Paraneoplastic pemphigus in a patient with follicular non-Hodgkins lymphoma

K K M B K Silva[1], D M Munasinghe[2], M Dissanayake[3], W M Tilakaratne[4]

Sri Lanka Journal of Dermatology, 2005, 9, 23-24

Abstract

Paraneoplastic pemphigus is described as an autoimmune disease, which presents with polymorphous blistering eruption and mucocutaneous ulcerations in a patient with an underlying neoplasm, either malignant or benign. The cutaneous lesions of these patients are quite variable and consist of a mixture of blisters, erosions and target lesions. The most frequently observed clinical feature of this disease is an intractable stomatitis, which is usually the earliest presenting sign; and is extremely resistant to therapy.

Herein we report a 30 yrs old woman with follicular non-Hodgkin's lymphoma presented with severe erosions and ulcerations involving oropharyngeal and vaginal mucosae, and lichenoid papules over both palms with typical histopathological and direct immunofluorescence findings of paraneoplastic pemphigus. The lesions were recalcitrant to conventional therapy with oral corticosteroids but significantly improved with plasmapheresis followed by dexamethasone and cyclophosphamie pulse therapy as adjuvant treatment.

Introduction

Pemphigus describes a group of autoimmune disease characterized by blisters and erosions of the skin and mucosal membranes, acantholysis by histology and auto antibodies directed against epidermal cell surface components. Apart from the two classical types (pemphigus vulgaris, pemphigus foliaceous) there are some rare forms described since the early 1970's. These include pemphigus herpetiformis, IgA pemphigus, and paraneoplastic pemphigus[1].

Case

A 30 yr old female presented to the dermatology clinic, General Hospital, Kandy in June 2002, with a history of painful orogenital ulceration resulting in bleeding, dysphagia and dysuria. She complained of irritation of both eyes and reduced tear formation also.

Approximately two weeks prior to this illness she has been investigated for generalized lymphodenopathy.

Examination revealed severe oral ulceration and haemorrhagic crusts on lips, involving the vermilion border (Figure 1). Ulceration was noted on the genital mucosa also. Lichenoid papules were seen on the palms. Ophthalmological examination showed evidence of pseudomembranous conjunctivitis affecting both eyes. Except for cervical and inguinal lymphodenopathy rest of the examination was normal.

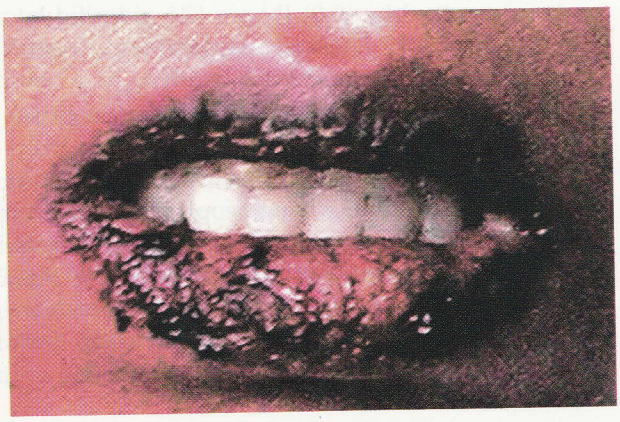

Figure 1. *Ulceration with haemorrhagic crusts over the lips*

According to the histology report of the lymph node biopsy which showed follicular non-Hodgkin's lymphoma, chemotherapy was commenced on her but the response was poor.

Further investigations done at this stage including ESR, full blood count, blood picture, renal function tests, liver function tests and bone marrow biopsy were normal. Ultrasound examination of the abdomen revealed extensive para-aortic lymphadenopathy and mild hepatomegaly. Oral mucosal biopsy showed parakeratinized stratified epithelium showing

[1]*Senior Registrar in Dermatology*, [2]*Registrar in Dermatology*, [3]*Consultant Dermatologist, Teaching Hospital, Kandy*, [4]*Consultant and Senior Lecturer in Oral Pathology, Department of Oral Pathology, Faculty of Dental Science, University of Peradeniya, Peradeniya.*

suprabasal separation, acantholysis, keratinocyte necrosis and interface dermatitis. Direct immunofluorescence revealed positive intercellular fluorescence with IgG. IgA, IgM and C3 were negative.

With these clinical, histopathological and immunofluorescence findings the patient was diagnosed as a possible case of paraneoplastic pemphigus. However further immunological tests including indirect immunofluorescence using transitional epithelium and immunoprecipitation were not carried out due to non availability.

She was started on oral prednisolone in addition to the chemotherapy. Although she improved initially, deterioration was noted with tailing off of steroids. Plasmapheresis was performed on her on two occasions. This was followed by the commencement of monthly intravenous pulses of dexamethasone and cyclophosphamide, in addition to daily prednisolone. With that treatment, skin and oral lesions improved significantly within next few weeks. Her lymphoma also is gradually resolving.

Discussion

In 1990 Anhalt et al originally described paraneoplastic pemphigus as an autoimmune disease with a polymorphous blistering eruption, mucocutaneous ulcerations, and an underlying neoplasm[2]. Since then more than 60 patients with paraneoplastic pemphigus have been reported. According to our knowledge, in SriLanka this is the first reported case of Non-Hodgkin's lymphoma patient presenting with paraneoplastic pemphigus.

The actual cause of paraneoplastic pemphigus has always been a matter of speculation. One hypothesis described the tumor antigens evoking an immune response that leads to the development of an autoimmune response to plakins. This autoantibody response leads to blistering in mucosa and other epithelia. Affected organ systems include the integument, the respiratory tract, and the gastrointestinal tract.

Most patients with paraneoplastic pemphigus have had malignant tumors. The most common malignancy associated with paraneoplastic pemphigus is non-Hodgkin's lymphoma. Other associated malignancies include chronic lymphocytic leukemia, Castleman tumor, giant cell lymphoma (reticulum cell sarcoma) and Waldenstrom macroglobulinemia and thymomas.

Patients usually present with painful oral erosions, often accompanied by a generalized cutaneous eruption. The eruption can assume a wide variety of morphologies, including morbilliform, urticarial, bullous, papulosquamous, or erythema multiforme-like lesions. Some patients present with mucocutaneous lesions resembling lichen planus.

Some patients experience oral lesions only. The erosions can occur anywhere in the mouth, including the buccal, the labial, the gingival, and the lingual mucosae. Erosions and subsequent crusting on the vermilion of the lips are similar to that seen in Stevens-Johnson syndrome. Mucous membranes of the pharynx, nose, eyes and genitalia also are known to be involved.

Camsia and Helm proposed modified criteria for diagnosis of paraneoplastic pemphigus in 1993[3]. According to these criteria, our patient had polymorphous mucocutaneous eruption with concurrent internal neoplasia, positive direct immunofluorescence and histological findings which fulfill two major and two minor criteria.

There is no consensus on a standard effective therapeutic regimen for paraneoplastic pemphigus. Corticosteroids produce partial resolution of lesions. Cutaneous lesions respond more quickly to therapy, whereas stomatitis is generally refractory. Induction of chemotherapy has occasionally resulted in complete resolution of malignancy and slow resolution of the skin lesions. Other attempted treatments are generally less successful. These include immunosuppressive treatment with cyclophosphamide or azathioprine, cyclosporine, gold, dapsone, plasmapheresis and photopheresis. Intravenous immunoglobulin was increasingly used in high doses as monotherapy or as an adjuvant. It is costly and time consuming to administer. However only few controlled trials are published regarding the use of this.

References

1. Neha D. Robinson, Thakashi Hashimoto, Masayuki Amagai, Lawrence S. Chicago. The new pemphigus variants. *Journal of American Academy of Dermatology* 1999; **40**: 649-71.

2. Anhalt GJ, Kim SC, Stanley JR, Korman NJ, Jabs DA, Kory M. Paraneplastic pemphigus: an autoimmune mucocutaneous disease associated with neoplasia. *N. England Journal* 1990; **323**: 1729-35.

3. Camsia C, Helm TN, Paraneoplastic pemphigus is a distinct neoplasia induced autoimmune disease. *Arch Dermatology* 1993; **129**: 883-6.