

Squamous Cell Carcinoma and Multiple Bowen's Disease in a Patient with a History of Consumption of Traditional Chinese Herbal Balls

Joon Seok^a Kui Young Park^a Kapsok Li^a Beom Joon Kim^a
Joo Hyun Shim^b Seong Jun Seo^a Myeung Nam Kim^a
Chang Kwun Hong^a

Department of Dermatology, ^aChung-Ang University College of Medicine and
^bNational Police Hospital, Seoul, Republic of Korea

Key Words

Arsenic · Arsenic keratosis · Bowen's disease · Chinese herbal ball · Squamous cell carcinoma

Abstract

Arsenic has been classified as a class I human carcinogen, meaning that there is sufficient evidence of carcinogenicity to humans. Arsenic, however, remains a common contaminant in a number of traditional Chinese herbal balls. A 64-year-old man presented with an erythematous erosive patch on the left palm, multiple yellowish scaly patches on the right palm and an erythematous hyperkeratotic patch with bleeding on the left foot dorsum. He also had similar skin lesions on the back and buttock. He had a past medical history of chronic exposure to arsenic through consumption of traditional Chinese herbal balls. Skin biopsy revealed Bowen's disease on the left palm and squamous cell carcinoma on left foot dorsum. We report this case to emphasize that we should investigate patient's history thoroughly, including the use of Chinese herbal balls to find out arsenicism.

© 2015 S. Karger AG, Basel

Introduction

With the discovery of the multisystem toxic effects of arsenic, including cutaneous and visceral malignancies, its therapeutic use has declined over the past half-century [1]. Arsenic remains an ingredient in a number of traditional Chinese herbal balls. Espinoza et al. [2]

Seok et al.: Squamous Cell Carcinoma and Multiple Bowen's Disease in a Patient with a History of Consumption of Traditional Chinese Herbal Balls

reported that they had detect arsenic in all products in the form of traditional Chinese herbal balls, patented medicinal agents manufactured in mainland China and confiscated at U.S. ports of entry, with arsenic ranging from 0.1 to 36.6 mg per ball. Moreover, chronic arsenicism from the consumption of traditional Chinese herbal balls in Singapore has been reported in patients ingesting 10 mg per day [3]. There is a direct dose-response relationship between the amount of arsenic exposure and the development of skin cancer [4].

Case Report

A 64-year-old male presented with an erythematous erosive patch on the left palm, yellowish scaly patches with multiple hyperkeratotic papules on the right palm and an erythematous plaque with bleeding on the left foot dorsum (fig. 1). He presented with skin thickening with hyperkeratotic papules on both palms regarded as arsenic keratosis for 15 years. His past history revealed chronic exposure to arsenic through consumption of traditional Chinese herbal balls taken daily for 30 years for treatment of myelitis for which he had undergone surgery several times. He was not exposed to any risk factor for other diseases. In addition, he had had to have his right leg amputated for diabetes mellitus.

We performed a skin biopsy on the left palm. The histopathologic findings were hyperkeratosis, acanthosis and full-thickness atypia in the epidermis. Higher magnification showed pleomorphic atypical cells with prominent nucleoli. While the epidermis showed marked atypical cells, the border between the epidermis and dermis remained intact (fig. 2). A skin biopsy was also performed on the left foot dorsum, and pathology revealed hyperkeratosis, acanthosis and inflammatory cell infiltration throughout the dermis. A high-power view showed atypical cells of prominent nucleoli throughout the epidermis and malignant tumor cell nests with an irregular border in the dermis (fig. 3). Histopathologic examination established the diagnosis of Bowen's disease on the left palm and squamous cell carcinoma (SCC) with Bowen's disease on the left foot dorsum. When considering excision of the SCC, however, he refused treatments other than topical ointment. Considering his age and lesion size, imiquimod was first applied topically to the Bowen's disease lesion.

Discussion

Hyperkeratosis can appear due to short periods of arsenic exposure, and these lesions give rise to the majority of arsenic-induced skin cancers. Arsenic-related SCC can develop either de novo or progress from Bowen's disease [5]. In our case, hyperkeratosis was observed on the cancer site and SCC was assumed to originate from Bowen's disease on the patient's left foot dorsum. Arsenic-related Bowen's disease can appear 10 years after arsenic exposure, while other types of skin cancer can have a latency period of 20–30 years [6]. Therefore, follow-up is advised to detect malignancy at an early and curable stage. Meanwhile, the patient had had to have his right leg amputated for diabetes mellitus, and arsenic as a potential risk factor for type 2 diabetes has received attention recently [7].

Arsenic-induced oxidative stress results from upregulating nicotinamide adenine dinucleotide phosphate oxidase, from uncoupling nitric oxide synthase and from depleting natural antioxidants such as nitric oxide and glutathione. It provokes immune dysfunction and tissue inflammatory responses, involving activation of the unfolded protein response signaling pathway. DNA damage with upregulated signal transduction molecules may cause apoptosis, promote proliferation and enhance cell survival. Genomic instability via direct DNA

damage and weakening of several cellular DNA repair mechanisms could also be important cancer development mechanisms in arsenic-exposed populations [8].

In our case, SCC and multiple Bowen's disease resulted from consumption of traditional Chinese herbal balls. Dermatologists need to bear in mind that exposure to arsenic is not uncommon, and that symptoms such as hyperkeratosis, hyperpigmentation and hypopigmentation may disappear with time, concealing possible exposure to arsenic. Thorough investigation of the patient's history, including the use of traditional Chinese herbal balls, may be needed to determine the source of arsenic exposure.

Statement of Ethics

The authors state that the patient gave informed consent to have his case report published.

Disclosure Statement

The authors have no conflict of interest for this publication and there was no funding.

References

- 1 Sommers SC, McManus RG: Multiple arsenical cancers of the skin and internal organs. *Cancer* 1953;6:347–359.
- 2 Espinoza EO, Mann MJ, Bleasdel B: Arsenic and mercury in traditional herbal balls. *N Engl J Med* 1995;333:803–804.
- 3 Tay CH, Seah CS: Arsenic poisoning from anti-asthmatic herbal preparations. *Med J Aust* 1975;2:424–428.
- 4 Wong SS, Tan KC, Goh CL: Cutaneous manifestations of chronic arsenicism: review of seventeen cases. *J Am Acad Dermatol* 1998;38:179–185.
- 5 Castrén K, Ranki A, Welsh JA, Vähäkangas KH: Infrequent p53 mutations in arsenic-related skin lesions. *Oncol Res* 1998;10:475–482.
- 6 Yoshida T, Yamauchi H, Sun GF: Chronic health effects in people exposed to arsenic via the drinking water: dose-response relationships in review. *Toxicol Appl Pharmacol* 2004;198:243–252.
- 7 Katherine MH, Ritesh KS, Craig AE: The mechanistic basis of arsenicosis: pathogenesis of skin cancer. *Cancer Lett* 2014;354:211–219.
- 8 Wang W, Xie Z, Lin Y, Zhang D: Association of inorganic arsenic exposure with type 2 diabetes mellitus: a meta-analysis. *J Epidemiol Community Health* 2014;68:176–184.

Seok et al.: Squamous Cell Carcinoma and Multiple Bowen's Disease in a Patient with a History of Consumption of Traditional Chinese Herbal Balls

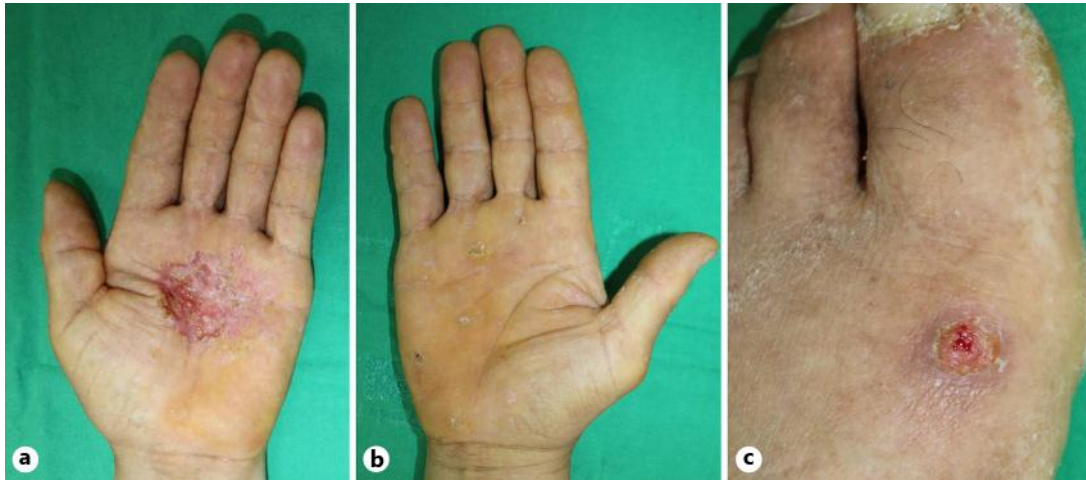


Fig. 1. **a** Erythematous erosive patch on the left palm. **b** Multiple yellowish scaly patches with hyperkeratotic papules on the right palm. **c** Yellowish to erythematous plaque with bleeding on the left foot dorsum.

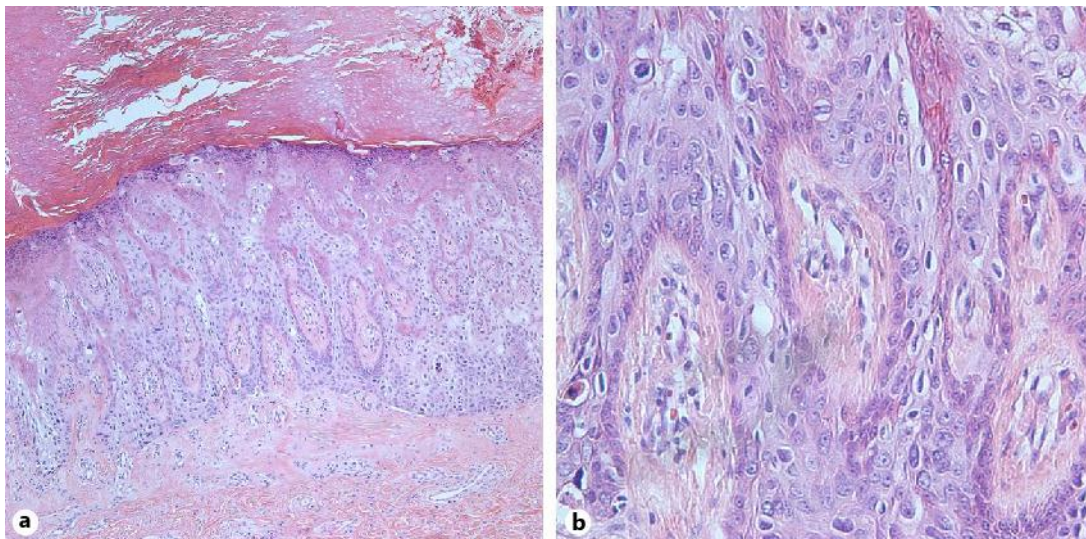


Fig. 2. **a** Skin biopsy showing hyperkeratosis, acanthosis and full-thickness atypia of the epidermis (H&E, $\times 100$). **b** High-power view of prominent nucleoli and pleomorphic atypical cells (H&E, $\times 400$).

Seok et al.: Squamous Cell Carcinoma and Multiple Bowen's Disease in a Patient with a History of Consumption of Traditional Chinese Herbal Balls

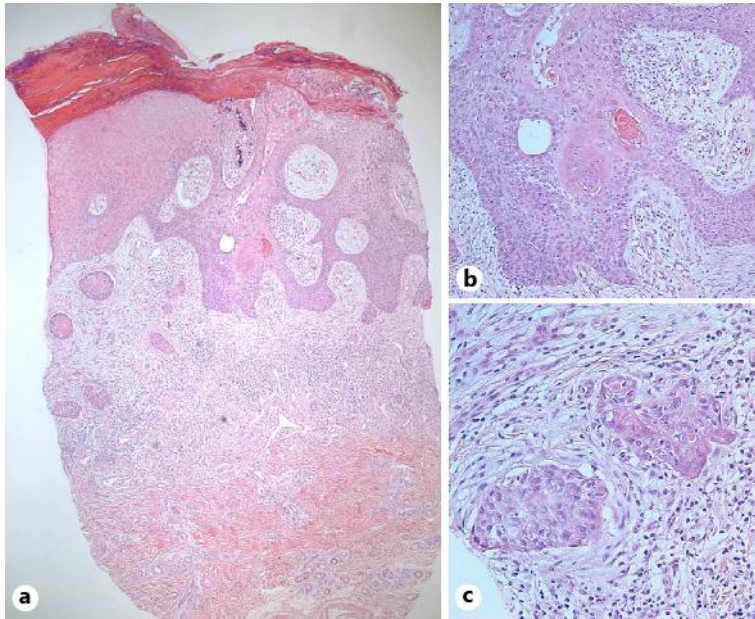


Fig. 3. **a** Skin biopsy showing hyperkeratosis, acanthosis and inflammatory cell infiltration throughout the dermis (H&E, $\times 100$). **b** High-power view of atypical cells of prominent nucleoli throughout the epidermis (H&E, $\times 200$). **c** Higher magnification showing malignant tumor cell nests with an irregular border in the dermis (H&E, $\times 400$).