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Case Report

Metastatic testicular cancer in a patient with arsenical keratosis

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Abstract Arsenicosis is a multisystem disorder, with many cutaneous features. The cutaneous manifestations take the form of pigmentary changes, hyperkeratosis, and skin cancers (Bowen's disease, squamous cell carcinoma, and basal cell carcinoma). It is a known carcinogen and there is association between chronic arsenic exposure and malignancy of bladder, lung, liver, kidney and other visceral malignancies. Our patient came from an endemic area where levels of arsenic are high in drinking water and had features of arsenical keratosis for past fifteen years along with metastatic testicular cancer at the time of presentation. Arsenic exposure may increase the risk of testicular cancer.

Key words
Arsenic, testicular cancer, punctate keratoses.

Introduction

Arsenic was earlier used empirically for the treatment of a variety of diseases, including leprosy, syphilis, and yaws. The art of arsenic therapy suffered a blow when this metalloid was identified as the culprit for major public health problem after exposure via drinking water in the early 1900s in Argentina, Chile, Mexico, and Taiwan.[1] Arsenicosis is a chronic multisystem disorder, arising out of high levels of arsenic in the body and has been defined by the WHO working group as a chronic health condition arising from prolonged ingestion (not less than 6 months) of arsenic above a safe dose, usually manifested by characteristic skin lesions, with or without involvement of internal organs.[2] The safe dose is quantified by the "maximum permissible limit" of arsenic in consumed water, which differs in different countries.[3] Skin lesions are found to be the commonest and earliest manifestation in arsenicosis patients.[4] Arsenic has carcinogenic potential. Skin, lung, bladder, kidney, prostate, liver, uterus, and possibly lymphatic tissues are considered as sites for arsenic-induced malignancies, and the skin is thought to be, perhaps, the most sensitive site.[2,5]

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Case report

A 38-year-old male presented to the oncosurgery department with history of swelling in the scrotum and left leg for 2 years. Testicular carcinoma was suspected which was confirmed by histopathology of the specimen obtained from bilateral orchidectomy. X-ray chest had revealed cannon-ball opacities suggestive of pulmonary metastasis (**Figure 1**). CT scan of chest and abdomen revealed pulmonary metastasis and involvement of pre- and para-aortic lymph nodes. Post-surgery he was started on chemotherapy with bleomycin, etoposide and cisplatin which were given every 4 weeks. He was referred to dermatology OPD for cutaneous manifestations. A detailed history was taken and

Figure 1 X ray chest showing cannon-ball secondaries.

Figure 2 Palmar keratoses.

Figure 3 Plantar keratoses with tinea pedis.

Figure 4 The characteristic rain-drop pigmentation on the back.

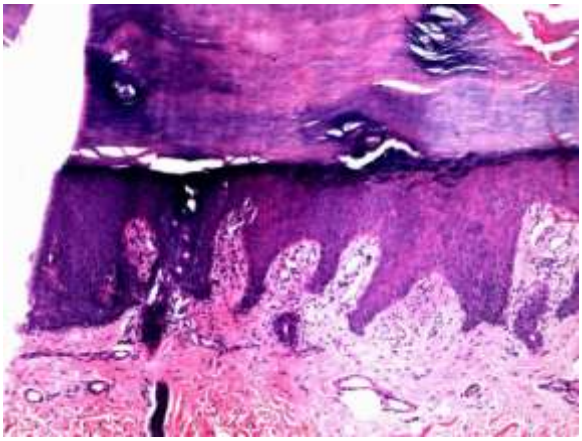

Figure 5 Histopathology showing epidermal hyperplasia, orthokeratosis, thickened granular layer and absence of inflammatory infiltrate.

thorough clinical examination was done. Patient complained of thickening of palms and soles and changes in skin color for 15 years.

Examination revealed multiple 5mm to 10mm keratotic papules on bilateral palms and soles (**Figure 2** and **3**). The lesions on the soles had coalesced to form thick plaques with superficial scales. There were hyperpigmented patches with small areas of hypopigmentation resembling raindrops in the dust mainly over the abdomen and back (**Figure 4**). Patient also had dry gangrene affecting few toes bilaterally. Patient came from an endemic area where arsenic levels are high in drinking water. Skin biopsy was taken from the sole of left foot which on histopathology revealed complete absence of

inflammatory infiltrate with moderate irregular epidermal hyperplasia, the granular layer was slightly thickened and the stratum corneum showed marked compact orthokeratosis with vertically oriented and spiralled acrosyringium, around which the orthokeratosis appeared blue. This had lead to alternating pink and blue type of orthokeratosis. A few fungal elements and cocci were also seen in stratum corneum (**Figure 5**). These features were consistent with arsenical keratosis with superimposed dermatophytosis.

Discussion

Arsenic is consumed mainly in 2 forms, arsenite (As^{+3}) and arsenate (As^{+5}). The absorption takes place mainly through ingestion of water, food, beverages, medicines, and sometimes, swallowing of the inhaled particulate matter with arsenic.[5] Skin lesions are found to be the commonest and the earliest manifestation in arsenicosis patients.[2] Prolonged ingestion of arsenic results in pigmentation, which is most intense on the trunk, which can be diffuse hyperpigmentation/melanosis or localized (or patchy pigmentation), particularly affecting skin folds.[6] Fine freckles of spotted pigmentary changes are also seen, known as *'raindrop pigmentation'*. Arsenic is known to be a carcinogen. Hypermethylation of DNA, particularly the promoter region, results in inactivation of the tumor suppressor genes involved in DNA repair, leading to uncontrolled cell proliferation leading to carcinogenesis. It has been suggested that the gene product or component within the ubiquitin system is targeted by arsenic, which results in alteration leading to genotoxicity and carcinogenicity.[8] Review of literature reveals that long-term arsenic ingestion can cause palmar and plantar keratoses and skin cancer, particularly basal cell carcinoma. It is suspected to cause visceral cancers.[9] Arsenic may play a role in testicular cancer.[10] In our patient, there was chronic exposure to arsenic with development of many features of arsenical keratoses and subsequent development of testicular cancer.

References

1. Zaldivar R. Arsenic contamination of drinking water and foodstuff causing endemic chronic poisoning. *Beitr Pathol.* 1974;**151**:384-400.
2. *Arsenicosis. Case-Detection, Management and Surveillance. Report of a Regional Consultation*. New Delhi: WHO Regional Office for South-East Asia; June 2003.
3. Saha KC, ed. *Arsenicosis in West Bengal. 1st ed*. Kolkata: Sadananda Prakashani; 2002. p. 11-52.
4. Khan MM, Sakauchi F, Sonoda T *et al*. Magnitude of arsenic toxicity in tube-well drinking water in Bangladesh and its adverse effects on human health including cancer: evidence from a review of the literature. *Asian Pac J Cancer Prev.* 2003;**4**:7-14.
5. Gomez-Caminero A, Howe P, Hughes M *et al*. Kinetics and metabolism in laboratory animals and human. Arsenic and arsenic compound. Environmental health criteria 224. International Programme on Chemical Safety. Geneva: World Health Organization; 2001. p. 112-67.
6. Tay CH. Cutaneous manifestations of arsenic poisoning due to certain Chinese herbal medicine. *Australas J Dermatol*. 1974;**15**:121-31.
7. Rossman TG, Wang ZL. Expression cloning for arsenite resistance resulted in isolation of tumor suppressor fau cDNA: possible involvement of the ubiquitin system in arsenic carcinogenesis. *Carcinogenesis.* 1999;**20**:311-6.
8. Ahmad Y. The largest mass poisoning in recorded history. *Int Health.* 2004;**82**:57-8.
9. Rosset M. Arsenical keratoses associated with carcinomas of internal organs. *Cancer Med Assoc J*. 1958;**78**:416-9.
10. DuMond JW Jr, Singh KP. Gene expression changes and induction of cell proliferation by chronic exposure to arsenic of mouse testicular Leydig cells. *J Toxicol Environ Health A*. 2007;**70**:1150-4.