

# Skin Cancer Caused by Chronic Arsenical Poisoning — A Report of Three Cases

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## Summary

The association of arsenical poisoning with the development of skin cancer is well-known. In Malaysia, arsenic has been shown to coexist with tin in tin-mining land. Our preliminary investigation has shown that the level of arsenic in well water from a tin-mining area is high. We report 3 patients with cutaneous lesions typical of chronic arsenical poisoning such as hyperpigmentation, keratoses and skin cancer. These patients have positive histories of previous domicility in tin-mining areas. We conclude that these patients developed chronic arsenical poisoning from drinking well water polluted with arsenic from the tin-mining soil.

**Key words:** *Chronic arsenical poisoning, cutaneous lesions, skin cancer, tin mining land, well water.*

## Introduction

The role of arsenic as an aetiological agent for skin cancer and related dermatosis has long been known<sup>1</sup>. Chronic arsenical poisoning could occur from ingestion of arsenical medicinal preparations or water contaminated with arsenic, and in certain occupations<sup>1,2</sup>. Chronic arsenical poisoning patients tend to develop characteristic cutaneous lesions as well as internal malignancies<sup>2</sup>. The typical cutaneous lesions include skin hyperpigmentation or melanosis, keratotic lesions, usually over the palms and sole, carcinoma *in situ*, and frank squamous cell as well as basal cell carcinomas<sup>2,3</sup>.

Endemic chronic arsenical poisoning caused by a high content of arsenic in public drinking water has been reported in many parts of the world<sup>1,2,3</sup>. In Malaysia, where tin-mining is an important industry, arsenic is found to coexist with tin in these mining areas<sup>4</sup>.

We present 3 patients who developed cutaneous lesions characteristic of chronic arsenical poisoning after a variable period of domicility in a tin-mining area.



**Fig 1a: Pigmented basal cell carcinoma with the characteristic rolled edge; the surrounding skin showing raindrop-like or diffuse dappling typical of hyperpigmentary changes due to chronic arsenical poisoning.**

## Patient Reports

### Case 1

A 55 year old Malay musician presented with a history of hyperpigmentation, mainly over the trunks and limbs, which developed over a period of 40 years. Subsequently, he noticed thickening and scaling (hyperkeratosis) over the palms and soles. The hyperpigmentation gradually spread to involve larger areas of the skin and the hyperkeratotic lesions increased in number and thickness over the years. About 25 years ago he underwent surgical treatment for swellings and ulceration on the middle and ring fingers of his right hand and the sole of his right foot. About one and a half years ago the patient came to see us with an enlarging growth over the tendoachilles area of the left leg. The growth measured 3 cm x 3 cm and was slightly tender and mobile. There were large areas of hyperpigmentation on the trunk and limbs (Fig 1a), interspersed with normal skin, giving a mottled appearance. We found numerous early hyperkeratosis over the soles (Fig 1b) and palms. A biopsy of the fungating lesion over the tendoachilles showed well-differentiated squamous cell carcinoma. We excised the lesion widely and grafted with good result.

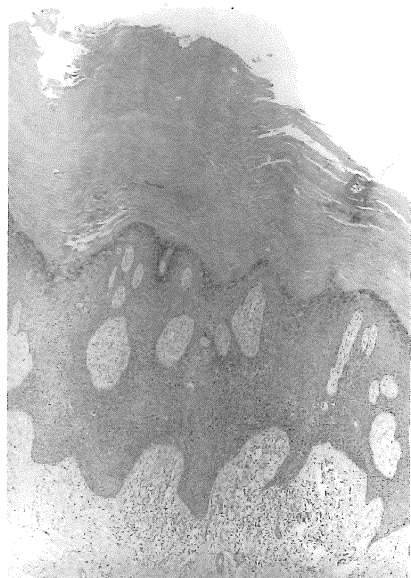
The patient was seen 6 months later for a non-healing ulcer over the middle and ring fingers of the right hand. He also complained of painful lesions over the plantar aspect of both heels which made walking difficult. Otherwise, he was in good health. We found that the hyperpigmentation and hyperkeratosis were more extensive than before. In addition, a Bowenoid lesion was seen over the left shoulder (Fig 1d). There was also a 2 cm x 2 cm pigmented lesion at the upper medial border of the left scapula (Fig 1a), which appeared to be pigmented basal cell carcinoma. On the palms and volar surfaces of the fingers were found multiple hyperkeratotic protuberant lesions, and on the ring and little fingers of the right hand, the lesions were ulcerated.

Based on these findings, we suspected that the patient had chronic arsenical poisoning. However, he denied ever taking arsenical medications. Therefore we reviewed the history for environmental exposure to arsenic. His family moved to Sentul, Kuala Lumpur, in 1935. From a migrant farming community, Sentul subsequently developed into a large tin-

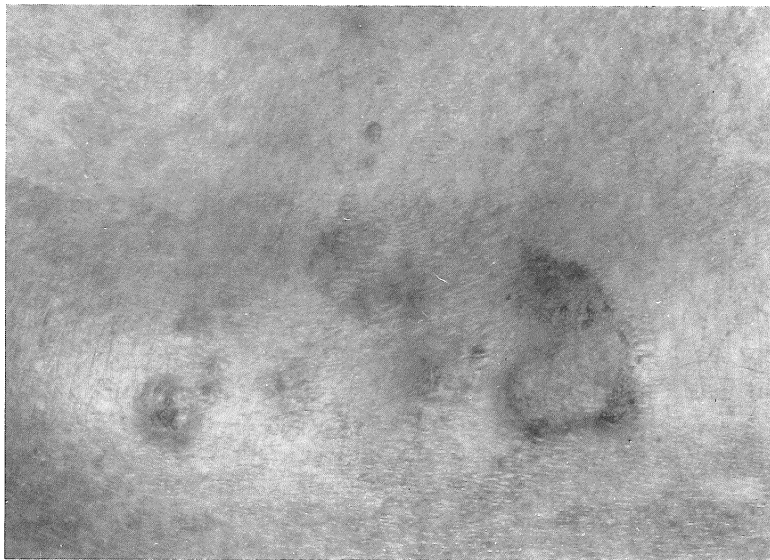
CASE REPORT



**Fig 1b:** Numerous punctate hyperkeratotic lesions on the sole, with a large lesion on the lateral border.



**Fig 1c:** Section taken from plantar lesion showing marked hyperkeratosis and hypergranulosis typical of carcinoma *in situ* (Haematoxylin and eosin stain, x 100).



**Fig 1d:** Bowen's disease of the skin.



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**Fig 2: Showing ulceration over the left palm. Multiple keratotic lesions typical of arsenical poisoning can be seen in the palm and volar surfaces of the fingers.**

At surgery in February, 1992, the left palmar growth was found to have infiltrated the base of the fourth metacarpal. The left palmar lesion was widely excised, to include the fourth metacarpal, and the fourth digital phalanges were filleted out and the digital skin flap was used to close the defect. A wide excision of the left epitroclear lymph node was done together with left axillary clearance during which the central group of lymph nodes were found to be enlarged. Histopathological examination of the resected specimen confirmed squamous cell carcinoma and the epitroclear as well as left axillary lymph nodes confirmed metastatic deposit. Post-operative irradiation was given to the left hand and arm but the axilla was spared as the metastatic tumour had not breached the lymph node capsules. The patient was found to be well at 1 month follow-up.

### **Case 3**

A 44 year old Malay housewife complained of a non-healing ulcer in both hands since 2 years, and another lesion over the left tendoachilles. She denied taking arsenical medications. She and her family had been staying in Sentul for more than 20 years since 1969 and they relied on well water for their daily needs. Her husband also developed a similar lesion in the right middle finger which was amputated at another hospital. He later developed a swelling in the right axilla and subsequently died in December 1991.

On examination of this lady, we found a 1.5 cm x 3 cm ulcer on the dorsal aspect of the proximal interphalangeal joint of the middle finger of the left hand, which was mobile and had a raised edge. There were multiple hyperkeratotic lesions on the palms and soles. Hyperpigmented areas were seen over the trunk and limbs. A non-ulcerating lesion was seen over the left tendoachilles, measuring 2 cm x 1.5 cm (Fig 3). The regional lymph nodes were not palpable and she was otherwise well. Biopsy of the dorsal left hand ulcer showed a well-differentiated squamous cell carcinoma. Wide excision of the ulcer as well as some of the hyperkeratotic lesions and the lesion over the tendoachilles was done in January 1992. The histopathological report showed that the lesion over the tendoachilles was an intraepidermal carcinoma. She is still attending our follow-up clinic.



**Fig 3: Showing lesion over the left tendoachilles which proved to be intraepithelial carcinoma.**

### Discussion

The relationship between arsenical poisoning and skin cancer has long been known. Hutchinson (as reported by Neubauer)<sup>1</sup>, in 1887, was the first to direct attention to this association. In those days, inorganic arsenic, such as Fowler's solution, Asiatic pills, "bromide" mixtures and others were commonly used to treat various conditions such as asthma, hay fever, nervous disorders and psoriasis<sup>1,6</sup>. Hutchinson observed that long-term therapeutic use of these drugs led to the development of keratosis and skin cancer. This observation was later confirmed by many others. In fact, it was found that other forms of long-term exposure to arsenic, such as occurs during occupational and dietary (from drinking water) exposures, could also give rise to the same conditions<sup>1,2,6</sup>.

The first report of arsenical skin cancer caused by polluted drinking water was by Geyer in Reichenstein, 1898<sup>1,2</sup>. Endemic chronic arsenical poisoning due to the high content of arsenic in public drinking water has more recently been reported in Taiwan, Argentina, Chile and Oregon, USA<sup>2,3,6,7</sup>. In an epidemiological study from Taiwan<sup>7</sup> involving a population of about 40,000 from an area with relatively high content of arsenic in potable water obtained from artesian wells, 18.54% of the population surveyed showed skin manifestations of chronic arsenicism, i.e., hyperpigmentation, keratoses and cancer, at the rate of 183.5, 74.0 and 10.6 per thousand respectively. Hyperpigmentation, keratoses and cancer are the 3 main skin lesions in chronic arsenicism, regardless of the source<sup>1,3</sup>. The hyperpigmentation occurs all over the body, often showing a raindrop-like appearance or diffuse dappling of dark brown, especially marked on the unexposed part of the body<sup>2</sup> and usually precedes keratoses. In the Taiwanese study<sup>7</sup>, 90% of those with cancer were associated with hyperpigmentation.

Arsenical keratoses is characterised by multiple, small nodules most commonly found on the palms and soles. These nodules may coalesce to form larger verrucous growth. There may also be diffuse keratosis on the palms and soles which may coexist with the nodular form<sup>2</sup>. In the Taiwanese study, 80% of those with cancer had keratosis on the palms and soles. Arsenical keratosis may take more than 20 years to develop after exposure to inorganic arsenicals<sup>6</sup>. Histologically, the majority of arsenical keratoses, including most palmar and plantar lesions, show a completely benign pattern. Others display mild to moderate atypia with sparing of adenexal

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epithelium, indistinguishable from solar keratosis<sup>6</sup>. Persistent ulceration, erosion, fissuring or induration may signal invasive malignancy. Arsenical cancers of the skin are often multiple and are usually located on unexposed parts of the body, palms, soles, extremities and trunk. The histological types of arsenical skin cancer include squamous cell carcinoma, basal cell carcinoma, intraepidermal carcinoma and combined forms.

Two of the patients we presented showed all typical features of arsenical dermatosis. Although the second patient had no hyperpigmentation, he had keratotic lesions on the palm and soles and a single skin cancer in an unexposed part. These clinical findings are compatible with a diagnosis of arsenicism. None of these patients were occupationally or pharmaceutically exposed to arsenic. They, however, shared 2 common features:

1. a variable period of domicility in a tin-mining area, using well water from that area;
- and*
2. typical features of chronic arsenical skin cancer.

The evidence thus appears to point towards the tin-mining environment as the source of arsenical poisoning in these patients. Ismail<sup>4</sup> stated that in Malaysia, arsenic coexists with tin and is used as a path-finder in tin prospecting. This view was also subscribed to by Hosking<sup>5</sup>. If the soil in tin-mining areas in this country contains arsenic, then it is very likely that arsenic could contaminate well water in these areas by the process of leaching. Our initial investigation has shown that in one area in Sentul Dalam, the well water contained a high level of arsenic (5.0 mg/litre). This level is 100 times the permissible level of arsenic in drinking water, which is 0.05 mg/litre<sup>8</sup>. We therefore concluded that the 3 patients presented developed chronic arsenical poisoning from ingesting well water contaminated with arsenic. Although the initial supporting evidence linking chronic arsenicism to the drinking of well water from tin-mining areas has been presented, further study is needed to determine:

1. the levels of arsenic in well water in several other tin-mining areas;
2. the prevalence of arsenic keratoses and cancers in inhabitants of other tin-mining areas.

### Conclusion

We presented 3 patients with features of arsenical skin cancer and demonstrated the source for the occurrence of chronic arsenical poisoning. A proper epidemiological study is necessary to further confirm these initial findings.

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