Photosensitivity due to Ampiroxicam

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Key Words

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Piroxicam is known to induce photosensitivity. Ampiroxicam has been developed as an ethoxycarbonyl ether prodrug of piroxicam. We describe here a case with photosensitivity due to ampiroxicam.

An 84-year-old woman was seen in July 1996 with pruritic and well-delineated erythema and papules on sun-exposed areas that had started 4 days before. She had no history of photosensitivity. She had started taking ampiroxicam (Flucam®, Toyama Chemicals Co. Ltd., Tokyo, Japan) 13.5 mg b.d.s. orally because of arthritis of both knees 7 days before. There were no abnormal findings on hematological examination, blood chemistry or urinalysis, including porphyrins of peripheral erythrocytes and urine. Histological findings of erythema on the right forearm demonstrated intercellular edema and perivascular lymphohistiocytic dense infiltration. We performed a screening phototest, as described before [1], with a Dermaray Model M-DMR-1 (Eisai Co. Ltd.) as a light source [2, 3] 3 months after she had stopped the drug. The UVB minimal erythema dose for this patient was normal (50 mJ/cm²), and irradiation of 13.5 J/cm² for UVA elicited no response, suggesting that photosensitivity of the patient had become normal. Patch and photopatch tests were made with ampiroxicam and piroxicam (10, 1 and 0.1% in petrolatum). Ampiroxicam (10 and 1% in petrolatum) and piroxicam (10, 1 and 0.1% in petrolatum) with UVA irradiation (4.5 J/cm²) on photopatch test showed erythema 1 and 2 days after irradiation. Patch tests with thiosalicylic acid (1 and 0.1% in petrolatum) and thimerosal (0.05% in petrolatum) were positive 2 days after application, while a patch test with mercuric chloride (0.05%) was negative. Patch and photopatch tests with ampiroxicam and piroxicam in 6 normal subjects showed no response 2 days after application or 1 day after irradiation. Ampiroxicam, a prodrug of piroxicam, has been in use since 1994 as a nonsteroidal anti-inflammatory drug. Inactive ampiroxicam is hydrolyzed to active piroxicam by an intestinal carboxyesterase during absorption through the intestinal wall [4]. Our case and 2 reported cases

[5, 6] with photosensitivity due to ampiroxicam showed a positive photopatch test in which irradiation was performed after 2-day closed patch testing, indicating that 2-day application was appropriate for ampiroxicam. Kurumaji [5] suggests that the positive photopatch test is due to conversion of ampiroxicam to piroxicam in the skin. However, we have postulated another hypothesis, i.e. that UVA irradiation of ampiroxicam could produce a similar photoproduct to that from piroxicam, because the carboxyesterase is specifically located in the intestine [4]. Piroxicam-induced photosensitivity is related to contact sensitivity to thimerosal and thiosalicylic acid [7-11]. All 3 cases with photosensitivity to ampiroxicam show positive patch tests with thimerosal and thiosalicylic acid, indicating a common pathogenesis in photosensitivity due to piroxicam and ampiroxicam.

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- Dideoxyinosine-Associated Ofuji Papuloerythroderma in an HIV-Infected Patient
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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 0.040×10^9 CD4/ 10^9 , 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. β -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/cnr) 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 patient 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.

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