Chronic Arsenicism and Multiple Skin Cancers

Waranya Boonchai, M.D.* Sorawuth Chu-Ongsakul, M.D.** Vutisiri Veerasarn, M.D.*** Summon Chomchai, M.D.****

*Department of Dermatology, ** Department of Surgery, *** Department of Radiology, **** Department of Preventive and Social Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Abstract: We report a case of skin cancer who presented with an ulcerated nodule at left arm and finger. The patient was previously diagnosed Bowen’s disease at left calf one year ago, skin cancer at hand and foot nine years ago. He also received herbal medicine every month for 1 year since 50 years ago for herpes treatment. Multiple skin cancers were suspected to be induced by chronic arsenicism. High level of arsenic was identified from nails. Bowen’s disease at finger was treated with CO2 laser and squamous cell carcinoma at left arm was removed by surgical excision. Chronic arsenicism was treated by supportive care.

Key words: chronic arsenicism, skin cancer, Bowen’s disease

Multiple skin cancer including Bowen’s disease (BD), squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) are induced by several factors. One of the most common causes is chronic arsenical poisoning. Arsenic is an abundant element in the earth’s crust. It was once widely used as a medication to treat syphilis and many skin conditions. Nowadays, arsenic is increasingly used in the microchip industry; it is also used as a pesticide in ant killers and pressure treated wood. Arsenic might be exposed by industrial emissions via water from direct contact with geologic arsenic, via soil contaminated by pressure treated wood and via diet, primarily seafood, which is a minimal toxic form. Chronic arsenic toxicity may induce vascular effects by endothelial destruction, artherogenesis and carotene and zinc deficiency, ultimately causing a deficit of capillary blood flow. In addition, DNA repair which is arsenic-induced, combined with such carcinogens as sunlight may cause skin cancer1. Here we report a case of chronic arsenic exposure associated with skin lesions. The investigation and management are to be discussed.

CASE REPORT

A 79-year-old Thai man was presented with a progressive enlarged ulcerated nodule on his left arm and an erythematous rash on the left middle finger. About 1 year prior to this admission, he had a chronic ulcer and was diagnosed as having Bowen’s disease from another hospital and treated with irradiation. A physical examination revealed rain-drop hypo and hyperpigmentation on the trunk (Fig 1.), palmoplantar punctuate keratosis on both sides, and the erythematous keratotic papules at the back, forearms and leg. There were ulcerated nodules 4x5 cm on the left arm (Fig 2.), an erythematous scaly plaque on the left middle finger (Fig 3.), back and left arm and hyperpigmented, pearly-border plaque on the right forearm; inguinal lymph nodes of 1x1 cm. were palpable without tenderness on both sides. The complete blood count, blood chemistry, chest radiography and bone scan showed normal findings. Arsenic level from nails was higher than normal [4.124 mcg/g, normal 3 mcg/g] but from pubic hair the level was normal.

The patient was treated by surgical modalities. A biopsy-proven SCC from the left arm nodule was removed by surgical excision and a biopsy-proven BD rash on the left middle index was treated by carbon dioxide laser.

DISCUSSION

Skin manifestations in chronic arsenicism include pigmentary anomalies, arsenical keratoses, Bowen’s disease, squamous cell carcinoma and basal cell carcinoma.25 Pigmentary anomalies are found in 90% of exposed patients. It is a sensitive marker only in certain ethnic groups. The lesion looks like a “rain - drop in the dust” and localizes in unexposed parts such as the trunk and buttocks5.

Arsenical keratoses are found in 80-100% of the patients. The latency period for development is 2-30 years, depending on dose, source of arsenic and race. The lesion is a small verrucous punctiform papules without peripheral inflammation. The size is about 0.2-1 cm. in diameter. It is most frequently found on the palms and soles. The important marker for chronic arsenicism is palmoplantar arsenical keratoses. This lesion can evolve into squamous cell carcinoma after a latency of 10 years with low incidence of metastasis25.
Chronic Arsenicism and Multiple Skin Cancers

Bowen’s disease or intraepidermal carcinoma or in situ squamous cell carcinoma is usually multifocal and randomly distributed but is more commonly found on the trunk. The lesion is erythematous, crusted, fissured, keratotic, round plaques, with or without ulceration. The size is about 0.1 - 10 cm. The occurrence of palmoplantar Bowen’s disease would suggest a diagnosis of chronic arsenicism. The mean latency period for development varies from 10 to 40 years.

SCC can arise in antecedent arsenical keratoses, Bowen’s disease or de novo. The prevalence is 20 - 40%. The lesion is more common in non sun-exposed areas. Arsenic - induced SCC is much more aggressive than sun-induced SCC. SCCs which arise from BD are more aggressive than those from arsenical keratoses. Fatal metastases from arsenic - induced SCC have been reported.

BCC is most commonly found on the trunk and is multiply distributed. The histopathology of arsenic-induced BCC is not different from that of sun - induced BCC but the superficial type is the most common. The prevalence of arsenic - induced BCC is 6 - 20%.

A past history of prolonged ingestion of herbal medicine for herpes treatment might induce chronic arsenic poisoning which is associated with several malignancies including adenocarcinoma and liver, skin, and bladder cancer. Arsenic levels can be investigated from blood, urine, hair and nail. Arsenic in blood has a very short half - life; the blood level returns to a normal range within 24 hours. The diagnosis of acute, subacute and chronic poisoning is summarized in Table 1. This patient was exposed to arsenic 50 years ago; the high arsenic level in his nails supported the diagnosis. However, chronic arsenic poisoning could not be excluded if there was a negative finding.

Management of this patient consisted of management of arsenic poisoning and management of skin cancer. Management of arsenic poisoning depended on the phase of exposure. Treatment of acute poisoning included decontamination, chelation and supportive care. Decontamination is not necessary in the subacute phase of chronic poisoning; only supportive care was needed in treating this patient.

Management of arsenic-induced skin cancers consists of medical, surgical and radiation treatment. The first line of treatment for multiple and recurrent skin cancers is medical treatment which is available in topical and systemic forms. Imiquimod is the topical immunotherapy in the imidazquinolone group which is also antiviral, antitumor and immunomodulator. Imiquimod was reported effective in the treatment of actinic keratoses, Bowens diseases and basal cell carcinoma. Systemic retinoids such as Etretinate and Acrinet are also effective in chemotherapy of precancerous disorders and chemoprevention of new skin cancer in patients prone to the development of multiple tumors just as it was in this patient. Its beneficial effects persist only as long as therapy is maintained. The predictable dose-related side effects and chronic toxicity limit their use for long - term therapy.

Surgical treatment of skin cancer should be considered if an oncological safety margin could be obtained, i.e., complete tumor removal, maximizing a curative outcome and lessening the chance of recurrence. Optimized tissue preservation to achieve minimal compromised function and acceptable cosmetic effect should also be considered. Surgical management includes field destructive therapies, surgical excision and Mohs micrographic surgery.

Field destructive therapies are best preserved for superficial tumors of the trunk and extremities. Tumor and surrounding non cancerous tissue are superficially damaged by using electrodessication and curettage, cryosurgery and laser. Healing occurs by second intention. The disadvantage of this technique is that no specimen is available for an evaluation of histology and margin. Surgical excision is suitable for a tumor which is extended deeper beyond the dermal junction and requires tissue for histological diagnosis. Mohs micrographic surgery is indicated for a tumor with a high risk of local recurrence, a tumor in irradiated areas or conservative areas, a recurrent tumor and tumor with an ill - defined margin.

Radiotherapy is indicated for a large lesion of more than 2 cm. in diameter, deep tissue infiltration, multiple lesion, for elderly or inoperable patients, for cosmetic results of the eyelids, nose, external ear and postoperative lymph node involvement, positive resected margin or perineural invasion. Radiation is contraindicated in bone or cartilage involvement, for young patients and for cosmetic results. The purpose of radiotherapy is to eliminate or shrink a localized cancer by inducing cancer cell death since possible healthy tissue suffers little damage and subsequently completes the repair. Radiation treatment can be used as single or combined modalities with other options.

CONCLUSION
We report a case of a patient with multiple skin cancer and a history of chronic arsenism from prolonged use of herbal medicine 50 years ago. Arsenic level was detected from the nails. Skin cancer on the left arm and finger were successfully treated by surgical excision and CO\textsubscript{2} laser.

COMMENT : From Head of Department of Dermatology
The major aspect in the management of this patient is patient education. All of the treatments in this patient were symptomatic. The patients who are exposed to arsenic should be educated so they can know about the clinical course of the disease. Periodic examinations and screening for precancerous lesions and malignancies on the skin and internal organs should be done. Unfortunately, this patient did not receive the correct information and screening for malignant skin lesions so the malignancies were detected late in their course. Most important of all is public education about the environmental source of arsenic, because prevention is better than cure in every disease, including arsenic poisoning.

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<th>Table 1. Diagnosis of arsenic poisoning at various phases.</th>
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<td><strong>History</strong></td>
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<td><strong>Clinical manifestations</strong></td>
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<td>GI symptoms Cardiac sign Peripheral neuropathy</td>
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<td><strong>Laboratory</strong></td>
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Chronic Arsenicism and Multiple Skin Cancers
REFERENCES