

“Clown Nose” as a First Manifestation of Lung Carcinoma

Sir,

Lung carcinoma is responsible for the majority of skin metastases in men and is second only to breast cancer as source of skin metastases in women (1, 2). There is a broad variety of clinical features, including nodules, papules, ulcers, inflammatory and sclerotic lesions, as well as lesions with a vesicular pattern (1). We report the case of a 58-year-old man with cutaneous metastasis located on the tip of the nose (“clown nose”) from a previously undiagnosed lung carcinoma.

A 58-year-old man was examined for a rapidly growing nodule on the tip of the nose, which had developed 1 month earlier. The lesion was red-yellowish, dome-shaped, partially ulcerated and measured 2.5 cm in diameter (Fig. 1). The patient was otherwise asymptomatic. Histologic examination showed a dense infiltrate located in the entire dermis, composed of neoplastic cells with pleomorphic nuclei, one or more nucleoli and abundant, eosinophilic cytoplasm. Some cells were arranged in cords and isles, whereas others were distributed in glandular-like structures, separated by thin fibrous bundles (Fig. 2). Immunohistochemical studies, performed with a standard three-step immunoperoxidase technique on routinely fixed, paraffin-embedded tissue sections, showed reactivity of neoplastic cells for pan-cytokeratins, carcinoembryonic antigen and epithelial membrane antigen. Negative staining was observed with S-100, HMB-45 and leukocyte common antigen. Routine laboratory investigations showed moderate sideropenic anaemia and an erythrocyte sedimentation rate of 80 mm/h. A chest X-ray detected a nodular lesion in the left upper lobe of the lung, and a computed tomographic scan with contrast revealed the presence of an ipodense mass,



Fig. 1. Nodular metastatic lesion on the tip of the nose from lung carcinoma.



Fig. 2. Dense infiltrate of neoplastic cells located in the entire dermis. Some cells were arranged in cords and isles, whereas others were distributed in glandular-like structures (hematoxylin-eosin stain; original magnification $\times 250$).

consistent with a diagnosis of lung cancer. However, no signs or symptoms related to the primary tumour were present in our patient. The past history was remarkable for smoking 20 cigarettes a day but not for professional hazards. Based on clinicopathologic findings, the diagnosis of cutaneous metastasis from lung carcinoma was made. The patient died of widespread disease 3 months after the onset of the nasal lesion. Autopsy was not performed.

Lung cancers frequently metastasize to the anterior chest wall, abdomen, back, face and scalp, in decreasing order (1, 2). The “clown nose” manifestation, as observed in our patient, has been rarely described (3, 4). In the reported cases, the cutaneous lesion developed after the diagnosis of the visceral malignancy. In contrast, in our patient, the metastatic

skin lesion was the first sign of a previously undiagnosed lung carcinoma. The clinical differential diagnoses included, among others, keratoacanthoma, basal cell carcinoma and lymphoma.

The prognosis of patients with cutaneous metastasis depends on the type and biological behaviour of the underlying primary tumour and on the particular response to treatment. In cases of skin metastases from lung cancer the prognosis is poor, since involvement of other organs such as brain, liver, bone and adrenal glands may be observed. The average survival after diagnosis of skin involvement from a lung tumour ranges from 3 to 5 months (2). Our patient died of widespread disease 3 months after the appearance of skin metastasis.

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Ketoconazole as a Therapeutic Modality in Subcorneal Pustular Dermatitis

Sir,

Subcorneal pustular dermatosis (SPD), first described by Sneddon and Wilkinson in 1956 (1), is characterised by 1) superficial flaccid pustules occurring singly or in groups forming annular or gyrate patterns with spreading serpiginous edges, located in the groins, axillae, submammary areas and the flexures of the limbs, 2) subcorneal location of the bulla filled with neutrophils and occasional eosinophils but no acantholysis or spongiosis, 3) negative immunofluorescent studies, and 4) sterile cultures. A majority of the patients respond to dapsone, while corticosteroids are less effective. Some workers have, however, reported treatment failures with dapsone in more than 50% of the patients (1, 2). We report a patient who failed to respond to dapsone and oral corticosteroids but experienced complete remissions on three occasions with ketoconazole. Ketoconazole has not been used earlier in SPD. A 30-year-old housewife had been having asymptomatic superficial grouped pustules in annular patterns with mild background erythema on the neck, trunk and extremities for the last 3 years. The lesions would appear in crops, which used to dry up in 5–7 days. The severity of the disease was greater in the summer months, with no complete remission at any time. There were no systemic or constitutional symptoms. Cutaneous examination revealed multiple grouped annular flaccid pustular lesions of 2 mm to 4 mm in size, located on the neck, upper chest, back, abdomen, inframammary areas and flexure surface of the upper and the lower extremities. There were no mucosal lesions and the systemic examination was normal. Histopathological examination of a lesion revealed a subcorneal bulla filled with neutrophils. There were no acantholytic cells or eosinophils in the bulla. The dermis was unremarkable. Immunofluorescence could not be performed because of non-availability of the services at that time, and culture was not attempted. A diagnosis of SPD was made and the patient was given 100 mg dapsone twice a day with 3 mg betamethasone on alternate days. After 2 weeks of therapy there was no improvement and new lesions continued to appear. At that stage 200 mg ketoconazole per day orally

was started and oral corticosteroids were withdrawn. Within 3 days the lesions started subsiding and in 2 weeks all the lesions had subsided completely. The dose of dapsone was reduced to 100 mg per day but ketoconazole was continued in the same dose. After another 4 weeks, while the patient was in remission, ketoconazole was stopped but dapsone was continued. After 2 months the patient had another relapse of the same disease, while she was still receiving 100 mg dapsone per day. She was again given 200 mg ketoconazole per day and the dapsone was stopped. This time also the lesions disappeared completely within 2 weeks. Ketoconazole was continued for 6 weeks, when the patient conceived and the drugs had to be withdrawn. She remained in remission till 2 weeks postpartum when she again had a severe relapse. This time she was treated with 200 mg ketoconazole alone for 3 months and she has now been in remission for about 1 year.

Ketoconazole is primarily used for dermatophytes, *Candida* and *Pityrosporum ovale*. The drug acts by inhibiting the cytochrome P-450 enzyme lanosterol 14-demethylase, which is required for conversion of lanosterol to ergosterol (3). It has also been reported to block testosterone synthesis (4), and the sex hormones have been found to influence the function of T-lymphocytes (5), which in turn can cause a variety of immunological effects. We do not know the mechanism of action of ketoconazole in our patient, but complete remissions on three occasions coinciding with the institution of ketoconazole therapy suggest that the remissions could be attributed to ketoconazole.

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