

Case 3: Arsenic Keratosis

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CASE SUMMARY

History

A 57 year-old man developed corn-like papules on the palms and soles since he was a teenager. These lesions were neither itchy nor painful and he did not seek medical advice. Thereafter he noticed more and more hyperpigmented macules on the chest and the back. By the end of 1996 he found a non-healing ulcer over his right middle finger and a number of hyperkeratotic pigmented papules and nodules over the anterior chest wall. Skin biopsy performed in November

1997 revealed intraepithelial squamous-cell carcinoma. He was a known asthma patient since childhood. His mother who practiced medicine in China prescribed to him several herbal medicines as well as western medicines. He is now on salbutamol inhaler. Apart from an operation for cataract his past medical history was unremarkable. There was no history of drinking well-water, excessive sun-exposure, or Human Papilloma Virus infection. There was no family history of cutaneous malignancy.

Physical examination

On physical examination there were multiple hyperpigmented macules over the chest and the back. There were some papules with adherent keratotic scale over the anterior side of the chest, the ankles and the buttocks. A 0.5cm ulcer was found over the right middle finger. There was no sign of solar damage and the exposed areas were relatively spared. (Figure 1, 2 and 3).



Figure 1: Multiple hyperpigmented macules over chest and back.



Figure 2: Papules with adherent keratotic scale on palm.



Figure 3: Non-healing ulcer over right middle finger.

Investigations

Multiple skin biopsies done in February 1998 revealed the following histological findings:

1. Sacral nodule - section showed a piece of skin with epithelial dysplasia and marked hyperkeratosis. No definite evidence of carcinoma seen.
2. Right cell wall nodule - section showed in-situ squamous-cell carcinoma with no definite evidence of invasion. The excisional margins were clear. Diagnosis was compatible with Bowen's disease.
3. Right hand nodule - section showed in-situ squamous-cell carcinoma with no definite evidence of invasion.
4. Left hand nodule and sacral nodule - both sections showed a keratinizing well-differentiated squamous-cell carcinoma invading the dermis.
5. Right middle finger ulcerated area - sections of the ulcerated areas showed invasion cords of squamous-cell carcinoma with surrounding inflammation. The lateral margin was free, while the deep margin clearance measured 1mm, compatible with invasive squamous cell carcinoma with a clearance margin of 1mm.

Other investigations including chest x-ray, complete blood picture, liver and renal function test were normal.

Differential diagnosis

The clinical features of multiple Bowen's disease and squamous-cell carcinoma are rare in Chinese. Most of the cutaneous signs were found on unexposed areas which did not suggest a solar etiology. The presence of melanosis and palmoplantar keratosis suggested arsenic as a cause. The history of chronic intake of Chinese

herb was the possible source of inorganic arsenic. Although screening of blood, urine, nail and hair for arsenic were not applicable, as he no longer took the herbal medicine after childhood, the clinical manifestations and relevant history were compatible with a diagnosis of chronic arsenicism.

REVIEW ON ARSENIC INDUCED SKIN DISEASES

Arsenic has been used as a medicine for many centuries both in the Orient and the West. It was previously used as a treatment for asthma, psoriasis, syphilis, various dermatoses and as a tonic. Fowler solution was a well-known medicine in the eighteenth century and Sin Lak pills¹ was a famous anti-asthmatic proprietary herb. Other herbs containing arsenic had been used for non-specific conditions such as epilepsy, sore throat and joint pains. There were reports of well water as a source of arsenic, causing Black foot disease in Taiwan.

There were many Chinese herbs containing arsenic. Many of these have been banned in the late 1970s. However, legislative loopholes allowed unsupervised manufacture, sale and distribution of these herbal medicines to continue. Continual surveillance programs to detect the unrestricted, unsupervised manufacture and sale of drugs should be imposed.

Clinical Features

The clinical manifestations include arsenic keratosis (70%), hyperpigmented macules (80%),

hypopigmented macules (30%), Mee lines (5%), diffuse alopecia, acrodermatitis and thromboangiitis-like changes of legs (5%).

There are two types of arsenic keratosis: 1) multiple, hard punctate cornlike papules at sites of friction especially palms and soles; and 2) elevated scaly hyperpigmented patch on the exposed areas.

A long list of malignancies had been reported to be associated with chronic exposure to arsenic. The most common types are skin cancers including Bowen's disease, squamous-cell carcinoma and basal cell carcinoma. Other internal malignancies which are related to chronic arsenicism include squamous-cell bronchogenic carcinoma, tumours of bladder, kidney, breast, pancreas, stomach, hepatic angiosarcoma and leukaemia. The latent period for arsenic induced malignancies can be more than thirty years.²

Other stigmata of chronic arsenic include toxic sensorimotor polyneuropathy, mild iron deficiency anaemia, leukopenia, thrombocytopenia, malabsorption and liver cirrhosis.

Pathogenesis

Arsenic is not an initiator or tumor promoter. However arsenic and its metabolites have been shown to cause chromosomal abnormalities and single-stranded breaks in DNA.³ The carcinogenicity has also shown to be related to gene amplification.⁴ Recent studies found dysfunction and loss of Langerhans cells in arsenic skin lesions.⁵ Other studies showed altered cytokeratin expression in arsenic skin cancers.

Diagnosis

The diagnostic criteria of arsenicism due to Chinese herbal product are as follows:-

1. A recent or past history of continuous or intermittent intake of a known or unknown preparation of Chinese herbal products.
2. A classical clinical picture together with histology, showing features of arsenic keratosis.
3. Evidence of high arsenic content (>25ppm) in the herbal preparation taken.
4. Evidence of increased tissue content in hair, nail (>1.0ppm) or in the urine (>0.01ppm). This last criterion is applicable only to recent exposure.

Treatment

Destructive treatments such as cryotherapy and excision are the mainstay of therapy for arsenic keratosis. Etretnate has been reported to be effective in treating arsenic keratoses. Etretnate also has the advantage of possibly reducing the chances of cancer formation.

Prognosis

The incubation period of major cutaneous manifestations of chronic arsenicism is more than thirty years, therefore we expect a certain number of patients still being at risk of developing cutaneous changes of chronic arsenicism. If a patient has chronic arsenicism, follow up with regular skin and systemic examination is necessary to monitor for skin and internal malignancy.

Learning points:

Chronic exposure to Chinese medicines containing inorganic arsenic increases the risk of cutaneous and systemic malignancies. The long incubation period means that long-term surveillance for malignant change is necessary.

References

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