Childhood-onset pityriasis rubra pilaris treated with methotrexate administered intravenously[1]

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Generalized pityriasis rubra pilaris developed in a male infant at the age of three weeks. He was treated at the Cleveland Clinic from the age of seven to 24 years, when he was lost to follow-up in 1981. His incapacitating disease stubbornly resisted many forms of therapy, including oral methotrexate, but responded satisfactorily to intravenous methotrexate given once every two weeks. Five attempts to withdraw the methotrexate resulted in prompt relapse into generalized, scaling erythroderma, accompanied by severe depression with suicidal tendencies. During the five years that he took intravenous methotrexate the patient had no discernible ill effects from the drug.

Index terms: Methotrexate • Skin, diseases
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Pityriasis rubra pilaris (PRP) is a rare cutaneous exfoliative disease characterized by follicular papules and scaling psoriasiform plaques. Of the two basic types, the acquired type has no apparent familial basis and occurs when an individual is middle aged.[1] This form tends to resolve in one to three years, and relapses are uncommon.[2] The childhood type is often hereditary and occurs shortly after birth or during early youth.[3] Redness of the face and seborrheic dermatitislike scaling of the scalp are the earliest signs. This form of PRP tends to persist throughout life.[4]

Experience with childhood-onset PRP is usually minimal and treatment is often difficult. We report a case of childhood-onset PRP treated with methotrexate administered intravenously for five years to control the disease. Although only rare cases require such drastic measures, it may be helpful to have such an alternative treatment when encountering particularly resistant cases.

Case report

A 24-year-old man was seen at the Cleveland Clinic with nonpruritic scaling plaques on the legs, trunk, face, scalp, and hands that had been present since he was three weeks old. The condition was not associated with seasonal variations. The family history revealed that the mother of the patient had a condition suggestive of PRP from birth until she was four years old. A 19-year-old brother and a 20-year-old sister had psoriasis; however, three other siblings and the father of the patient were normal. An examination revealed generalized, irregularly shaped erythematous scaling plaques with sparing of the intertriginous areas. The scalp showed moderate scaling. The face demonstrated a fiery red erythema with slight scaling and a marked bilateral ectropion. Follicular papules were present on the dorsal aspects of the fingers and in some scaling plaques in other areas. A few areas of normal skin (skip areas) were present on the back, chest, and extremities (*Fig. 1*).

Laboratory studies. The following laboratory studies were negative or within normal limits: complete blood count, fasting blood sugar, partial thromboplastin time, serum glutamic oxaloacetic transaminase, thymol turbidity, creatinine clearance, lactic dehydrogenase, serum carotene, VDRL, serum vitamin A level, uric acid, alkaline phosphatase, urinalysis, and prothrombin time. Total bilirubin levels were elevated at 2.0 mg/dl (normal, 0-1 mg/dl). Cephalin flocculation was 2+ after 48 hours. A chest roentgenogram was normal. Liver biopsy results revealed a "mild fatty change."

Histopathology. Results of skin biopsy from an involved area on the forearm showed hyperkeratosis; follicular plug-

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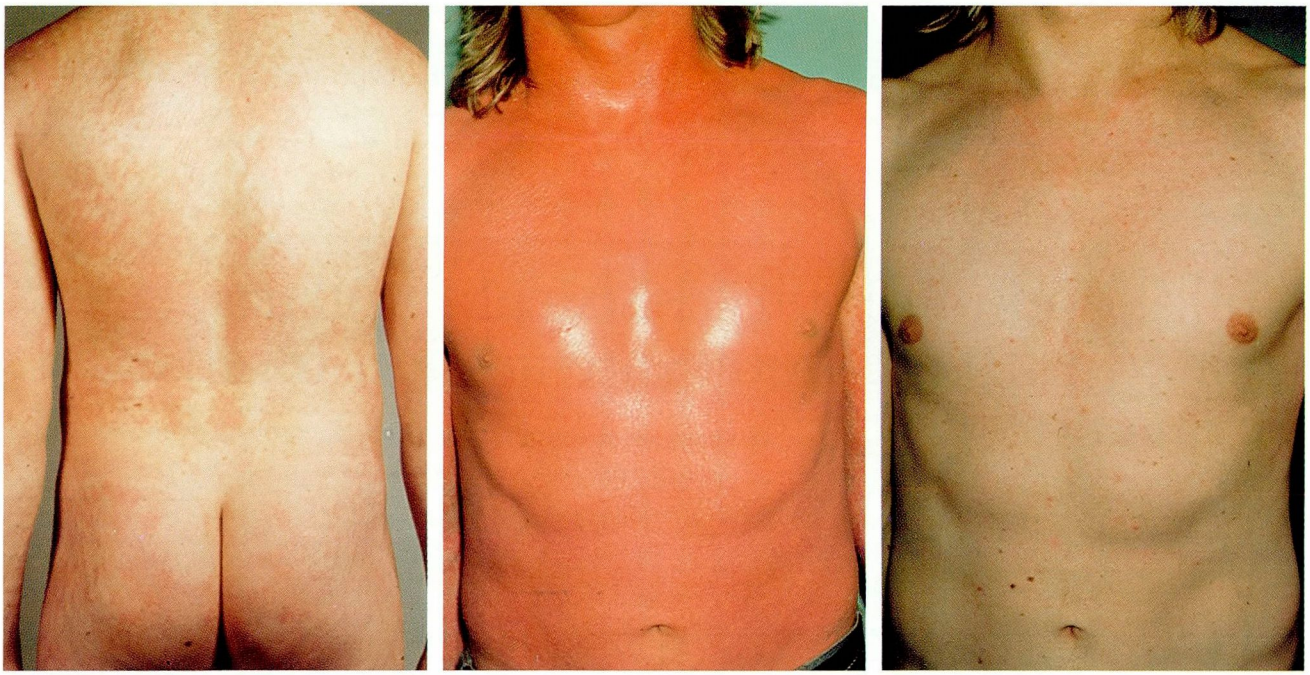

Figure 1. Erythematous scaling patches and plaques on the back of the patient with childhood-onset PRP. Note the typical clear areas (skip areas) of normal-appearing skin.

Figure 2. The patient's PRP had evolved into this generalized erythroderma before intravenous administration of methotrexate was prescribed.

Figure 3. The patient's PRP was maintained in this condition for five years with methotrexate (30–50 mg) given intravenously every one to three weeks.

ging; moderate, irregular acanthosis; focal perifollicular parakeratosis; and a mild upper-dermal perivascular mononuclear inflammatory infiltrate.

Clinical course. The disease gradually worsened and became increasingly resistant to treatment. Fifteen hospitalizations were necessary for treatment from 1964 to 1976. Many unsuccessful attempts included oral administration of vitamin A (500,000 units/day), topical vitamin A, topical and systemic corticosteroids, crude coal tar, and ultraviolet therapy. Because of the generalized erythroderma, the patient was often depressed and suicidal during these periods and was totally incapacitated for school attendance or work.

The patient was given mycophenolic acid on a trial basis for several months in 1975. Initially, the lesions improved, but then flared severely. Photochemotherapy with 8-methoxypsoralen and ultraviolet A (PUVA) was tried; the eruption worsened markedly. Methotrexate (25 mg, administered orally once each week) was restarted and was continued for six months without improvement. Generalized erythroderma became persistent (*Fig. 2*). Hyperkeratosis of the palms and soles became prominent as the erythroderma worsened.

In June 1976, methotrexate (50 mg, administered intravenously) was started on a weekly basis. The skin was 95% clear of lesions after three injections (*Fig. 3*). The patient then received methotrexate (30–50 mg, administered intravenously) every one to three weeks. One injection every one to two weeks was required as a maintenance dosage. The methotrexate was discontinued on five occasions; each time, a severe generalized erythroderma occurred within three weeks. During the second week after its discontinuation, scattered, well-marginated brown plaques appeared, enlarged rapidly, and became confluent. Generalized erythroderma regularly followed within two and one half to three weeks. The patient's depression and suicidal tendencies coincided with the severe erythroderma. When the disease was controlled with methotrexate the patient was happy and able to work effectively. PUVA was tried again on two occasions with marked flaring of the erythroderma. Orally administered methotrexate was reinstated on four occasions, and flaring of the erythroderma occurred each time within three weeks. Liver biopsies were performed at 12- to 18-month intervals during intravenous treatment; all showed a mild fatty change. The patient was lost to follow-up in June 1981. Until that time, no complications had occurred, except for occasional neutropenia, which necessitated a temporary reduction in the methotrexate dosage.

Discussion

PRP may result in the appearance of follicular papules in mildly affected patients or generalized erythroderma in severely affected patients.[5] Childhood-onset PRP with erythroderma is rarely seen. Davidson et al[6] reported 3 patients with this type of disease; generalized erythroderma developed in each case. In 2 of these patients, PRP began before the age of six months and was lifelong. Brown and Perry[7] reported 4 patients with acquired PRP who responded to

methotrexate given orally. Borrie[8] used orally administered methotrexate (5.0 mg, daily) to treat childhood-onset PRP and noted improvement, although not total clearing of the eruption. Anderson[9] treated a patient with severe erythrodermic PRP with methotrexate administered orally and noted a remission after seven weeks of therapy. The patient's sister had resistant psoriasis and after treatment with methotrexate, a one-year remission also occurred.

The multiple treatments and withdrawals of intravenously administered methotrexate in our patient for five years demonstrated a dramatic therapeutic effect. The erythroderma faded gradually to psoriasiform plaques and finally to normal-appearing skin. The assessment of various treatments for PRP is difficult because the natural history of the disease is usually unpredictable. However, for our patient, the course of the disease became known; severe erythroderma occurred invariably after intravenous administration of methotrexate was discontinued. Attempts to substitute other treatment, including systemic corticosteroids, orally administered methotrexate, and PUVA, failed.

After responding initially to weekly doses of orally administered methotrexate, our patient's condition became refractory to that treatment. Only when given intravenously, did methotrexate produce good results. Poor absorption of methotrexate in the intestine may have caused the orally administered methotrexate to become ineffective (personal communication, Van Scott EJ, 1980).

Van Scott et al[10] reported intravenously administered methotrexate to be safe in patients with psoriasis. Our patient's five years of such treatment attests to its safety. Nevertheless, we do not advocate the routine intravenous administration of methotrexate for extended periods, but it may be extremely beneficial in certain instances when all conservative and conventional therapies have been attempted without success.

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