Case 20
A 74-year-old Thai male from Nakornpathom.
Chief complaint: Multiple slow growing plaques for 10 years.

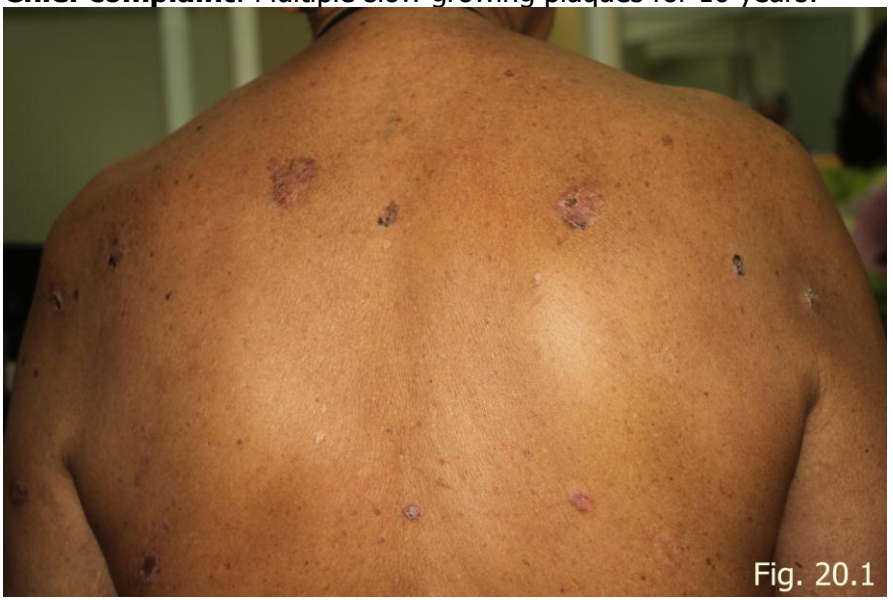

Fig. 20.1

Present illness: The patient initially presented to surgical department with a two-month history of dysphagia, and was subsequently diagnosed as having esophageal carcinoma. During his oncology visit, the oncologist noticed of multiple asymptomatic lesions on the patient's trunk and extremities and then referred him to our dermatology clinic. The skin lesions were asymptomatic, and gradually increased in size and number over the past ten years without bothering his livelihood. Further history taking revealed that around 20 years ago, he took unknown traditional medicines continuously for 2 years. The patient denied taking any other drugs and herbal medications. He also denied working in mine, electronic, or chemical manufacturers. No one in his family has skin cancer or other skin disorders.

Past history

He denied any significant past medical history or surgical history other than that mentioned above.

Physical examination

HEENT: Not pale, no jaundice

Lymph node: No palpable cervical, supraclavicular, axillary,and inguinal lymph nodes

Abdomen: No hepatosplenomegaly

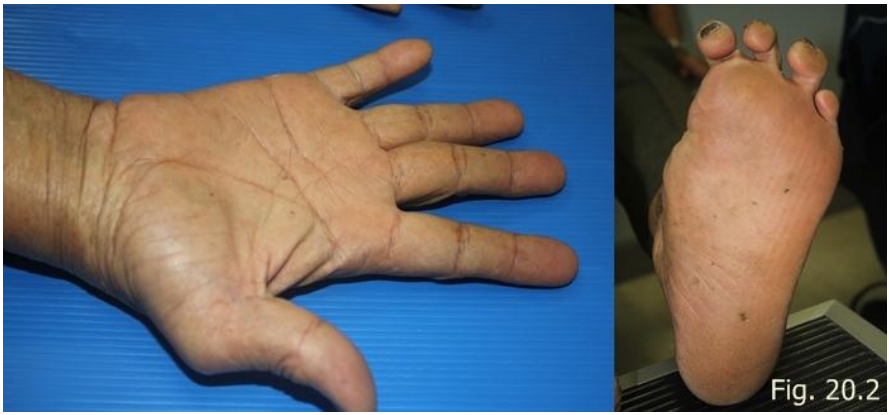

Fig. 20.2

Skin examination

- Multiple irregular friable erythematous plaques with scatter inhomogenous brown to black color, size range from 1- 15 cm. on chest, back, both arms, both thighs, right leg, and both dorsum of hands (Figure 20.1)
- Guttate hyperpigmented and hypopigmented macules, mostly on chest, back, and abdomen (Figure 20.1)
- Multiple small punctate yellow keratotic papules and pits on both palms and soles (Figure 20.2)

Histopathology

(S13-06936A, left chest; S13-06936C, left thigh)

- Downward growth of atypical squamous epithelium extending into the deep dermis
- Squamous epithelium composed of large hyperchromatic nuclei, scattered mitotic figures
- Dense inflammatory-cell infiltrate of lymphocytes and plasma cell in the dermis

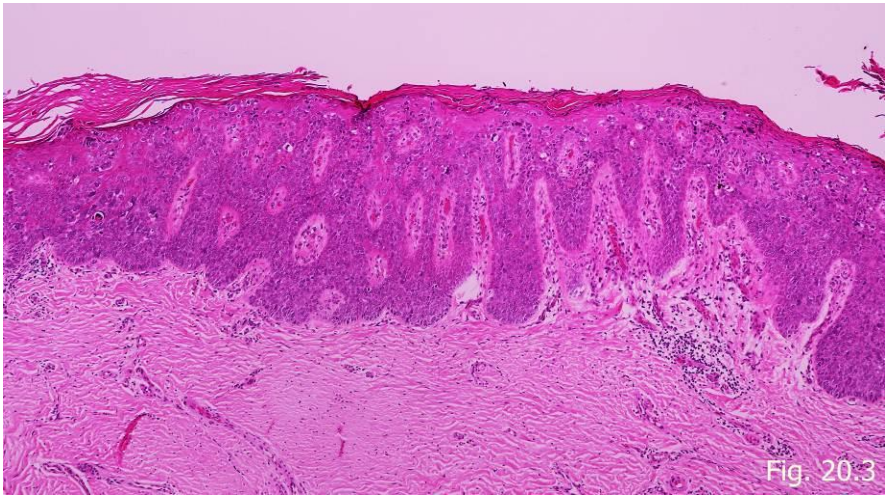

Fig. 20.3

(S13-06936B, left dorsum of 3rd finger) (Figure 20.3)

- Atypical keratinocytes with large, hyperchromatic, closely crowded nuclei at all layers of hyperplastic epidermis.

Investigation

CT chest and upper abdomen:

- Irregular circumferential mass at the midportion of the esophagus. Tumor invasion of periesophageal fat and local nodal metastasis are noted.
- Two micronodules at the left lower lung. The rest of the lung parenchyma is normal.
- Liver and bone are unremarkable.

Diagnosis: Chronic arsenism with esophageal cancer
Treatment: Chemotherapy and radiation for esophageal cancer
Acitretin 10 mg/d and cryotherapy for skin cancers

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Discussion

Arsenic is a heavy metal well-known for its carcinogenicity. Humans can expose to arsenic via environmental (soil and well water contaminated by mining or agricultural fungicides, fertilizers, and pesticides), occupational (mining, computer microchip, forestry, and electroplating), or medicinal (Chinese herbal medicine and Thai traditional medicine) agents.[1-4]

In Thailand, there was major arsenic poisoning in Ronpibool District, Nakorn Sri Thammarat, the southern Province of Thailand. The area was famous for tin mine in 80's. Without proper waste management at that time, it caused contamination of arsenic in environment, especially water. The first case of skin cancer in the area associated with chronic exposure to arsenic was found in 1987. The estimated prevalence of skin lesions associated with arsenic was around 5,000 cases at that time.[5] Another event of arsenic contamination was found in Thai traditional medicine. In 2002, Thai Food and Drug Administration declared of contamination of arsenic in 4 brands of Thai traditional medicines. The contamination of arsenic occurred by using red arsenic instead of a rare red-color herb to produce the color of medicines.[6] Although, the contaminated products were withdrawn and recalled from the market, the effect of chronic arsenism could be left in victim body for years.

Arsenic overdose can cause both acute and chronic effects. In acute form, it is mainly caused by gastrointestinal, neurologic, and hematologic involvement that can lead to death.[1] On the

contrary, in chronic form, dermatologic manifestations are prominent clinical features. Chronic arsenism is characterized by dyspigmentation of skin (guttate hypopigmented macules on background of hyperpigmentation resembles "rain drop on a dusky road"), keratoses or pits of palms and soles (usually on pressure areas), diffuse alopecia, Blackfoot disease (peripheral vascular disorder affecting the lower extremities that eventually results in gangrene), and multiple non-melanoma skin cancers, particularly Bowen's disease. Skin cancers in chronic arsenism are usually multiple, and often founded in non-sun-exposed area, contrary to non-arsenic related skin cancers.[1-4, 7] Extracutaneous malignancies associated to chronic arsenism are lung, genitourinary, kidney, and liver cancer.[1, 3, 8] Even though these cancers are increasing in chronic arsenic cases, they are not suggestive features of chronic arsenism like skin manifestations. Other systemic manifestations are peripheral neuropathy, diarrhea, bone marrow hypoplasia, liver diseases, diabetes, and obstructive lung disease.[1, 3]

Histologically, arsenical keratosis of palms and soles demonstrates marked hyperkeratosis and parakeratosis with mild to moderate keratinocyte atypia resembles actinic keratosis of acral skin. Arsenic-related skin cancers have same histology to regular skin cancer, and cannot be distinguished by histopathology.[1, 3]

Chronic arsenic toxicity is primarily diagnosed on the basis of its cutaneous manifestations and history of contact to contaminated substances. In long term arsenic exposure, characteristic dermatological lesions are considered a good biomarkers, which has significant association with the risk of skin cancers.[9] However, the measurement of arsenic level is also helpful, but not necessary, in diagnostic arsenic toxicity. Important biomarkers of arsenic exposure are urine, hair, and nail. Arsenic concentration in blood is usually too low and transient, thus it is not considered a good maker for chronic arsenism. Chronic arsenic toxicity can be confirmed by measurement of arsenic content in hair

and nail above 1 μg/g and 1.5 μg/g respectively, or arsenic level in urine above 50 μg/L (without any history of taking seafood).[10] It should be noted that arsenic level is easily disturbed by many factors, such as seafood diet (increase urine arsenic level from non-toxic organic arsenic) and external contamination (increase in nail and hair arsenic level).[9, 10] Furthermore, there is no correlation between hair, nail, and urine arsenic level and clinical features of chronic arsenic toxicities.[11] Therefore, high arsenic level is indicative of arsenic exposure, but it is not conclusive for diagnostic of chronic arsenic toxicity.

All patients should stop using contaminated substances eg. traditional medicines, well water, etc. Up to now, no specific treatment is yet established to treat chronic arsenism. Using chelating agents, such as dimercaptosuccinic acid and penicillamine, is still controversy in improving clinical recovery, but may reduce arsenic storage.[1, 12] Systemic retinoids is helpful. It can cause regression of arsenical keratosis, and acts as chemoprevention for skin cancers. It is imperative to regular skin exam for early detection of skin cancer which upon excision, it can be curative.[1, 4, 5]

Our patient was diagnosed as having chronic arsenism on the basis of characteristic cutaneous manifestations and multiple skin cancers. Although, esophageal cancer in our patient is not frequent tumor observed in chronic arsenism, we believe that this internal cancer is also related to intake of arsenic. Our patient received chemotherapy for treatment of esophageal cancer which also caused regression of his skin cancer. In addition, he was treated with once daily oral dose of 10 mg acitretin and monthly cryotherapy to help clearing the residual skin cancer. Lastly, the source of arsenic in our patient is likely from traditional medicines that he used in the past. This emphasizes the important of continuously surveillance of traditional and chinese medicines in market which will help prevent this disabling and fatal disorder.

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