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Case Report

Arsenical keratosis caused by medication: a case report and literature

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Abstract: Medication-induced arsenical keratosis is a rare type of arsenical keratosis. We describe here a case of 70-year-old man to explore the clinical characters, diagnosis and treatment of medication-induced arsenical keratosis in order to improve the understanding of this disease and reduce the misdiagnosis rate. The clinical characters, signs, lab findings as well as progression, diagnosis and treatment in the case of arsenical keratosis were analyzed. The patient of medication-induced arsenical keratosis suffered from chronic eczema. He has taken realgar during the treatment. His medication caused arsenical keratosis. Medication-induced arsenical keratosis is rare. Making the medication history clear and using urine arsenic detection if necessary are of significance to understand the patients' condition. It is quite effective that using Sodium Dimercaptosulphonate during the treatment without delay.

Keywords: Herbal medication-induced, arsenical keratosis, arsenic trioxide

Introduction

Long-time exposure to arsenic pollution is the major cause of chronic arsenic poisoning. Being affirmed as one blastomogen by International Agency for Research on Cancer (IARC) and US Environment Protection Agency (EPA), the utilization of arsenic is strictly limited. Chronic arsenic poisoning caused by drug is rarely reported in western countries. Realgar has the effect of detoxification, eliminating dampness, relieving itching and removing putrefaction in Traditional Chinese medicine, so it is used to treat chronic skin diseases. However, since it contains arsenic compound, a few patients taking medicine containing realgar can be poisoned by arsenic and suffer from secondary arsenical keratosis. The clinical manifestation of the patients is worsening primary erythra which can lead to misdiagnosis. In this paper, we report a case of drug-induced arsenical keratosis and review the literature, aiming to improve the clinical understanding of herbal medication-induced arsenical keratosis.

Case report

The patient is a male farmer at the age of 70. He has never been engaged in any toxic or harmful work, nor arsenic ore smelting operation in his place of residence. The patient has been suffering from rash with pruritus for more than one year, followed by exacerbation with chromatosis for two months. This patient came to our hospital on May 17th, 2013. Red maculopapule appeared and worsened gradually at the beginning of 2012 and was diagnosed as "skin chronic eczema". The effect of external application of glucocorticoid is not evident. Two months before being hospitalized, he began to take traditional Chinese medicine. Instead of becoming better, it went worse: more rashes appeared and chromatosis with diffuse verrucous hyperplasia as big as granule or mung bean and Mees' lines appeared on finger nails (**Figures 1**, **2**). External application of glucocorticoid and antihistamine has no effect. Laboratory examination: urine arsenic test: 232 μg/L (reference value 2.62~22.7 μg/L), blood routine examination: blood platelet 69×109/L↓ and others normal, liver function: Alanine Aminotransferase (ALT) 26 U/L, Alkaline Phosphatase (ALP) 173 U/L↑, γ-glutamyl transpeptidase (GGT) 128 U/L↑, α-hydroxybutyric dehydrogenase (HBDH) 203 U/L↑, abdomen CT: diffuse enlargement and ascites formed in liver. After being hospitalized, the traditional Chinese medicine was

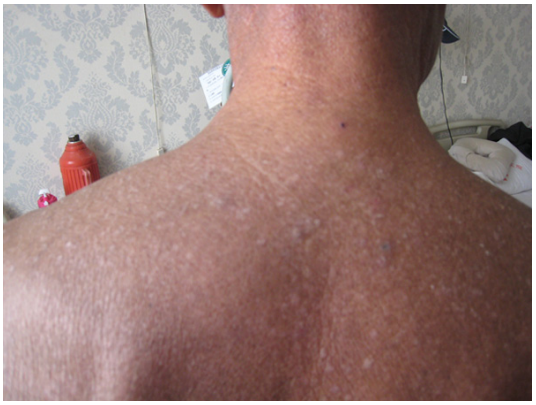

Figure 1. More rashes appeared and chromatosis with diffuse verrucous hyperplasia as big as granule or mung bean.

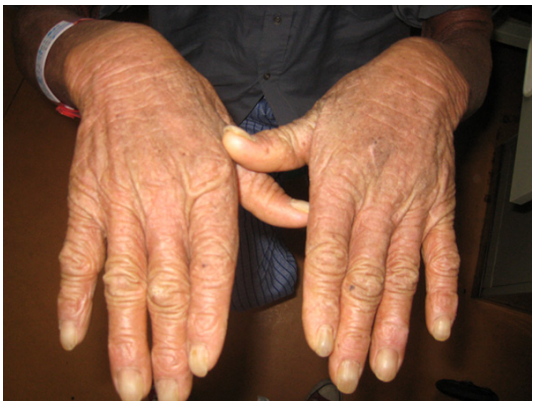

Figure 2. Mees' lines appeared on finger nails.

replaced by 0.25 mg Sodium Dimercaptosulphonate once a day (3 days is a course of treatment). We conducted two courses of removing arsenic treatment. After the first course, the urine arsenic was re-examined as 686 μg/L and after the second one, it was 76 μg/L. Because of personal reason, the third course was not conducted. After two courses of removing arsenic treatment, the pruritus was eased. Desquamation appeared on hands and no verrucous hyperplasia was observed on new skin. Abdomen B-ultrasound showed that dropsy disappeared. Blood routine examination showed that blood platelet was 108×10^9/L and liver function showed that ALP 60 U/L and GGT 102 U/L, and all indicators were improving. The patient is now in follow-up.

Discussion

Before Western medicine was introduced in China, traditional Chinese medicine played an important role in curing diseases and arsenic compound was widely used in treatment of many diseases such as dermatosis, nosohemia and trypanosomosis [1]. Zhang et al. in 1970 applied white arsenic in the treatment of leukemia and achieved satisfying curative effect [2]. Li et al. have found that arsenic trioxide (As_2O_3) is effective in the treatment of airway hyperresponsiveness [3]. All these divert scholars' attention to the mechanism of arsenic compound in human body. Many studies have revealed that arsenic compound can accelerate cell differentiation, induce apoptosis, inhibit tumor growth [4-6], thus in September of 2000, arsenic trioxide was approved to be used in the treatment of acute promyelocytic leukemia [7]. Pharmacology effect of arsenic compound being affirmed makes arsenic compound applied in many clinical filed, especially in some refractory chronic diseases.

However, as a toxic substance, the toxic reaction of arsenic compound in the treatment process attracts the attention of medical workers. If the long-term intake of traditional Chinese medicine containing arsenic reaches the toxic dose of arsenic, it will lead to excessive proliferation of skin keratinocyte, chromatosis, verrucous hyperplasia, Mees' lines or coilonychia on finger nails and skin keratosis [8, 9]. Hyperkeratosis and inflammatory cell infiltration will be observed. Khandpur has reported the case of curing arseniasis secondary skin lesion caused by epilepsy with the application of arsenic compound [10]. In China, many cases of applying traditional Chinese medicine containing arsenic compound in the treatment of skin diseases, such as psoriasis, leucoderma, arseniasis and arsenical keratosis have been reported [11, 12]. Drug-induced arseniasis and arsenical keratosis caused by the treatment of refractory chronic eczema and allergic dermatitis have been found in clinical practice. These patients began treatment because of chronic skin lesion, and at the early stage of arsenic compound poisoning, it is regarded as the poor effect of primary disease treatment, so the illness will become more serious. In addition to secondary typical skin lesions, arsenic compound poisoning can cause other system damages such as peripheral neuritis and cognitive function loss caused by damage in nervous system, peripheral neuritis, liver func-

tion lesion and emesis from digestive system lesions. Moreover, it can also lead to the reduction of blood platelet. Therefore, medication history should be firstly understood during the treatment. If arsenic compound has been used and skin lesion with damages on organs worsened, it is likely that the arsenic compound poisoning is the major cause and arseniasis will be diagnosed if the content of arsenic in patient's urine increases.

After that, Sodium Dimercaptosulphonate should be applied in removing arsenic. Studies have revealed that Vitamin C and E are antagonistic to cellular oxidation damage caused by arsenic poisoning [13-15] and the application of selenium (a microelement) can improve humans' ability of excreting arsenic [16].

Traditional Chinese medicine is mild in nature with fewer toxic and side effects and the dosage is dependent on clinical experience. Drug-induced arsenic compund poisoning may be caused by the long-term intake of traditional medicine for curing chronic dermatosis. Studies have revealed that 1 μM arsenic trioxide can cause cellular oxidation stress damage [17] and lont-term drinking water containing arsenic compound above 30 μg/L can increase the risk of cancer [18]. Therefore, the dosage of arsenic compound should be strictly limited in the treatment and the toxic effects should be observed. The pharmacological effects of toxic medicine will be optimized and intoxication accident will be avoided if the benchmark dose is inspected.

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Disclosure of conflict of interest

None.

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