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CHROMOBLASTOMYCOSIS WITH SQUAMOUS CELL CARCINOMA

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A 47-year-old male patient had extensive verrucous lesions on the right upper limb for 33 years. One of the lesions developed ulceration which had not healed for 6 years. A clinical diagnosis of chromoblastomycosis was confirmed histopathologically and mycologically, *Cladosporium cladosporioides* being the organism cultured. Combined treatment with amphotericin B and 5-fluorouracil gave good response with most lesions resolving. A few verrucous plaques and the ulcer persisted. Biopsy from the ulcer revealed a low-grade squamous cell carcinoma which was treated with excision and grafting. A year later, the patient developed metastasis in the axillary lymph nodes which also showed fungal granuloma at the time of biopsy. The axilla was irradiated with 4500 rads and three courses of bleomycin injections were given. However, he died 10 months later following a massive bleed from an axillary vessel.

Key words : Chromoblastomycosis, Cladosporium cladosporioides, Squamous cell carcinoma.

Chromoblastomycosis is a chronic subcutaneous mycosis caused by one of the several species of pigmented fungi. It is a slowly progressive disease characterised by warty nodules and plaques which may ulcerate. Dissemination of the disease may occur via lymphatics or blood stream. Main complications are ulceration, secondary infection, lymphoedema and elephantiasis. Spread to the central nervous system[1] and squamous cell carcinoma arising in the lesions have been rarely reported.[2] We report a case of squamous cell carcinoma with metastasis into the lymph node occurring in a patient who had extensive chromoblastomycosis of skin with lymphatic spread, caused by *Cladosporium cladosporioides* a hitherto unreported etiological agent in this disease.

Case Report

A 47-year-old male farmer from south India presented with skin lesions on the right upper limb for 33 years and restriction of movements at the right elbow for 6 years. The skin lesions started as a warty papule in the right cubital fossa with no preceding trauma. Over the years, new warty lesions appeared at adjacent sites on the arm and forearm which later coalesced to form large plaques. Fifteen years after the onset, the lesions were irradiated in another hospital with no significant improvement. Treatment with antitubercular drugs, thiabendazole and potassium iodide had also been tried without benefit. The lesions rather continued to spread slowly but relentlessly. The patient had noticed ulceration of the initial lesion at the right elbow with foul smelling purulent discharge for about 6 years. The patient was a moderately built adult in no obvious distress. Systemic examination was normal. Skin lesions were confined to the right upper extremity extending from the shoulder to the wrist. These consisted of multiple verrucous plaques and nodules with crusting and scaling. The plaque in the cubital fossa showed a tender ulcer about 5 cm in diameter with a raised border and the floor covered with granulation tissue. There was flexion deformity of the right elbow due to scarring and soft tissue contracture (Fig. 1). There was no significant lymphadenopathy.

A clinical diagnosis of chromoblastomycosis was made. Biopsy from one of the plaques on

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Fig. 1. Multiple verrucous plaques on the right upper limb with contracture at the elbow.

the arm showed verrucous chromoblastomycosis with the organisms seen in the dermal granuloma (Fig. 2). On culture, the fungus was identified as *Cladosporium cladosporioides*. He was treated for $2\frac{1}{2}$ months with intravenous amphotericin B, a total dose of 2 gm, along with topical 5-fluorouracil. A month later, there was a marked reduction in the size and thickness of the lesions, but thereafter some of the plaques visibly extended. The ulcerated lesion at the right elbow remained unchanged and the patient started having pain at the region of the ulcer. Right axillary lymph nodes were not significantly enlarged. Biopsies were repeated because of the clinical worsening during treatment. The plaque on the arm showed irregular downward proliferation of the epidermis with marked atypia of cells and many abnormal mitoses. The underlying dermis showed the fungal granuloma. Biopsy from the ulcerated lesion showed low-grade squamous cell carcinoma with early infiltration of the underlying tissue. A wide excision of the ulcerated lesion on the right elbow was done followed by skin grafting. Biopsy showed low-grade squamous cell carcinoma (Fig. 3). The graft site healed well. The patient continued the treatment with topical 5-fluorouracil.

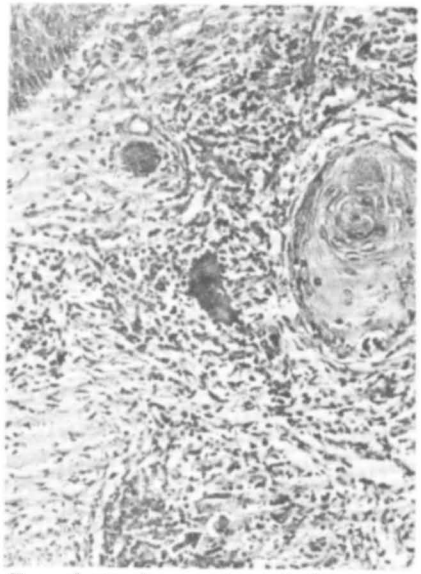

Fig. 2. Dermal granuloma. Arrow indicates organisms. (Hematoxylin and eosin stain×620).

One year after surgery, the patient developed gross lymphoedema of the right upper limb. Verrucous plaques were still present but confined

Fig. 3. Low-grade squamous cell carcinoma skin with early infiltration of underlying tissue (Hematoxylin and eosin stain×620).

to the right shoulder and wrist. The biopsied tissue from these plaques again grew *Cladosporium cladosporioides*. The central group of right axillary lymph nodes were found to be enlarged, 3 cm in size, hard and fixed. These, on histopathology, showed fungal granuloma (Fig. 4) as well as poorly differentiated squamous cell carcinoma. The axilla was treated with local irradiation of 4500 rads over a period of $4\frac{1}{2}$ weeks followed by 3 courses of bleomycin injection. Six months later, the patient came back with persisting edema of the whole right upper limb. He died 4 months later at home, following a massive hemorrhage from the right axilla, probably due to involvement of the axillary artery. At the time of death, all the skin lesions had regressed except a small plaque on the arm.

Comments

Squamous cell carcinoma complicating chromoblastomycosis is rare. Only 5 such case reports are available in the world literature.[2-5] This is the first case report from India. The carcinoma developed in a lesion which was 33-year-old. In 4 of the 5 earlier reported cases also, the carcinoma had developed in long-standing lesions of 10 years or more.[2,3,5] However, in one female patient the carcinoma appeared 5 months after the onset of the fungal granuloma.[4]

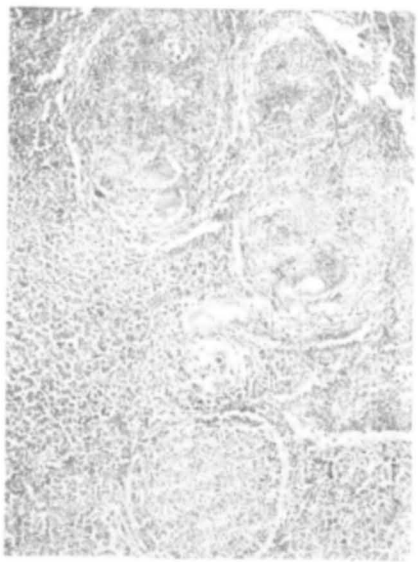

Fig. 4. Fungal granuloma in the lymph node (Hematoxylin and eosin stain×620).

Chromoblastomycosis is known to be caused by several fungi belonging to the genera *Phialophora*, *Hormodendrum* and *Cladosporium*. In our patient, *Cladosporium cladosporioides* was isolated from the lesion on two occasions (identified by CDC, Atlanta, Georgia, USA). This organism is a saprophyte but has rarely been recognized as a pathogen.[6] There are no earlier reports where this organism had been cultured from the lesions of chromoblastomycosis.

The therapeutic outcome on chromoblastomycosis has been frustrating and drugs like amphotericin B, 5-fluorouracil, thiabendazole, potassium iodide, ketoconazole have all been used with variable results.[7-9] Therefore the therapeutic response of our patient to a combination of amphotericin B and 5-fluorouracil was surprising. Almost complete regression of the lesions was seen with this combined therapy. Had the therapy been instituted earlier, dissemination of the lesion could have been possibly prevented.

Even though carcinomatous change in chromoblastomycosis is rare, clinicians should consider long-standing lesions, non-healing ulcerated lesions and painful lesions as danger signals. Multiple biopsies from suspicious sites are justified.

Excision of the low-grade squamous cell carcinoma at the elbow in our patient did not prevent the occurrence of poorly differentiated carcinoma in the axillary lymph node a year later. Seeding into the axillary lymph node had probably occurred even before excision was carried out or perhaps more than one skin lesion may have had malignancy.

Acknowledgement

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