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Excessive Cerumen Production Due to the Aromatic Retinoid Tigason in a Patient with Darier's Disease

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Abstract. A patient with Darier's disease is described, who developed excessive cerumen production and otitis externa in addition to general symptoms of adverse effects during treatment with the aromatic retinoid Tigason.

Oral vitamin A and topical vitamin A acid have been used to treat skin diseases with abnormalities of keratinization such as psoriasis ichthyosis and Darier's disease, but their use has been limited by their toxicity.

More recently the oral aromatic retinoid analogue of vitamin A (Ro-10-9359: Tigason) has been used for the same conditions, with good results (2-4). A limiting factor regarding the therapeutic use of retinoids is the frequency of side effects, most often cheilitis, mucosal dryness, exfoliation of palms and soles, pruritus, sweating, alopecia and severe liver damage, as well as general malaise, dizziness, nausea, etc.

This paper describes a patient with Darier's disease who developed excessive cerumen production resulting in otitis externa and loss of hearing during Tigason treatment, in addition to general symptoms.

CASE REPORT

A 35-year-old woman with a history of Darier's disease since the age of 6, was first seen as an out-patient in June 1979. From 3rd August, treatment was started with Tigason 75 mg daily until mid-September. She responded well, with almost total normalization of her skin, but suffered from adverse effects such as dry mouth and lips, and an intolerable feeling of deafness. Examination revealed excessive cerumen and otitis externa bilaterally.

The treatment was discontinued for 3 months, but the disease worsened, and Tigason treatment was started again, first with 75 mg daily for 2 weeks, then 50 mg daily. Her condition improved, but after 6 weeks' treatment she again developed a feeling of deafness and discharge from the ears. She also complained of general malaise, dizziness and nausea, and stopped the Tigason treatment.

There was a new recurrence of Darier's disease and several kinds of topical treatments were tried, but with little or no effect. She was admitted to hospital in August 1981 to try Tigason therapy once more. Before treatment was instituted, her ears were examined by an otolaryngologist, cerumen was removed and an audiogram proved normal.

After *one week* of medication the patient felt tired, complained of nausea, vertigo and general malaise, and the treatment had to be discontinued. A new audiogram failed to reveal any change, but quite a considerable amount of cerumen had already been produced.

DISCUSSION

Excessive production of cerumen and the development of otitis externa during Tigason treatment are not well known adverse effects. Burge et al. (1) mention in their study of 18 patients with Darier's disease treated with Tigason, that 2 patients complained of 'blocked ears'. Tsambaos & Orfanos (5) stated that after 2 weeks of treatment with oral retinoid, guinea pigs developed erythema, edema and scaling of the skin, with the changes most pronounced at the ear and snout.

The present case indicates that the known adverse effects such as dryness of the skin and scaling also may be seen in the ear, and that in predisposed persons this irritative condition may cause excessive cerumen production and otitis externa.

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Transepidermal Water Loss and Sweat Gland Response in Lamellar Ichthyosis before and during Treatment with Etretinate: Report of Three Cases

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Abstract. Despite its desquamative effect, oral etretinate had no normalizing effect on the increased basal transepidermal water loss in 3 patients with lamellar ichthyosis. Neither was any improvement achieved during treatment in the defective sweat gland function as measured after stimulation by intracutaneously injected methacholine chloride solution.

Key words: Etretinate; Transepidermal water loss; Sweat gland function; Evaporimetry

An increased transepidermal water loss (TWL) has been demonstrated in lamellar ichthyosis and other ichthyoses (4, 5). Furthermore, in lamel-

lar ichthyosis there is a failure in normal sweating which may cause hyperpyrexia in warm weather or during exercise. So far the mechanisms of these disturbances are not known.

Because of its desquamative effect, oral etretinate (an aromatic retinoid, Ro 10-9359) has proved useful in the treatment of various hyperkeratotic dermatoses including lamellar ichthyosis (for reviews, see 2, 7). In the present paper we report the effect of this treatment on TWL and on the activity of sweat glands in 3 adult patients with lamellar ichthyosis.

MATERIAL AND METHODS

Patients and treatment

Three adult patients with congenital lamellar ichthyosis were studied. Histological biopsies confirmed the clinical diagnosis. Three healthy persons served as controls. Age and sex distributions are presented in Table 1. The patients were given etretinate at an initial dose of 0.75–1.00 mg/kg/day. The dose was later reduced to a maintenance level of 0.50–0.90 mg/kg according to the clinical response.

Measurement of transepidermal water loss (TWL) and sweat gland function

Basal TWL and peak sweat response after stimulation were measured before and during treatment, using an evaporimeter (8) (Evaporimeter EP 1, Servomed, Stockholm) to record sweating, as described previously (9).

Sweat gland function was evaluated by injecting 0.1 ml of methacholine chloride (Mecholyt®, Sigma) in saline, 1:10³ dilution, intracutaneously in symmetrical sites of the upper back skin of the patients. This concentration has been used to reveal absence of active sweat glands (10). In healthy controls the dilution 1:10⁷ was used, since in normal skin high concentrations exceeded the measuring capacity of the apparatus.

The temperature of the test area was measured with an YSI 408 thermistor and was recorded on a Telco recorder. The local mean skin temperature in the patients was 33.3 (SD ±0.6)°C and in the control subjects 33.6 (SD ±0.3)°C. The temperature of the test room ranged from 20 to 23°C, and the relative humidity from 15 to 40%.

RESULTS

The results of TWL and sweat rate measurements in patients and controls are presented in Table 1. The basal TWL in ichthyotic patients was almost 3-fold compared with that in controls. A slight increase in TWL was observed during treatment. Methacholine stimulation with a 1:10³ dilution had virtually no effect on total cutaneous water loss in