

**Arsenic induced squamous cell carcinoma of skin – atypical presentation  
with aggressiveness.**

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**ABSTRACT**

A 68 year old gentleman from arsenic affected area presented with an ulceration at skin at the junction of neck and thorax (left side) and a lump at left upper neck. On examination, ulcer was 3×3 cm. In size. There was an enlarged lymph node at level I I cervical region. There were hyperkeratoses and hyperpigmentation at multiple site. Patient had lost one finger at left upper extremity. Biopsy and histopathological examination from the ulcer revealed squamous cell carcinoma. CT scan of whole abdomen showed multiple hypodence space occupying lesion in liver, consistent with metastasis. Patient was treated with chemotherapy with palliative intent. This case has atypical presentation with aggressiveness in behaviour. The case is described along with a review of literature.

**Key words:** Arsenic, carcinoma, skin.

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**INTRODUCTION**

Arsenic is twentieth most abundant element in earth's crust.<sup>1</sup> It has been used as therapy for syphilis and psoriasis (as Fowler's solution, in late 1940s).<sup>2</sup> But arsenic has proved itself from many years as poisonous element. Human being are exposed to arsenic primarily from air, water and food (particularly sea-food). Among these, elevated arsenic level in drinking water is the most important cause of arsenic toxicity. Tissues and organs which are affected due to chronic arsenic poisoning are skin, hair, nail, lungs, heart, liver, gastro-intestinal system, nervous system and haematological system. But arsenic tends to concentrate in ectodermal tissue, including skin, hair, nail. Skin is a primary target organ for chronic arsenic exposure. Reason has been behind this is predilection of arsenic for tissues with high sulphhydryl group. Ectodermal tissue like skin has high sulphhydryl group.<sup>3</sup>

Skin manifestation of arsenic poisoning is diverse. These are hyperpigmentation, hyperkeratosis, bowen's disease, basal and squamous cell carcinoma. Hyperpigmentation and hyperkeratosis are two different direction of manifestation. Hyperpigmentation does not lead to carcinoma. But hyperkeratosis is the station of a spectrum which leads to carcinoma. Hyperkeratosis usually appear as small corn-like

elevation, 0.4 to 1 cm. in diameter. Bowen's disease, an in-situ squamous cell carcinoma, represents continuation of dysmaturation process observed in keratoses. Basal cell carcinoma arise most frequently in normal tissue, many times this is multiple and occurs in trunk. On the other hand squamous cell carcinoma arise from normal tissue or from pre-existing hyperkeratosis or bowen's disease.

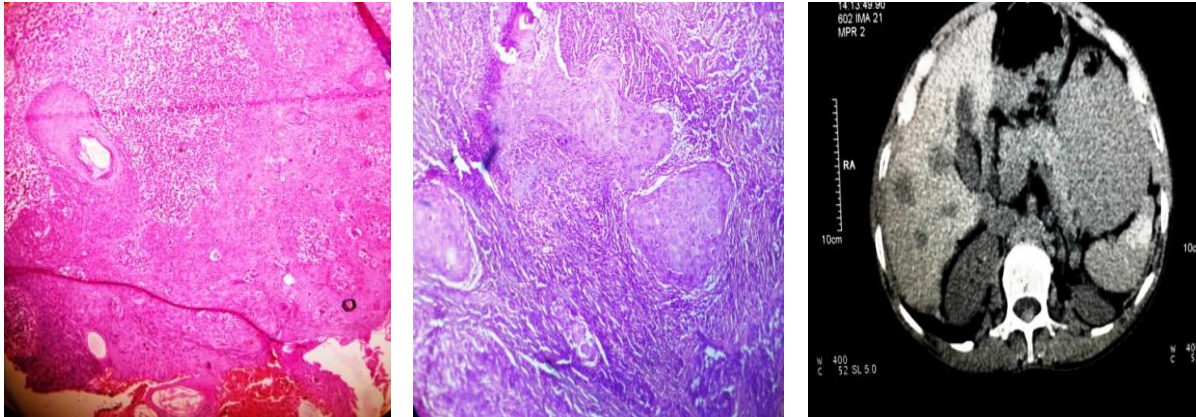
Arsenic induced and sun induced squamous cell carcinoma are histopathologically same. But site of occurrence are different. Sun induced carcinoma occurs mainly on sun-exposed areas (head,neck). Arsenic induced squamous cell carcinoma's common occurrence is palm, soles and trunk. Metastatic potential of sun-induced squamous cell carcinoma is low. Metastatic potential and behaviour regarding aggressiveness of arsenic induced carcinoma is not properly known. Here we present a case of arsenic induced squamous cell carcinoma of skin at sun-exposed area and aggressive behaviour with metastasis to lymph node and liver.

### **CASE REPORT**

68 years old gentleman presented in OPD with an ulcer at skin at the junction neck and thorax[(left side)(image 1)], which is sun-exposed area. It was of 7 months of onset. There was an enlarged hard lymph node at left cervical region, mobile, 6x5 cm. In size(image 2). Onset was of 3 months. There was hyperkeratosis and hyperpigmentation at multiple site. Patient had lost one finger at left upper extremity. Water of the area of patient's residence is known to be polluted with arsenic.

Biopsy and histopathological examination from the ulcerative growth revealed squamous cell carcinoma. Skin tissue shows full thickness dysplasia with focal breaching of basement membrane and microinvasion of dysplastic cells into dermis(image 3). Deep dermis shows sheets of malignant cells with squamous differentiation surrounded by desmoplastic stroma(image 4).

Chest imaging reveals no obvious abnormality. But CT scan of whole abdomen showed multiple hypodense space occupying lesion, consistent with metastasis(image 5). Patient was first treated with chemotherapy containing cisplatin and 5-FU. After 2 cycles, clinical evaluation was done. It revealed stable disease. Chemotherapy regimen was then changed. It consisted paclitaxel and cisplatin. Again after 2 cycles, clinical evaluation was done. Size of both the ulcer and lymph node was reduced. Then another 2 cycles of same regimen were given. After 6 cycles, again evaluation was done. On clinical examination, disease had further reduced in size.



## **DISCUSSION**

Inorganic forms of arsenic are mainly toxic to human health.<sup>1</sup> Drinking water which is the main source of arsenic poisoning is contaminated by arsenical pesticide, arsenical chemical and natural mineral deposit. Arsenic occurs as both in trivalent and pentavalent forms. Trivalent form is more toxic. Mechanism of arsenic toxicity has been diverse. It induces sister chromatid exchange in DNA.<sup>4,5</sup> There has been chromosomal aberration in peripheral lymphocytes. It also inhibits DNA repair process by inhibiting DNA repair enzymes.<sup>6</sup> It also causes substitution of phosphorus in DNA backbone.

There is variety of symptoms in arsenic exposed population. Range of arsenic toxicity is wide. So disease manifestation is also diverse. Respiratory system affection may cause obstructive lung disease, interstitial lung disease, bronchiectasis. In case of gastro-intestinal system, nausea, vomiting, diarrhoea, anorexia and abdominal pain may occur. Liver disease occurs in the form of portal hypertension, liver fibrosis, cirrhosis.<sup>7</sup> In case of cardiovascular system, there is arteriosclerosis, dry gangrene, spontaneous amputation of affected extremity, thromboangitis obliterans. Nervous system affection may cause paresthesia. There may also be headache, vertigo, sleep disorder, lack of concentration, irritability.

However skin is the tissue which is most commonly affected by it. Range of affection in skin is also diverse. Ultimately disease may lead to carcinoma. Apart from skin cancer, arsenic can cause carcinoma of urinary bladder and lung.<sup>8</sup> Even in these cases, dermatological manifestation has been found.<sup>9</sup>

Hyperkeratosis is the most frequent sign of arsenic toxicity.<sup>10</sup> Minimal latency period for hyperkeratosis has been reported to be 2.5 years. Hyperpigmentation, on the other hand, is a pathologic hallmark of chronic arsenic exposure.<sup>11</sup> Although hyperpigmentation is not considered to be precursor of malignancy. Bowen's disease is squamous cell carcinoma in situ. These are sharply demarcated round or irregular plaque. Size varies from 1 mm to more than 10 cm. Arsenic induced basal cell carcinoma most commonly arise from normal tissue.

Arsenic induced invasive squamous cell carcinoma may arise from normal tissue or within pre-existing precursor lesion.<sup>12</sup> Clinical manifestation is ulceration, erosion, induration and fissuring. In contrary to sun-induced carcinoma, arsenic induced squamous cell carcinoma commonly occurs in extrimities and trunk. They may be multiple. Sun-induced squamous cell carcinoma has low metastatic potential. But metastatic potential and aggressiveness of arsenic-induced carcinoma has not been well defined. There has been one study in Taiwan to assess aggesiveness. In this study by Yeh et al 5-year case-fatality rate is 14.7%.<sup>12</sup>

### **CONCLUSION**

Although arsenic-induced carcinoma occurs mainly in non-exposed area, in this case it has arised from sun-exposed area. So, in carcinoma of skin in sun-exposed area, arsenic as a causative agent should be kept in mind. Again, the disease has progressed very rapidly. Metastases to lymph node has occurred rapidly. No case till now has been reported with arsenic induced squamous cell carcinoma with liver metastasis. In this case, there is liver metastasis. So whenever there is arsenic induced squamous cell carcinoma of skin, thorough clinical examination and proper imaging are necessary to properly stage the disease before initiation of treatment.

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