ARSENICOSIS- A RARE CASE REPORT

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INTRODUCTION

Arsenicosis should be considered in the dermatologic patient presenting with leukomelanoderma, punctate palmar keratoses and/or numerous non-melanoma skin cancers at a relatively young age. Arsenic ingestion is an important public health issue that should not be overlooked. The possible sources of arsenic vary in different localities. Agricultural workers may be exposed to arsenic salts used as a fungicide, weedkiller, sheep dip or pesticide, and they frequently take inadequate precautions against accidental ingestion or inhalation. It may be a hazard in smelting and other industrial processes. In some countries, notably parts of Argentina, Bangladesh and Taiwan, the water supply has been contaminated.1

CASE REPORT

History

A 60 year old male agricultural worker came to the skin outpatient department with complaints of thickening and roughness of the palms, soles, knee and elbow joints; and whitish and dark coloured skin lesion over the trunk, back, arms, forearms, thighs and legs. He also complained of dark coloured lesions over the tongue and skin lesions over the genitalia and perianal region and loosening of teeth, all of this approximately for a duration of 4 years. The patient was apparently normal 4 years back, he initially developed skin lesions over the arms and forearms that spread to the whole body. There is no history of pain or itching, history of exposure to agricultural pesticides, history of taking treatment for pulmonary tuberculosis for 6 months two years back, and gave history of long term homeopathic treatment for general well being and for the skin lesions, which was stopped after cutaneous lesions started increasing, history of smoking, quit two years back. Patient was nonalcoholic and denied any history of extramarital sexual exposure. There was no history suggestive of underlying malignancy. Family history failed to reveal any malignancy or any sign suggestive of arsenic toxicity.

Physical Examination

Systemic examination was unremarkable and vitals were stable. On cutaneous examination, pitted hyperkeratotic palmoplantar papules resembling syphilitic cornee, firm, spiny and pigmented in areas were noticed[Fig 1]. Multiple discrete keratotic pigmented papules and plaques seen over the dorsum of hands, knees, elbows and legs[Fig 2]. Hypopigmented macules with a background of diffuse pigmentation is seen over the chest, back and thighs[Fig 3]. Diffuse pigmentation seen over the tongue and buccal cavity with loss of teeth. Broad, raised, gray, confluent, papular lesions over the anogenital areas resembling condyloma lata were noticed. Few erosions and ulcers with hypo and hyperpigmented macules were noticed over the penis [Fig 4].

Investigation

The following investigations were done -complete blood count ,liver function test, blood sugar, lipid profile, which had values within the normal limit. RPR was non reactive, TPHA and HIV I AND II were negative. Quantitative analysis of arsenic in hair was done which revealed 0.28 mcg arsenic/gram of hair (Reference Range:> 16 Yrs = 0-0.9 mcg/g of hair).

Histopathological Study

On histopathological examination, epidermis revealed hyperkeratosis, parakeratosis, acanthosis,full thickness cellular atypia with loss of normal maturation (wind blown pattern), cells appeared large , irregular, in size and shape, with large, dark, pleomorphic nuclei[Fig 5].

1. Fig.1: Multiple,small,firm,spiny, skin colored and pigmented keratotic papular lesions with few warty nodules on palms.
2. Fig. 2: Multiple discrete keratotic pigmented papules and plaques over the [A] dorsum of hand,[B] elbows and forearms, and [C]knees and legs.
3. Fig.3: Rain-drop pigmentation (discrete,numerous hypopigmented and few pigmented macular lesions) and leukomelanosis (few distinct hypopigmented
macules with a background of pigmented areas) over trunk.

4. Fig 4: [A] Spotted pigmentation on tongue with loss of teeth; and [B] spotted pigmentation with erosions and ulcers on penis and keratotic papular and nodular lesions over scrotum.

5. Fig 5: Histopathology of skin 5[A] H and E section of the skin (Magnification x100) showing hyperkeratosis, irregular acanthosis and inflammatory infiltrates in the dermis. 5[B]: H and E section of the skin (Magnification x 250) showing hyperkeratosis, parakeratosis, acanthosis and full thickness cellular atypia. 5[C]: Acanthotic epidermis showing full thickness cellular atypia with loss of normal maturation (Wind blown appearance). The cells appear large, irregular in size and shape with large dark pleomorphic nuclei. (H and E section, Magnification x400).
DISCUSSION

Arsenosis, as defined in a WHO field guide, ‘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.’

Both hyper and hypopigmented macule and/or patch, generally <1cm in size, few to numerous, occur commonly over trunk, arm and thigh but other areas like forearm, face, legs and genitalia are also found to be affected. Fine freckled or spotted melanosis known as “rain-drop pigmentation” and depigmented macules on normal skin or hyperpigmented background known as “leukomelanosis” are also seen in chronic arsenicosis. Diffuse or spotted pigmentation of oral mucosa; and diffuse pigmentation of palms, trunk and limbs are also known to occur.

Arsenical hyperkeratosis appears predominantly on the palms and soles. Keratoses are graded as mild, moderate, or severe depending on the extent and severity. In the early stages of keratosis (i.e., the mild variety), the involved skin has an indurated, gritlike character with papules less than 2 mm in size that can be best appreciated by palpation. In the moderate variety, the lesions usually advance to form raised, punctate, wartlike keratoses >2-5 mm in size that are readily visible. When the keratosis becomes severe, it may form keratotic elevations more than 5 mm in size and sometimes become confluent and diffuse and sometimes result in cracks and fissures too. Though palms and soles are primarily affected by hyperkeratosis, dorsa of the extremities and trunk may also be affected by it.

Other cutaneous manifestations reported are Mees lines (transverse white bands on finger nails), gangrene or ‘black-foot disease’ (peripheral occlusive vascular disorders) and peripheral neuropathy.
As mentioned above, any person with cutaneous manifestations of melanosis and keratosis should be suspected to have arsenicosis. Any history of exposure to known source of arsenic in atmosphere, soil, water, medications may help. Once suspected, arsenicosis is confirmed by laboratory methods.

There have been several methods described for the detection of arsenic in the samples (water, hair, nails, and urine), which include colorimetric methods, atomic absorption spectrometry, inductive coupled plasma (ICP) methodology, voltammetry, x-ray spectroscopy, hyphenated techniques, etc. Most of them suffer the inadequacy of being semi-quantitative or having low sensitivity. Presently atomic absorption spectrometry is considered the standard reference method because of its high specificity and sensitivity. Nails and hairs provide circumstantial evidence of arsenic exposure within the preceding 9 months.[5]

The WHO expert committee recommended that cutaneous markers of arsenicosis as identified by the expert dermatologist who can rule out other simulating conditions should be considered as ‘gold standard’ in case definition.[2] Clinical diagnosis, indeed by an expert dermatologist offers almost minimal error in fields with known history of contamination.

There is real dearth of reports regarding the types and patterns of histopathological changes in skin lesions of chronic arsenicosis.[3] The histopathological study from Bangladesh wherein hyperkeratotic lesions of 70 patients with chronic arsenicosis were compared with 20 controls, revealed hyperkeratosis (100%), parakeratosis (97%), acanthosis (95.7%), and papillomatosis (74%) to be significantly more ($P<0.001$) in the patients than in controls. They also found basal cell pigmentation in 42.8% ($P>0.05$) and dysplasia and malignant changes in 7% ($P>0.1$).[3]

Another study, also from Bangladesh, documented hyperkeratosis, parakeratosis, acanthosis, papillomatosis, hypergranulosis, and dysplastic changes to be the most important and constant findings; and on the other hand, basal pigmentation and dermal changes, to be the inconstant features.[6]

Study on the neoplastic manifestations of arsenicosis revealed pre-cancerous skin lesions in 6.6% and cancerous lesions in 0.8% of the patients.[5] Arsenical hyperkeratosis has been classified histologically into benign type A and malignant type B according to the absence or presence of cellular atypia.[5] None of the available studies focused on the histopathology of the pigmented lesions.

Arsenic exposure toxicity due to several medications including homeopathy has been reported in the past. Our case had both occupational exposure suggestive of arsenic toxicity and long term homeopathic medication in the past. Estimation of blood arsenic level was futile because it tends to normalize within a short span of 6 months after nil arsenic exposure. It is known that gradual improvement occurs in signs of chronic arsenicism over a period of 18 months if no further exposure to arsenic occur. However diffuse pigmentation may remain in such patients.

**CONCLUSION**

Arsenicosis is primarily diagnosed on the basis of its cutaneous manifestations, but the manifestations can, at times, be confused with other dermatoses. Histopathological examination plays a pivotal role in the final diagnosis of arsenicosis, in patients with history suggestive of arsenic exposure and characteristic cutaneous manifestations.

Our case is noteworthy for its unusual and widespread clinical presentation. Chronic arsenicism is a therapeutic dilemma and in paucity of clearcut guidelines for chronic arsenicosis, the present case raises a valid argument. Though the available literature indicates that serum arsenic level returns back to normal after a period of nil arsenic exposure, its noteworthy that the lesions of chronic arsenicosis may progress with time even if there is no further exposure to arsenic and diagnosis and treatment of arsenicosis requires multi-disciplinary input.

**REFERENCES**