DISCUSSION

Juvenile xanthogranuloma has been described in adolescents and young adults (5). In this setting, the entity may present as isolated or multiple lesions. Multiple lesions are frequently irregularly scattered in distribution. Both of our patients presented with a localized clustering of papules. This agminated appearance, a finding which initially led to some diagnostic confusion, has not been well described in the literature. Recently, the occurrence of coalescing papules was described on the nape of the neck of an infant (6). The authors suggested the term "clustered juvenile xanthogranuloma" for this entity. We report 2 additional cases occurring in adults. The presence of alopecia mucinosa, surrounding induration and satellite papules extending in a linear array from the tumor were additional worrisome clinical features in one of the patients. Histologically, juvenile xanthogranulomas are characterized by nodular dermal infiltrates, composed primarily of histiocytes, with foam cells and multinucleated and Touton-type giant cells. The infiltrate may be admixed with lymphocytes, neutrophils and eosinophils. A previous study of juvenile xanthogranulomas noted that foam cells and giant cells may not always be present in these lesions and are not requisite for diagnosis (7). Follicular mucinosis was observed in one of our patients, and this has not previously been reported in xanthogranulomas. Electron microscopy supported the diagnosis of xanthogranuloma and was helpful in excluding histiocytosis X.

These 2 cases provide additional clinical and histological features which may occur as part of the spectrum of juvenile xanthogranulomas and should not be mistaken as signs of malignancy.

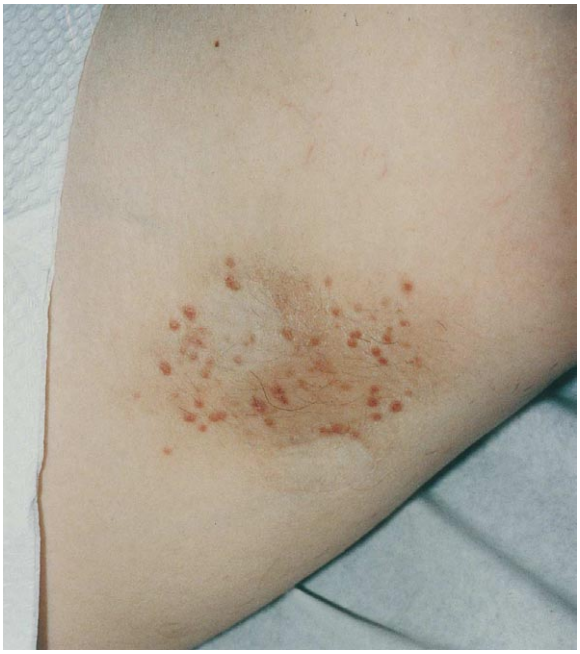

Fig. 2. A multinodular plaque is present on the left inner thigh.

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Ibrahim A. Tangoren[1], Jeffrey M. Weinberg[2]*, Tatanya Humphreys[1], George F. Murphy[1], David J. Margolis[1] and Elizabeth M. Spiers[1]
Departments of Dermatology, [1]University of Pennsylvania School of Medicine, Philadelphia, PA, and [2]New York Medical College-Metropolitan Hospital Center, New York, NY, USA
*Metropolitan Hospital Center, Department of Dermatology, 1901 First Avenue, New York, NY 10029, USA.

Fixed Drug Eruption Due to Melatonin

Sir,

Melatonin is a hormone synthesised by the pineal gland. Its secretion is principally controlled by the prevailing light-dark environment, and for this reason it is called the "hormone of darkness" (1). It has recently been synthesised in the laboratory, and the oral form is now available for investigational use.

The physiological role of melatonin in humans is still unknown. It has been hypothesized that this hormone has an anticancer activity and is a good treatment for some mental diseases, sarcoidosis, rheumatoid arthritis, AIDS, insomnia and headache. It also seems to delay or prevent ageing ("pill of youth"). The most satisfying results with exogenous melatonin have been obtained for jet lag syndrome (2, 3), delayed sleep-phase syndrome (4) and some kinds of chronic insomnia.

Here we present two cases of fixed drug eruption of the genitalia due to melatonin.

CASE REPORTS

A 35-year-old man was referred to our department to evaluate the presence of itching, burning and sharply marginated, erythemato-

vesicular plaques on the glans. Physical examination also showed well-demarcated similar erosions, 2–3 cm in diameter, on the shaft.

The anamnesis revealed that during a business trip in the U.S.A. the patient had purchased "Nature's Bounty Natural melatonin" in order to prevent jet lag syndrome. These tablets contain 3 mg of melatonin and also magnesium stearatum, stearic acid and silica.

Furthermore, the anamnesis revealed that the patient used to take these pills at the dosage of one pill a day every time he went abroad and that he had experienced an episode similar to the one observed by us 4 months earlier.

In the same period we observed another businessman, 42 years of age, who presented a well-marginated, round, 4 cm in diameter, erosive plaque on the ventral surface of the shaft. In this case too fixed drug erythema developed after the beginning of a treatment with "Nature's Bounty Natural" for preventing jet lag.

In both patients we performed a peroral provocation test, consisting of administration of 1 mg of pure melatonin, supplied by our hospital pharmacy. The patients looked for any reaction over the next 24 h. Six to 8 h after taking the melatonin, plaques appeared in both patients in the previously affected sites, accompanied by a burning sensation. The lesions disappeared within 10 days without any sequelae.

Since the patients refused to perform an open test on the previously involved genitalia skin, melatonin powder in ethanol, at a concentration of 10%, was applied to normal skin of the back, and the patients were followed up for 24 h. In both patients the results were negative.

DISCUSSION

The clinical diagnosis of fixed drug eruption is usually easy. Although oral provocation is usually a safe method for in-patients, there is always, however, a potential risk of anaphylaxis or severe cutaneous reactions. Unfortunately, challenge testing with the suspected drug is still the only reliable method; in fact, attempts to demonstrate the specific causative agent with a patch test on the affected skin have so far been unsuccessful. When a patch test is performed at the site of such a lesion, if anatomically possible, a positive response occurs only in about 30% of patients.

In the U.S.A., melatonin is an over-the-counter drug, which can be found in any supermarket or drugstore. Even though both of our patients purchased the same brand of melatonin, we believe that this was most likely a coincidence.

In Europe many countries such as the U.K., Switzerland, France and now also Italy have blocked the uncontrolled sale of melatonin.

We are unaware of any other cases of fixed drug eruption due to melatonin in the literature. The widespread use of melatonin all over the world has led us to report these two cases, in order to inform physicians that this hormone too can be included among drugs responsible for fixed drug eruption. Intake of this drug should therefore be investigated in the anamnesis.

We believe, in fact, that in the future there will be many new cases of drug eruptions due to the use of melatonin, since it is the new fashionable drug and is easy to purchase, especially in the U.S.A.

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F. Bardazzi, F. Placucci, I. Neri, A. D'Antuono and A. Patrizi
Department of Dermatology, Bologna University, Via Massarenti,1, IT-40138 Bologna, Italy.

Rosacea Fulminans with Extrafacial Lesions

Sir,

Rosacea fulminans, previously called pyoderma faciale, is a rare conglobate, nodular disease reported to be restricted to the face, only occurring in women (1). The condition responds to topical and systemic corticosteroids, unlike ordinary rosacea. Here we present an unusal case conceived as rosacea fulminans with extensive extrafacial lesions.

CASE REPORT

The patient was a 35-year-old woman with rheumatoid arthritis, who had been treated with oral methotrexate 10 mg weekly for 2 months. She had no history of skin disease. In April 1995 she developed erythema and papulo-pustules on her left cheek. Her rheumatologist stopped the methotrexate treatment and gave her oral prednisolone, decreasing from 30 mg/daily to 5 mg/daily during the next 2 weeks. The lesions spread to the other cheek, with gradual aggravation of the eruptions. From the beginning of May she was treated with tetracycline 1 g daily for rosacea by a dermatologist. In the next 5 days she considerably worsened, with exudative exanthema, lesions on the trunk and fever, 38°C. At hospitalization in the Department of Dermatology her face and chest were covered by oozing crusts, erythema and papulo-pustles (Fig. 1A). The backs of her hands showed multiple papulo-pustules and erythema (Fig. 1B). There were fewer, but the same type of lesions on the flexor sides of both arms and on the thighs. The oral and the genital mucosa were unaffected. Treatment was started with saline-soaked dressings on the face. Triamcinolone acetonide cream was applied twice a day to her body. Acyclovir and dicloxacillin were given orally until negative microbiological tests were received and tetracycline was again started up. Prednisolone 5 mg daily was continued during hospitalization. The CRP and the sedimentation rate were raised and there was leukocytosis (27,700 WBC/mm^3) with neutrophilic granulocytosis (23,600 cells/mm^3). All the other laboratory investigations were within the normal range. PCR examinations were negative for both varicella zoster and herpes simplex. Bacteriological investigation of the content of the pustules was negative. Histopathological examination showed superficial pustular folliculitis and *Demodex folliculorum* were not seen. The temperature normalized and the eruptions began to remit after 2–3 weeks. When discharged, the patient had erythema and a few papulo-pustules in the face; she was still receiving