Treatment of Arsenical Keratosis with Etretinate

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Treatment with oral etretinate is reported in a case of arsenical keratosis with Bowen's disease. Good (80%) clearance in keratoses was obtained, which is maintained after 15 months' follow up. *Arsenical keratosis; Bowen's Disease: Etretinate.* (Received February 1, 1983.)

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Inorganic arsenic has been used in medical and dermatological therapy right up to mid-twentieth century in spite of the correlation between arsenic intake and development of

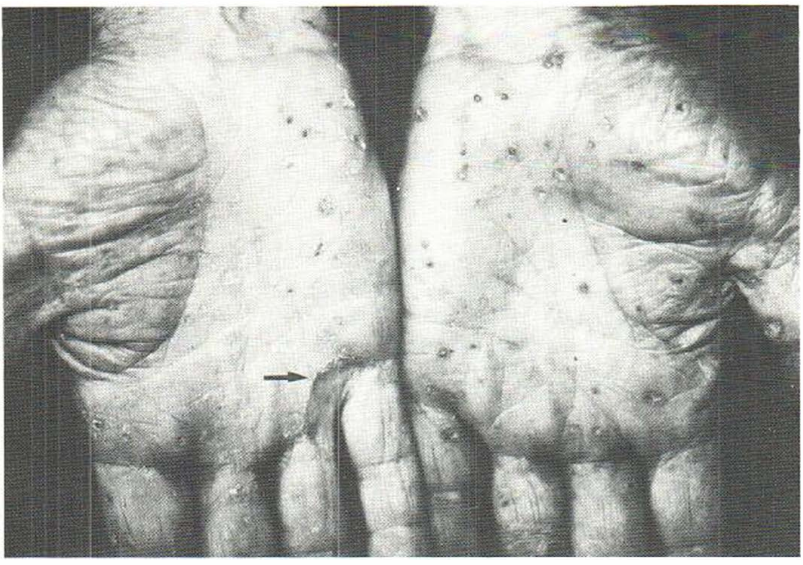

Fig 1. Palms of the patient before therapy, showing multiple corn-like arsenic keratoses. Arrow indicates site of previous excision of infiltrating squamous cell carcinoma.

pre-cancerous keratosis and malignant skin tumours, reported as early as 1887 by Hutchinson (4). Extensive reviews on arsenic exposure and skin cancer have since been reported (3, 6, 8). So far, no treatment has proved satisfactory for arsenical keratosis. There are two reports in the literature describing the use of oral aromatic retinoids in basal cell carcinoma in relation to arsenic exposure (1, 7) but neither of them mentions arsenical keratosis. Clinical effectiveness of etretinate is reported in a case of arsenical keratosis with Bowen's Disease.

CASE REPORT

J. H., a 65-year-old retired telephone engineer presented in July 1981 with a 21-year history of corn-like lesion on palms and soles and a few scattered lesions on the trunk and limbs. He reported a history of taking arsenical tonic (mixture of inorganic arsenic and bromide) for 6 months in 1950 for insomnia. Between 1950 and 1976 he developed seven intra-epidermal squamous carcinomas of the Bowen type on hands, trunk, scrotum, right upper thigh and left sole, which were treated with surgical excision or topical 5 Fluoro-uracil. In addition, an infiltrating squamous cell carcinoma from the base of the ring and little finger on the right hand was excised locally, followed by dissection of lymph nodes from right axilla and radiotherapy. Past treatment for his multiple arsenical keratoses included topical keratolytics, a course of Dimercaprol (100 mg intramuscularly three times daily for 7 days) in 1964 and topical retinoic acid. There was no significant family history. He was not taking any drugs.

Examination of the skin revealed yellowish, corn-like punctate keratoses on palms and soles (Fig. 1) with a few similar scattered lesions on the trunk, limbs and groin. In addition he had two scaly cursted, erythematous plaques on the left thoraco-lumbar region, measuring 10×6 mm and 7×3 mm respectively. The remainder of the physical examination was normal.

Diagnostic biopsies from the two plaques confirmed Bowen's Disease. Estimation of arsenic content in the hair, nails and urine showed levels of 0.039, 0.063 and 0.014 parts arsenic per million respectively, but these were within normal limits. Pre-treatment haematological, hepatic and renal laboratory tests and lipid profile were within normal limits. These laboratory parameters were monitored during and after therapy at 4-weekly intervals.

Therapy with etretinate was begun at 1.0 mg/kg/day in three divided doses after meals and clinical progress was assessed at fortnightly intervals. The dose was reduced to 0.75 mg/kg/day after 4 weeks

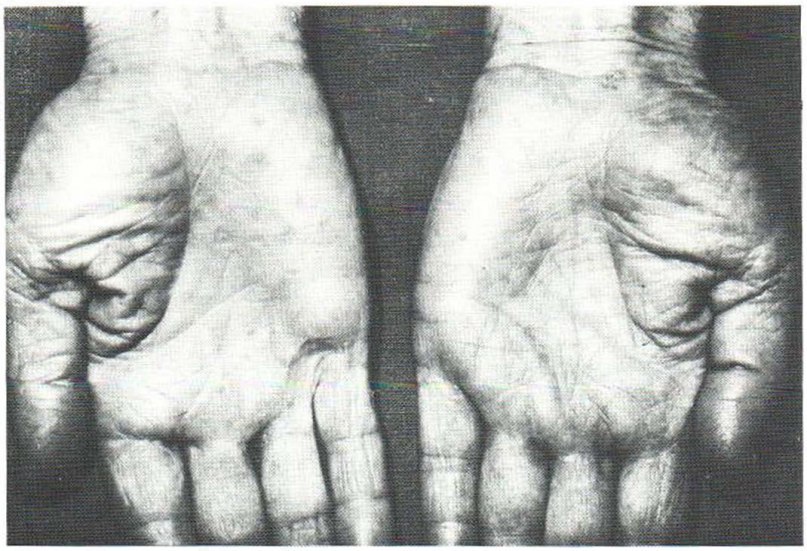

Fig 2. Palms of the patient 8 weeks after therapy with etretinate, showing good regression in arsenic keratoses.

because of cheilitis, conjunctivities, xerosis, dryness of nasal mucosa and pruritus. The punctate keratosis started to flatten after 4 weeks therapy and showed 80% clearance after 8 weeks (Fig. 2). However, the plaques of Bowen's Disease showed only partial clearance. Retinoid therapy had to be discontinued after 12 weeks when he developed elevated levels of serum aspartate and alanine aminotransferases (SGOT, SGPT). The rest of the laboratory parameters at this stage, including serum bilirubin, lactic dehydrogenase, alkaline phosphatase, total protein and albumin, were within normal limits. SGOT and SGPT continued to rise for one week after stopping the retinoid therapy and then gradually returned to normal levels after 35 weeks. After a 15-month follow-up, 80% clearance of arsenical keratoses has now been maintained. His laboratory parameters remain normal. Two plaques of Bowen's Disease which showed only partial clearance during therapy recurred 4 weeks after stopping etretinate and have subsequently been treated successfully with topical 5 Fluoro-uracil.

DISCUSSION

Arsenic exposure in man, whether medicinal, environmental, or occupational, is both mutagenic and carcinogenic (3, 4, 6, 8). Treatment and chemo-prevention of basal cell carcinoma associated with arsenic exposure with retinoids have proved to be of some benefit, though continuous long-term therapy seems to be required to prevent recurrence (1, 7). We have obtained a good clearance with aromatic retinoid in arsenical keratoses which have carcinogenic potential and this clearance has been maintained for more than a year. Although the patient developed transient muco-cutaneous side effects and transient hepatoxicity as has been previously reported (9) with retinoid therapy, the therapeutic results have outweighed the transient side effects. The exact mechanism of action of retinoids in the treatment and chemo-prevention of cutaneous tumours is not known. Considering the diversity of biological effects of retinoids, it is unlikely that any single mechanism is responsible. It is probable, though, that the action of retinoids on the cells to maintain their normal phenotype and to inhibit the growth of transformed and tumour cells,plays an important part (2, 5, 7). The use of aromatic retinoids in skin cancer prevention seems to be of significant value.

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