

An Elderly Gentleman with Multiple Squamous Cell Carcinoma

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CASE SUMMARY

History

A 75-year-old gentleman was referred to our clinic for a non-healing ulcer on his right ring finger for over one year. He also complained of another ulcer over his left thumb, which was present for two months. He was known to suffer from diabetes mellitus complicated by retinopathy, hypertension, stroke and dementia. He was bed bound and lived in an old age home.

He had been a farmer in Mainland China till he was nineteen. He then worked as a bone-setter in Hong Kong for the next twenty years before retiring. There was no history of psoriasis, asthma, or long-term intake of herbal medicine.

Physical examination

An ulcer was seen at the dorsum of the right ring finger between the proximal and distal interphalangeal joints (Figure 1). It had an irregular base with yellowish discharge. Its edge was irregular, indurated and was covered with pigmented friable tissue. At the left thumb, there were erosions, crusting and swelling at the proximal nailfold. The nail plate was dystrophic and a fleshy nodule was found at the distal end of the lateral nailfold (Figure 2). Ill-defined scaly thin erythematous plaques were present over the dorsum of the left index, middle and ring fingers (Figure 3) and also over the right middle and ring fingers. No lymph nodes were palpable.

There were also no palmoplantar hyperkeratotic papules, no Mee's line and no abnormal hyperpigmentation or hypopigmentation of the skin. No signs of excessive solar damage were seen at exposed areas.

Differential diagnosis

The differential diagnoses include: vasculitis, atherosclerosis (as a result of the underlying diabetes mellitus), cutaneous malignancies and infections.

Investigations

The complete blood picture and renal biochemistry were normal. Anti-nuclear factor was positive at 1/160 while anti-DNA, anti-ENA and ANCA were all negative. Skin swab from the right ring finger ulcer grew a moderate mixed growth of *Staphylococcus aureus*. Nail clipping from left thumb for fungal microscopy and culture were negative. Midstream urine for microscopy and chest X-ray were normal.



Figure 1: Ulcer at the dorsum of the right ring finger



Figure 2: Nail dystrophy, erosion and nodule at the left thumb

The first skin biopsy was taken from the margin of the right ring finger ulcer. Atypical squamous proliferation was seen at the epidermis characterized by enlarged and irregular nuclei. As no definite diagnosis of malignancy could be made, skin biopsy was repeated. Specimens were taken from the right ring finger ulcer as well as from the left thumb nodule at the second skin biopsy. Both specimens showed a highly dysplastic epithelium with irregular islands of squamous cells in the underlying dermis. A diagnosis of squamous cell carcinoma was made for both specimens. Incisional skin biopsy from the scaly erythematous plaque on the dorsum of the left middle finger showed features of dysplasia with marked parakeratosis and nuclear pleomorphism of epidermal cells. The overall epithelial maturation was, however, still observed and there were no stromal invasion.

Diagnosis

The multiple squamous cell carcinomas could be



Figure 3: Scaly erythematous thin plaques over the dorsum of the left index, middle and ring fingers

related to previous exposure to arsenic, either from an agricultural source or from bone-setting preparations, as there were no other obvious predisposing factors.

Management

The patient was referred to orthopaedic surgeons. Radiation therapy was given to the lesions on the right ring finger and left thumb. A repeated biopsy of the ring finger ulcer after radiotherapy revealed only inflammation without signs of malignancy. Partial thickness skin graft was subsequently performed for the right ring finger ulcer.

REVIEW ON CHRONIC ARSENICISM

Source of chronic arsenicism

Arsenic can be absorbed orally, through inhalation, or percutaneously.¹ The most common cause of chronic arsenicism is medicinal exposure. Fowler's solution previously used in the treatment of psoriasis contains 1% potassium arsenite, whereas asiatic pills used for treating asthma contain arsenic trioxide. Many chemicals used in agriculture contain arsenic and they can give rise to chronic arsenicism. These include pesticides,

fungicides, herbicides, rat poisons, and weed-killers. Industrial exposure to arsenic can occur in the manufacturing of glass, wood preservatives, pigments dyes, and enamels. Drinking well-water contaminated with arsenic is an important cause of chronic arsenicism in some places like Taiwan.

Diagnosing chronic arsenicism

The diagnosis of chronic arsenicism is usually based on the relevant clinical findings together with a history of exposure to arsenic. Objective evidence to demonstrate chronic arsenic poisoning is often not possible unless there is still on-going exposure to the agent.

Laboratory diagnosis of chronic arsenicism

There are two forms of arsenic, organic and inorganic arsenic. Organic arsenic is non-poisonous and can be found in seafood. Arsenic that can cause acute or chronic poisoning is in inorganic form, mainly arsenic 3- or arsenic 5-compounds.

Measuring the arsenic level in urine is only useful for acute exposure. Specially treated bottles are needed for specimen collection to avoid contamination. It is possible to differentiate between the poisonous inorganic form and the non-poisonous organic form from urine samples. The hair is a poor tissue source for measuring arsenic level, due to the high contamination rate from environmental exposure. Hair testing is useful only for relatively recent exposure that occurred during the growth of the hair sample and it cannot differentiate between organic and inorganic arsenic.

Histologically, there are no arsenic related pathognomonic features for pre-malignant and malignant cutaneous lesions.

Cutaneous stigmata of chronic arsenicism

Pigmentary changes in chronic arsenicism include generalised hyperpigmentation and hypopigmented raindrop-like macules with the size of one to two millimetres. Mee's lines are transverse whitish nail bands and can be found if exposure to arsenic is recent. Diffuse alopecia, acrodermatitis and thromboangiitis-like changes in legs are other non-neoplastic changes seen in chronic arsenicism.

Arsenical keratosis is often regarded as pre-malignant and there are two types. The first type is found

in sites of friction, for example the palms and soles, and consists of multiple, punctate, hard, yellowish, corn-like papules. The second type can be found in unexposed body areas with slightly elevated, scaly, erythematous or pigmented patches. Arsenical bowenoid lesions can be found in both sun exposed or non-exposed sites. Squamous cell carcinoma and basal cell carcinoma are the cutaneous malignancies associated with chronic arsenic exposure.

The frequencies of cutaneous lesions associated with chronic arsenicism vary between studies. The reported prevalence of arsenical keratosis ranged from 7% to 44%, hyperpigmentation from zero percent to 18%, and skin cancers from one percent to 12%.²⁻⁴ Squamous cell carcinomas were found to be 1.2 times to 6.8 times more frequent than basal cell carcinomas.^{4,5}

Extracutaneous features of chronic arsenicism

These include neuropathy, anaemia, leukopenia, thrombocytopenia, metallic breath odour, diarrhoea, malabsorption, hepatic cirrhosis, and electrocardiographic changes. Internal malignancies can have a latent period of up to 50 years and can affect the nasorespiratory, gastrointestinal and genitourinary tracts.

Learning points:

In patients with multiple skin cancers, chronic arsenicism should be considered. Occupational and medical histories are important, as laboratory confirmation is not possible if arsenic exposure occurred many years ago.

References

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