesis. The complete clearing obtained after the drug withdrawal without recurrence 2 years later, in addition to the presence of eosinophils in the cutaneous infiltrate, suggests that OPE could also be a peculiar form of drug reaction [10]. We think that the dose of 69 J/cm² of PUVA was probably too low to induce the resolution of the rash.

Contrary to previous observations [3, 8], we do not think that HIV-related OPE must be considered an ominous sign since our patients is still alive 2 years after the diagnosis. This case supports the hypothesis that OPE must be considered a nonspecific pattern of cutaneous reaction related to multiple causative factors, such as neoplasms, infections and probably drugs too, which may occur at any age.

References

Letters to Dermatology
Chemotherapy in HIV-Infected Patients with Kaposi’s Sarcoma

Marc Pechère
Clinique de Dermatologie, Hôpitaux Universitaires de Geneve, CH-1211 Geneva 14 (Switzerland),
Tel. +41 22 372 9423, Fax +41 22 372 9470

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Plettenberg et al. [1] suggest that chemotherapy for Kaposi’s sarcoma increases the risk of opportunistic infection in HIV-infected patients. They conclude that the probability of an
increased risk of opportunistic infections should be taken into account when considering systemic chemotherapies. Several new elements should certainly moderate this conclusion. First, this study was conducted before the era of modern antiretroviral strategies. Combined therapies with protease inhibitors have resulted in a profound and persistent decrease in HIV RNA plasma levels and reduced morbidity and mortality even in very immuno-suppressed patients [2]. Furthermore, regression of Kaposi’s sarcoma following treatment with protease inhibitors has been reported by several groups [3]. In the study of Plettenberg et al. [1], patients were mainly treated with zidovudine monotherapy which is not recommended any more [4]. Thus, the observations of this trial can certainly not be transferred to patients treated according to current guidelines [4].

Second, we have recently shown that systemic antitumoral chemotherapy did influence neither HIV RNA levels nor CD4 cell counts [5]. Furthermore, none of our patients developed any opportunistic infection. Thus, these patients were safely treated simultaneously with potent double or triple combinations of antiretroviral agents and antitumoral chemotherapies without significant toxicity. The same obser-

We agree with Pechère and Rutschmann that improved antiretroviral therapy significantly influences the course of HIV infection. Corresponding to recent published studies we observed in our outclinic department a decrease in AIDS-defining events of more than 50% during the last 18 months. We believe that this is a result of the improved antiretroviral therapy, especially the use of protease inhibitors. On the other hand, it should be considered that even today a marked number of patients develop opportunistic infections and that generally patients with advanced Kaposi’s sarcoma have a poor prognosis. The data of the study published by Rutschmann et al. [1] described viral load and CD4 cell counts before and 1 week after chemotherapy for 10 patients with Kaposi’s sarcoma. The study had no control group and the period of observation was only 1 month. In our prospective trial, the clinical courses of 35 HIV-infected patients with Kaposi’s sarcoma treated with chemotherapy were compared with courses of 35 matched-pair patients without chemotherapy. The observation period was 6 months. We focused on clinical markers and observed that chemotherapy was associated with an increased risk of opportunistic infections (11 vs. 5). We did not find any influence of chemotherapy on the course of CD4