CAN OPIUM CAUSE CHRONIC ARSENIC POISONING?

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INTRODUCTION :

More than 2400 years ago arsenic was used in Greece and Rome as a therapeutic agent and as a poison.[1] Hippocrates and Aristotle knew about the medicinal effects of arsenic. As early as the 17th century, arsenic was known to cause cancer. In modern times arsenic is a common environmental toxicant, found in soil, water, and air. Arsenic-related diseases are common in areas of the world where the drinking water has a high arsenic content.[2-7] In India more than 220000 people are said to be suffering from arsenic related diseases ranging from melanosis to skin cancer. At least 38 million people in eight districts and 830 villages are at risk in West Bengal state alone. The conditions in Bangladesh may be much worse. People with arsenical skin lesions have been identified in 18 of the 20 districts surveyed for arsenic patients.[8]

Acute arsenical poisoning may cause cerebral edema and is often fatal. In the past acute arsenical dermatitis occurred mostly from the treatment of syphilis with arsphenamine. Chronic arsenical toxicity is a systemic disease. Skin lesions include hyperpigmentation, focal "raindrop" depigmentation, hyperkeratosis of palms and soles, Mees transverse linear discolourations of nails, Bowen's disease, basal cell carcinoma, and squamous cell carcinoma. [9&10] There is also an increased risk of internal malignancies, especially of the lung and bladder. [5&6] Other manifestations of chronic arsenical toxicity are peripheral neuropathy, liver dysfunction, cardiopathy and gastrointestinal complaints. The blackfoot disease is an arsenic-related peripheral vascular disorder endemic in the southern coast of Taiwan, resulting in gangrene of the extremities. [11, 12]

Arsenic poisoning may be the result of ingestion or percutaneous absorption, [13] generally traced to contaminated water and food, environmental, occupational or medicinal exposures. Opium is not a widely recognized source of arsenical intoxication, although arsenic in opium has been used in many countries as an aphrodiastic and for treatment of diverse illnesses. [14-16] The effects of opium are essentially those of morphine but unexpected toxicities, such as esophageal cancer associated with "dross opium" and polyneuropathy due to deliberate addition of arsenic are problems in some specific regions. [17] Unpredictable ill effects of chronic opium usage are skin manifestations of chronic arsenic poisoning such as hyperpigmentation, keratosis and malignancies. [18]

This article reports two patients, both heavy chronic opium addicts of long duration, with skin manifestations of chronic arsenic poisoning including malignancies.

CASE 1 :

A 58-year-old male public-bath worker presented with hyperkeratosis and papillomatous plaques of the palms and soles (figures 1-3) of three years duration, which did not respond to the many topical karatolytic agents applied. He also complained of multiple scaling erythematous plaques on the trunk. He was a heavy opium addict both by smoking and ingestion with daily usage of 10-30 grams per day for about 30 years. He had worked for 20 years in public baths where a large amount of a traditional hair remover known as 'NOOREH' (composed mainly of calcium carbonate and arsenic) is used topically for removal of pubic hairs. He had hyperpigmentation mostly on the trunk and associated with "rain-drop" hypopigmented macules, palmoplantar keratosis and multiple erythematous scaling plaque also on the trunk (Figures 1-5). Histopathological examination of skin biopsies from right plantar plaques showed hyperkeratosis as well as Bowen's disease and squamous cell carcinoma (Figures 6-10). Abdominal sonography and CT scan revealed a mass in the lower pole of the left kidney which, on histopathological examination of the nephrectomy specimen, proved to be a renal cell carcinoma.

CASE 2 :

A 55-year-old female farmer, a heavy opium addict of 25 years, presented with multiple plantar corn-like lesions of about 5 years duration, some of

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Fig. 1.   Arsenical plantar punctate hyperkeratosis .

Fig. 2.   Arsenical palmar hyperkeratosis.

Fig. 3.   Arsenical palmar hyperkeratosis, note superficial ulceration of the skin of the inner aspect of the arm.Arsenical keratosis of the soles.

Fig. 4.   Arsenical Bowen's disease, chest wall.

Fig. 5.   Arsenical hyperpigmentation and " rain-drop" hypopigmentation on the back.
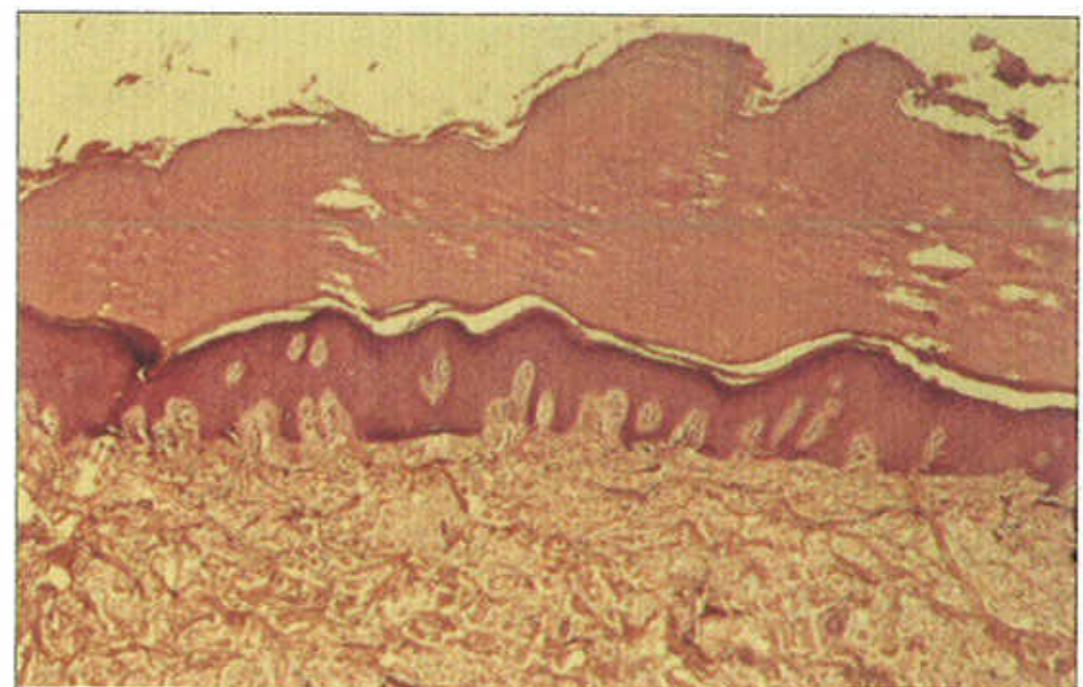

Fig. 6.   Hiatological appearance of arsenical keratosis of the palm. H&E.
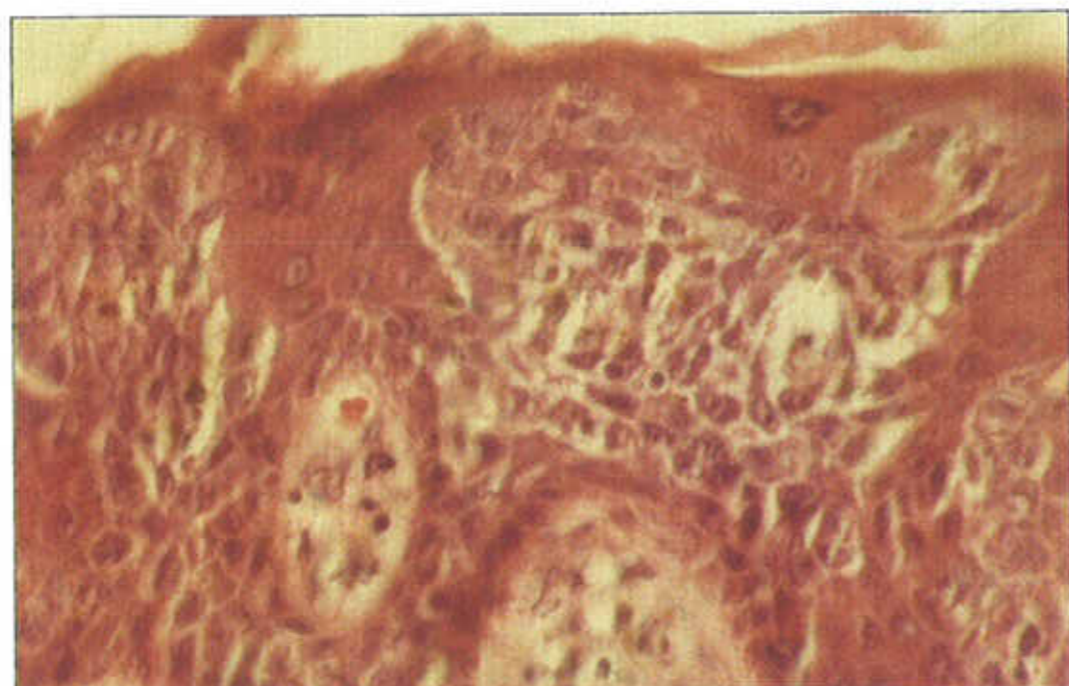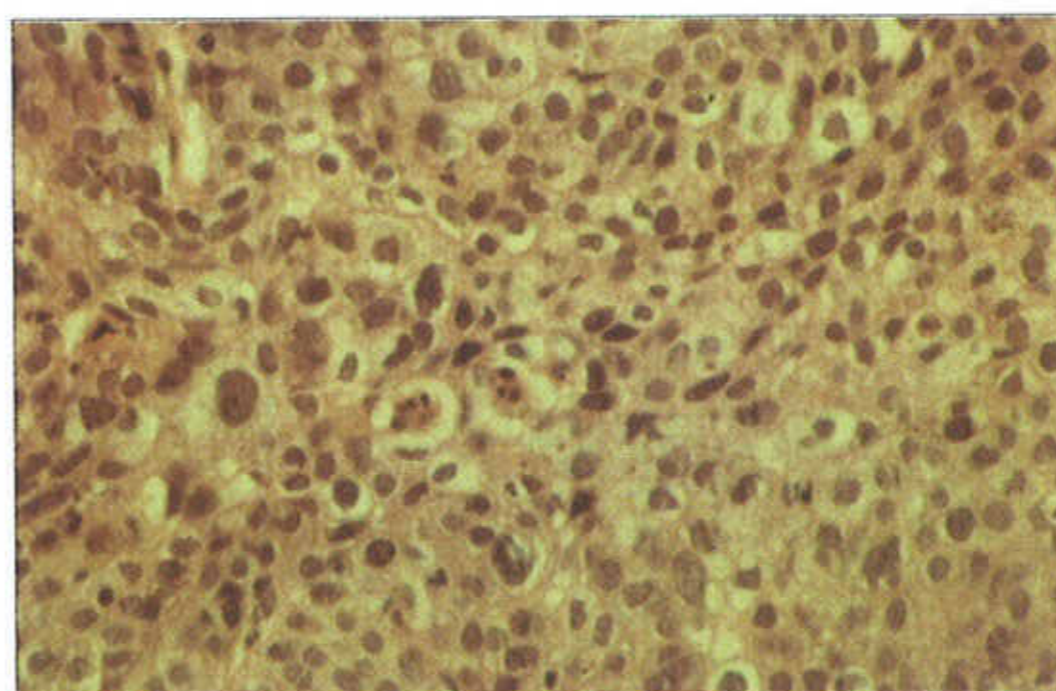
Fig. 7. *Arsenical dysplastic changes of the epidermis. H&E.*

Fig. 8. *Arsenical Bowenoid squamous cell carcinoma invading the dermis. H&E.Fig.*

9. *Higher power of arsenical Bowenoid invasive squamous cell carcinmoma. H&E.Fig.*

10. *Cytological details of arsenical Bowenoid invasive squamous cell carcinmoma. H&E.*

which were tender. Topical therapy for corns had produced no improvement. She had been a farmer for about 30 years, exposed to large amount of pesticides during her work without any protective coverings. Histopathological examination of the corn-like lesions showed squamous cell carcinoma. Multiple Bowen's plaque on the forearms and trunk and punctate palmar hyperkeratosis had been present for about 10 years. Measurement of arsenic by graphite-furnace atomic absorption spectophotometry showed a high serum arsenic level of >7.3 microgr/l and the arsenic content of nails and hair was more than normal controls. All other paraclinical work-ups were within normal limits.

DISCUSSION :

Arsenic is a common environmental toxicant (table 1) found in soil, water, and air. Well water in some parts of the world contains high concentrations of arsenic. Manufacture and application of arsenical herbicides and pesticides are major sources of occupational exposure in industrial and agricultural workers. [19] Fruits and vegetables sprayed with arsenicals may be a source of this element and it is concentrated in many species of fish and shellfish. Arsenicals sometimes are added to the feed of poultry and other livestock to promote growth. Arsenic is used as arsine trioxide in the manufacture of most computer chips using silicon-based technology. Galium arsenide is used in the production of compound semiconductors used in LEDs, lasers and solar devices. [1]

Arsenic may be absorbed after topical, respiratory or gastrointestinal exposures. It is excreted mainly by the kidneys but other pathways of excretion include the skin, hair, nails and Faeces. [20] The metabolism and toxicity of arsenic depend on whether it is organic or inorganic (pentavalent or trivalent), inorganic arsenic being the most potent tumorgenic form in humans . The arsenite ion (ASO2) generated by in vivo metabolism is thought to be responsible for the carcinogenic effect. [6, 21, 22] Diagnosis

of chronic arsenic poisoning is based on clinical presentation and laboratory findings. Analysis of tissues and body fluids can be difficult but arsenic persists in hair and nails.

Arsenical palmar and plantar keratosis usually takes many years to develop. In a follow-up study of 262 cases who had been taking Fowler's solution for 6 to 26 years, arsenical keratoses of the palms and soles were found in 40%, and arsenic-induced carcinomas of the skin in 8%. In the study from Taiwan, 80% of the 428 patients with arsenical carcinomas of the skin had arsenical keratosis of the palms and soles. [23] The minimal latent period between the beginning of arsenic intake and the onset of arsenical keratoses of the palms and soles has been found to be 2.5 years, and the average latent period 6 years. As the majority of these keratosis persist for years without malignant transformation, prophylactic removal does not appear justified. [6] Arsenical carcinomas of the skin are usually multiple and about three quarters are located on the trunk, but can arise on the palms and soles. The latency between the beginning of arsenic intake and the onset of cutaneous carcinoma has ranged from 3 to 40 years (average 18 years). [4]

Arsenic exposure has been associated with carcinomas of nasopharynx, esophagus, stomach, lung, bladder, kidney, prostate, [5] and hepatic angiosarcoma . [24] The latency period is long, ranging from 13 to 50 years (average 24 years). A recent study of the levels of arsenic in drilled wells in Finland did not find a statistically significant association with the risk of kidney cancer but arsenic levels were generally low. The same study found some evidence of an association between arsenic and the risk of bladder cancer but concluded that more studies are needed to confirm this association at such low levels of exposure. [25] Given the increased incidence of epithelial malignancies, patients with a history of arsenic exposure should be observed for a long time in order to detect early signs of cancer development.

Both of our patients had been exposed to dual potential sources of chronic arsenic toxicity related to their occupations and their opium addiction. The first case, a heavy opium addict of many years, had worked for 20 years in public baths where large amounts of a traditional hair remover 'NOOREH' which contains arsenic is used topically. He developed Bowen's disease and squamous cell carcinoma of the skin as well as a renal cell carcinoma. The second case, a farmer and also a heavy opium addict of long duration had been exposed to pesticides for 30 years and had a high serum level of arsenic. She developed multiple plaques of Bowen's disease and squamous cell carcinoma.

We were unable to obtain samples of opium used by our patients to analyse for arsenical content. However, we suspect that opium is a potential source of chronic arsenic toxicity in some regions. Opium used orally or by smoking has a long history of medical and social acceptance in many parts of the world. Major constituents of opium are morphine (10%), noscapine (6%), papaverine (1%), codeine (0.5%) and thebaine (0.2%) [26] but, in various places, opium is adulterated with arsenic in the belief that it is both a tonic and an aphrodisiac. [27] The arsenic content of opium measured in India ranged from 16.0 to 74.1 microgram per 100 g but the precise source of arsenic in opium could not be traced. It is, however, quite commonly used in India as an aphrodisiac and for treatment of illnesses of diverse nature. [15, 16] There is a need to investigate the arsenical content of opium used in other geographical regions in order to take the necessary steps for the prevention and treatment of long term opium addicts.

Table 1. Sources of cryptic arsenic exposure

Medicinal
       Chinese herbal balls, Fowler's solution
       Asiatic pills, Aphrodisiacs
       Poison (homocide, suicide)
Occupational
       Mining and smelting
       Wine-making, Carpentery
       Agriculture, Electroplating
       Computer chip production
       Fishermen (marine plywood,
        eating contaminated seafood)
Environmental
       Contaminated well water
       Burning plywood
       Contaminated shell fish
       "Moonshine" alcohol

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