INTRODUCTION

Paraneoplastic dermatoses are cutaneous reaction patterns to internal neoplasms which can closely resemble a number of dermatoses. These may represent the first sign of an underlying neoplasm or the earliest symptom of relapse of a previous cancer.1

Multiple myeloma is characterized by clonal proliferation of plasma cells that produce a monoclonal immunoglobulin protein. Dermatological associations can be due to extension and proliferation of malignant plasma cells in the skin, deposition of protein(s) related to the primary M protein or as paraneoplastic syndromes, which are neither due to malignant cell infiltration nor because of deposition of biologic material.2 These paraneoplastic syndromes include scleromyxedema, sclerodema, necrobiotic xanthogranuloma, plane xanthoma, Schnitzler syndrome, pyoderma gangrenosum, sweet syndrome, leukocytoclastic vasculitis, erythema elevatum diutinum and sub-corneal pustular dermatosis.3

Classical Addisonian pigmentation is seen in Addison’s disease and comprises of generalized black brown pigmentation which is accentuated in sun exposed areas, over pressure points and palmar creases. In addition there is nail and oral mucosal pigmentation. This type of pigmentation may also be seen as a paraneoplastic phenomenon in bronchogenic carcinoma. Such typical pigmentation has not been reported previously in multiple myeloma. Acquired ichthyosis has also very rarely been associated with multiple myeloma.4

We report a unique combination of Addisionian pigmentation and acquired ichthyosis as presenting features in a patient with undiagnosed multiple myeloma. To the best of our knowledge this combination of paraneoplastic dermatosis has not been documented before in multiple myeloma. It is concluded that the presence of more than one suspicious dermatosis may be an indicator of being paraneoplastic requiring necessary work-up.

CASE REPORT

A 36 years old male was referred to Dermatology Department of Combined Military Hospital, Bahawalpur, in January 2006 for evaluation of progressive pigmentation over body for the last 2 years. There was a history of generalized weakness, arthralgias and weight loss for the same duration which had aggravated in the last 3 months. He had been treated for pulmonary tuberculosis 10 years ago.

On examination a generalized black brown pigmentation was noted on the body. The pigmentation was more prominent over the face and in the palmar creases. Finger nails showed linear pigmented bands. Oral examination showed spotted and diffuse black pigmentation of the buccal and labial mucosa (Figure 1). The pattern of pigmentation conferred to that seen in Addison’s disease. Examination of the thighs and lower legs revealed changes of ichthyosis (Figure 2). His blood pressure was 120/80 mmHg with no postural drop. Examination of the systems did not reveal any abnormality. Keeping in view the pattern of pigmentation, weight loss and past history of tuberculosis, the patient was investigated for Addison’s disease. Morning and evening serum cortisol levels were within normal limits. Plain X-rays abdomen did not reveal calcification of adrenal glands. Instead permeative pattern of bone

ABSTRACT

Black brown hyperpigmentation of the mucosae, sunexposed skin, palmar creases and frictional sites (Addisonian pigmentation) is characteristic of Addison disease. However, it can also occur as a paraneoplastic manifestation of tumours like bronchogenic carcinoma. Acquired ichthyosis starts later in life and can also be a paraneoplastic presentation. We report a unique combination of paraneoplastic Addisonian pigmentation and acquired ichthyosis as presenting features in a patient with undiagnosed multiple myeloma. To the best of our knowledge this combination of paraneoplastic dermatosis has not been documented before in multiple myeloma. It is concluded that the presence of more than one suspicious dermatosis may be an indicator of being paraneoplastic requiring necessary work-up.

Key words: Multiple myeloma. Skin pigmentation. Ichthyosis. Paraneoplastic syndromes. Addisonian pigmentation.

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Paraneoplastic Addisonian Pigmentation and Acquired Ichthysis as Presenting Features of Multiple Myeloma

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destruction was seen in the lower ribs bilaterally. X-rays of the dorso-lumbar spine showed collapse of third lumbar vertebra and multiple lytic lesions in the ribs and vertebrae. X-rays of other areas showed lytic lesions in the skull (Figure 3), mandible, medial end of the clavicles and body of fifth cervical vertebra. The skull and mandibular lytic lesions revealed classical rain drop pattern of multiple myeloma. Multiple calculi were seen in left kidney. Abdominal CT scan did not reveal any abnormality of the adrenal gland. However, the osseous lesions seen on plain X-rays were better revealed. Serum protein immuno-electrophoresis showed monoclonal paraprotein consisting of IgG kappa. Serum IgG level was 65 g/l, serum albumin level was 35 g/l and serum albumin/globulin ratio was decreased. Bone marrow examination revealed abundant abnormal plasma cells (40%). Urine for Bence John proteins was negative. Haemoglobin was 8.2 g/decilitre. Serum calcium and other blood chemistries were within normal limits. On the basis of these findings, the patient was diagnosed as a case of multiple myeloma with skin pigmentation in an Addisonian pattern and acquired ichthyosis and was referred to the department of internal medicine for further management. He refused treatment and died after 2 months of diagnosis.

DISCUSSION

Pigmentation seen in Addison's disease is black brown in colour which is accentuated over light exposed areas, pressure areas and in flexures. Buccal mucosa is essentially involved and the nails show longitudinal melanonychia.

Hyperpigmentation of nipples and scars is also a feature. The pigmentation results from melanogenic action of melanotrophic hormones secreted by the pituitary. Similar pigmentation is also a paraneoplastic feature of tumours which produce ectopic adrenocorticotropic hormone and alpha MSH like bronchogenic carcinoma. Atypical Addisonian pigmentation without the involvement of buccal mucosa is a feature of many inflammatory and neoplastic disorders including chronic infections, lesions of diencephalon and substantia nigra, liver cirrhosis, primary biliary cirrhosis, porphyria cutanea tarda, hyperthyroidism and chronic renal failure and tumours like carcinoids, pheochromocytoma, and Hodgkin's disease.

In multiple myeloma different patterns of pigmentation have been described. The strongest association of skin pigmentation and multiple myeloma is seen in POEMS syndrome. The pigmentation is diffuse but may be accentuated over extensor surfaces, the back, neck, and axillae. Multiple myeloma has been associated with Cronkhite-Canada syndrome in which the pigmentation is diffuse and accentuated over face, neck, palms, and extremities but with oral involvement occasionally. Multiple myeloma and diffuse pigmentation can occur with sclerema. Yellow skin and yellow hair have been reported in an elderly patient with multiple myeloma. The black brown pigmentation seen in our patient which was accentuated over light exposed areas, areas of pressure and in flexures with involvement of buccal
mucosa and longitudinal melanonychia, was typical of that seen in Addison’s disease and different from all the above patterns. The etiology of pigmentation in this patient remains obscure but probably can be related to ectopic MSH like compounds or ACTH precursors that can be secreted by the tumour cells.  

Acquired ichthyosis is a non-hereditary cutaneous disorder characterized by dry, rough skin with prominent scaling. It has rarely been associated with multiple myeloma. Exact cause is not known but can be due to production of transforming growth factor - alpha by the tumour cells or there may be neoplastic disruption of any of the critical enzymes involved in keratinocyte differentiation. Metabolic derangements like malnutrition and malabsorption which occur in malignancy may also contribute to the problem.

Paraneoplastic syndromes can closely resemble a number of dermatoses and sometimes it becomes difficult to discern clinically whether the dermatosis is a paraneoplastic manifestation or otherwise. This case was initially suspected to be suffering from Addison’s disease on the bases of the characteristic pigmentation and previous history of tuberculosis but during investigations was found to be suffering from multiple myeloma and there was no evidence of adrenal dysfunction.

It is suggested that multiple myeloma may be included in the differential diagnosis of classical Addisonian pigmentation. Presence of more than one suspicious dermatosis may be a strong indicator of them being paraneoplastic and should alert the physician for necessary work-up.

REFERENCES