

# Multiple cutaneous carcinoma arising from arsenic-containing traditional Chinese medicine in a patient with psoriasis: A case report

Wenyi Li <sup>a</sup>, Xue Li <sup>a</sup>, Chuanjie Xu <sup>b</sup>, Songjia Sun <sup>a</sup>, Chunli Yao <sup>a,\*</sup>

<sup>a</sup> Department of Dermatology, The Second Hospital of Jilin University, Changchun, 130041, China

<sup>b</sup> Department of Pathology, The Second Hospital of Jilin University, Changchun, 130041, China

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## ABSTRACT

**Background:** Arsenic exposure is closely related to keratosis and cutaneous carcinoma, but a few studies have focused on patients with psoriasis presenting carcinoma after long-term medication of arsenic-containing traditional Chinese medicine (TCM).

**Case description:** We presented a psoriasis patient showing multiple cutaneous carcinoma arising from arsenic containing TCM. A 60-year-old gentleman with psoriasis for nearly 30 years presented to our department with severe keratosis in hands, trunk and feet. He received oral administration of realgar (with As<sub>4</sub>S<sub>4</sub> as the major component) for at least 15 years. There were keratotic plaques, ulcer and exudate in the middle finger and forefinger of left hand, and middle finger, forefinger and ring finger of the right hand. Moreover, brown papule was seen in right sole, together with keratotic plaques and ulcer in the left heel. Pathological analysis revealed basal cell carcinoma (BCC) in the anterior chest, right hand and right foot, Bowen disease in left hand and right hand, as well as squamous cell carcinomas (SCC) in right hand.

**Conclusion:** This is a rare arsenic-exposure psoriasis patient showed coexistence of Bowen disease in left hand and right hand, BCC in the thoracic site, right hand and right foot, as well as SCC in right hand.

## 1. Introduction

Psoriasis, characterized by erythematous plaques covered with silvery scales, is a multisystem inflammatory condition that predominantly involves the skin tissues. Unfortunately, there is no curative method for such condition despite the availability of a variety of treatment options such as topical vitamin D3 analog, photodynamic therapy (PDT), as well as topical corticosteroid [1]. To date, most arsenic-based drugs have been abandoned with the discovery of antibiotics since 1940s, and a few novel arsenicals are still utilized in combination with traditional Chinese medicine (TCM), serving as valuable alternatives for treating psoriasis [2,3].

Although arsenicals are suitable alternative in treating psoriasis, its toxicity should not be neglected. Arsenic ingestion triggers pigmentary changes in the skin of the trunk and extremities. Usually, skin lesions are acknowledged as the first sign for arseniasis, based on a survey involving the patients drinking arsenic-containing water in US, India, Bangladesh, Chile, Nepal, and China Taiwan

\* Corresponding author. Department of Dermatology, The Second Hospital of Jilin University, No. 218 Ziqiang Street, Nanguan District, Changchun, 130041, China.

E-mail address: [ycl@jlu.edu.cn](mailto:ycl@jlu.edu.cn) (C. Yao).

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[4–9]. With increased seeking out complimentary medicine, the use of arsenicals and its potential consequences should be considered. To date, a few studies have reported patients with psoriasis presenting carcinoma after long-term medication of arsenic-containing TCM. For instance, Zhu et al. reported a patient with psoriasis died from verrucous carcinoma due to arsenic ingestion [10]. Siefring et al. reported a chronic plaque psoriasis patient developing rapid onset of squamous cell carcinomas (SCC) that may be associated with the use of arsenic-containing TCM [11]. To our best knowledge, rare patients present multiple cutaneous carcinoma in a single patient after taking arsenic-containing herbal medicine. In this study, we reported a very rare psoriasis patient showing concurrent Bowen disease, basal cell carcinoma (BCC), and SCC after taking arsenic-containing TCM.

## 2. Case presentation

A 60-year-old gentleman presented to our department with psoriasis for nearly 30 years. He reported oral administration of realgar (with  $As_4S_4$  as the major component) for at least 15 years. On physical examination, diffused rain-drop like pigmentation was noticed in his trunk. A dark-red plaque with a size of  $5.0\text{ cm} \times 3.0\text{ cm}$  was seen in the skin tissues of left thoracic part, in which fine scales in a yellow-white color at the central part combined with enlarged capillaries (Fig. 1). There were keratotic plaques, ulcer and exudate in the left hand (middle finger and forefinger) (Fig. 2A and B) and right hand (middle finger, forefinger and ring finger) (Fig. 2C and D), respectively. Brown papule was seen in right sole, together with keratotic plaques and ulcer in the left heel (Fig. 2E and F). Keratosis was seen in neck, hands and feet and the histology of the keratitis lesions was only available in the neck (Supplementary Fig. 1). For the treatment, Mohs surgery was performed to the involved sites. Postoperative analysis indicated BCC in the thoracic site (Fig. 3A), right hand and right foot, Bowen disease in left hand and right hand, as well as SCC in right hand (Fig. 3B–F). The patient was lost in the follow-up as he refused to receive further treatment for financial causes. The study protocols were approved by the Ethical Committee of The Second Hospital of Jilin University.

## 3. Discussion

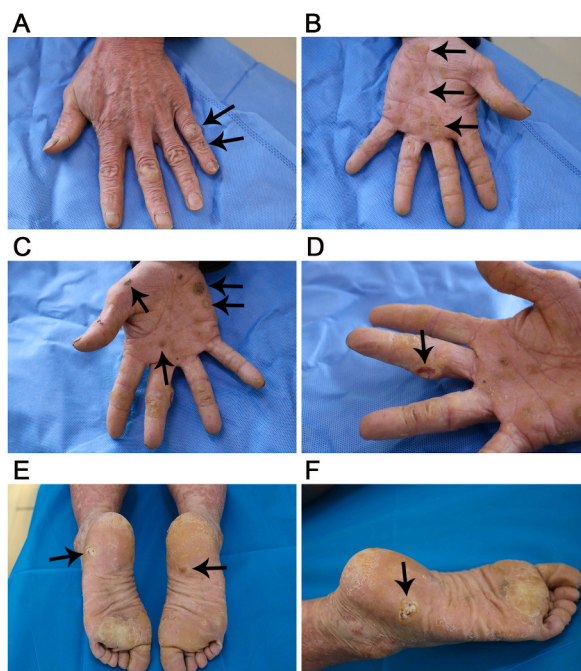
Arsenicosis, as defined by the WHO, is “a chronic health condition arising from prolonged ingestion of arsenic above the safe dose for at least 6 months, usually manifested by characteristic skin lesions of melanosis and keratosis, occurring alone or in combination, with or without the involvement of internal organs [12]. In clinical practice, its diagnosis is mainly based on the distinct cutaneous manifestations, including characteristic pigmentation in a rain-drop appearance and palmoplantar keratosis [13]. The majority of patients with arsenicosis would present cutaneous lesions characterized by thick, hard, rough hyperkeratotic skin in the palm and sole. Besides, they also present diffused, mottled pigmentation in a rain-drop appearance on covered areas mainly of the chest, back, and limbs. Based on the dermal hyperpigmentation and hyperkeratosis at palms and the feet, the patient in this study was diagnosed with arsenicosis. This case highlighted that the dermatologist should be aware of cutaneous manifestation of chronic arsenicosis.

Arsenic exposure has been well acknowledged to induce skin cancer [14], with Bowen’s disease, BCC and SCC as the most common types [15]. Hyperkeratosis has been described to give rise to the majority of arsenic-induced skin cancer [16]. In this case, the patient was diagnosed with concurrent keratosis and cutaneous cancer in palm and sole simultaneously. Indeed, the palm and sole are the major sites for keratosis. In a previous study, based on samples from the palms of subjects with arsenic keratosis and arsenic-exposed subjects without lesions, Guo et al. reported the high possibility of keratosis in palm and sole was closely related to the down-regulation of desmoglein 1 (DSG1), and up-regulation of keratin 6c (KRT6C) and fatty acid binding protein 5 (FABP5), respectively [17]. Although the evidence is not strong and further studies are needed to investigate the roles of these markers in skin pathogenesis under arsenic exposure, this can help to explain the high possibility of keratosis and skin cancer in the sole and palm.

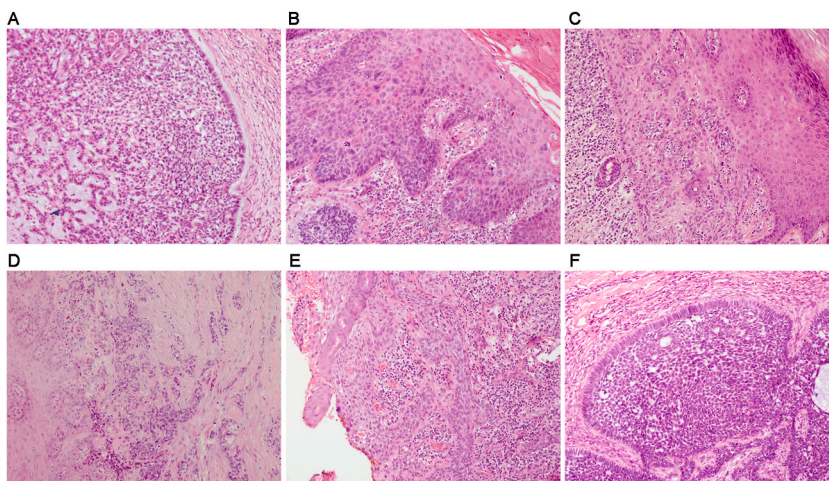
Rare cases showed simultaneous concurrence of Bowen’s disease, BCC and SCC, with most of them showed keratosis combined with single or two conditions. For instance, two studies reported patients with keratosis combined with BCC [18], or SCC [11], respectively.



**Fig. 1.** Diffused rain-drop like pigmentation was noticed in his trunk. A dark-red plaque with a size of  $5.0\text{ cm} \times 3.0\text{ cm}$  was seen in the skin tissues of left thoracic part, in which fine scales in a yellow-white color at the central part combined with enlarged capillaries.



**Fig. 2.** Keratotic plaques, ulcer and exudate in the left hand (A, B) and right hand (C, D). Brown papule was seen in right sole, together with keratotic plaques and ulcer in the left heel (E, F).



**Fig. 3.** Pathological findings for the involved lesions. (A) BCC in the thoracic site, under a magnification of  $40\times$ ; (B) Bowen disease in left hand; (C) Bowen disease in the forefinger of right hand; (D) SCC in middle finger of right hand; (E) BCC in right finger. (F) BCC in right foot. The images in (B) to (F) were observed under a magnification of  $100\times$ .

To our best knowledge, only one study reported the coexistence of these three conditions in a patient with 70-year-old Caucasian gentleman employed in the field of anticryptogamic pesticides (containing lead arsenate) [19]. In mainland China, arsenic-containing TCM is still used for treating psoriasis despite its reported toxicities [20]. According to our clinical experiences, some patients were diagnosed with cutaneous lesions and even malignancies after receiving arsenic medicine for treating psoriasis (data not shown). Our patient showed coexistence of BCC in the thoracic site, right hand and right foot, Bowen disease in left hand and right hand, as well as SCC in right hand, respectively.

For the treatment of psoriasis patient with arsenic keratosis, the cessation of arsenic was recommended. In addition, DMPS (sodium 2,3-dimercaptopropane-1-sulfonate) was recommended to chelate with the arsenic to form atoxic sulfhydryl compounds, which facilitated to the discharge of the arsenic compound. Some agents such as tretinoin [21], retinol [22], nicotinamide [23] and selenium [24] may contribute to the attenuation of keratosis. For the patients suspected with cutaneous carcinoma, pathological analysis is still

the gold standard for the diagnosis. Upon confirmation of Bowen disease, SCC or BCC, Mohs surgery was recommended, followed by close follow-up every three months together with regular color Doppler ultrasonography on the lymph nodes and abdomen. As the palm and soles are the commonly involved sites of arsenic keratosis, skin graft is necessary after taking the difficulty of incision suturing and repeated pathological analysis into consideration. Additionally, there would be a high possibility of recurrence, and PDT is a promising alternative for the treatment. For the patients with severe cutaneous lesions in palm and sole, carbon dioxide laser combined with PDT may contribute to the attenuation of the symptoms.

Our study has some limitations. In this study, we could merely provide clinical and histological data to support the diagnosis. However, we could not provide the evidence for long-term arsenic exposure based on nail or hair samples as the patient was lost in the follow-up.

#### 4. Conclusions

We reported a rare patient showed coexistence of Bowen disease in left hand and right hand, BCC in the thoracic site, right hand and right foot, as well as SCC in right hand after taking arsenic-containing TCM for treating psoriasis. We hope to raise the attention on the arsenic toxicity, especially those with a long-term history of taking realgar-containing medicine for treating psoriasis in mainland China.

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#### Ethics declarations

This study was reviewed and approved by the Ethical Committee of The Second Hospital of Jilin University, with the approval number: SB2020-139. The patient provided informed consent to participate in the study. The patient provided informed consent for the publication of their anonymized case details and images.

#### Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Acknowledgements

Not applicable.

#### List of abbreviations

PDT	photodynamic therapy
SCC	squamous cell carcinomas
BCC	basal cell carcinoma
DSG1	desmoglein 1
KRT6C	keratin 6c
FABP5	fatty acid binding protein 5

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2023.e22699>.

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