lymphocytes in some cases of PNP.[6]

Clinical Features

The mean age of onset is 60 years. Patients ranging in age from 7-76 years have been reported. Males and females are affected equally.[2]

Most patients affected by PNP are adults with sporadic occurrence in children. Exquisitely painful oral lesions are one of the first signs of the disease. Diffuse shallow ulcerations with irregular margins may involve any surface and the antecedent vesicles or bullae are rarely seen. The ulcers extend onto the vermillion zone of the lips, resulting in the hemorrhagic, crusted appearance suggestive of primary herpetic gingivo stomatitis. Infrequently patients may have a milder involvement suggestive of oral erosive lichen planus.[7,8]

Patients 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, papulos-quamous oe erythema multiforme like lesions. Some patients complain of pruritus or pain. The erosions can occur anywhere in the mouth including the buccal, the labial, the gingival and the lingual mucosa.[2]

Cutaneous lesions of PNP vary in their appearance reflecting the variety of cellular adhesion components against which the host antibodies are directed. Tense bullae develop on the trunk, proximal extremities and head and neck region. An interesting feature of PNP is the bullous involvement of palms and/or soles, uncommon in Pemphigus vulgaris.[5]

Lichenoid skin lesions consisting of erythematous papules may develop during the course of the disease. Approximately 70% of PNP patients develop conjunctival erosions and ulcerations, often resulting in cicatrizing conjunctivitis. It may be quite severe and debilitating due to significant crusting of the eyelids. In addition, vaginal ulcerations and erosions and penile lesions have been reported. Most serious aspects of PNP are respiratory involvement in about 20% of cases, which is often fatal.[5,9]

Investigations

Histopathologic examination

Sections from perilesional tissue shows suprabasilar clefting of the epithelium though the degree of acantholysis is not prominent as in pemphigus vulgaris. In addition, sub-epithelial clefting (like pemphigoid) is also seen. Vascular degeneration of the basal cell layer and keratinocyte necrosis are seen which results in a pattern suggestive of lichen planus, lupus erythematosus, graft versus-host disease etc. These epithelial changes are accompanied by an intense chronic inflammatory cell infiltrate in the superficial connective tissue.[1]

A distinctive feature of PNP is dyskeratosis. Dyskeratosis is a constant feature, but the number of dyskeratotic keratinocytes is variable. Dyskeratotic keratinocytes are found at all levels in the epidermis, especially within the zone of acantholysis, and they can be found in cutaneous adnexa. The presence of dyskeratosis in a suprabasal acantholytic bullous disorder is a clue to the presence of PNP.[2]

Immunofluorescence: Direct immuno fluorescence on perilesional skin shows deposition of IgG with or without C3 on the cell surface and at the basement. The IgG deposits are found on desmosomal plaques, hemidesmosomes and on both the extracellular part of desmosomes and keratinocyte plasma membrane.[5,10]

Indirect immuno fluorescence revealed a high titre of circulating auto antibodies when using monkey esophagus or rat bladder epithelium as substrate. A characteristic feature of PNP is that the auto antibodies bind to many desmosome containing epithelium including simple, columnar and transitional epithelium such as bronchiolar epithelium.[10]

Immunoprecipitation: These studies are considered the most definitive test for the diagnosis of PNP. Antibodies were identified complexed to proteins having molecular weights of 250 kD, 230 kD, 210 kD, 190 kD and 170 kD. The 250 kD and 210 kD proteins comigrate with desmoplakin I and II, the intercellular components of the desmosome, 230 kD proteins represents the major bullous pemphigoid antigen, a component of hemidesmosome, 190 kD represents periplakin another member of desmoplakin family. The 170 kD antigen is yet to be identified though antibody to this antigen alone may be sufficient for the clinical expression of PNP.[5,11]

Treatment and Prognosis

Management of PNP depends to a certain extent upon the associated neoplastic diseases. For benign lymphoid lesions such as thymoma excision of the tumor results in resolution of PNP as observed by Lemon MA et al but Anhalt GJ found that PNP in malignant disease do not resolve despite the apparent control/or cure of the malignant process. High dose systemic corticosteroids-prednisone orally 1-2 mg/kg daily remains the mainstay of treatment. Other immune modulating agents such as azathioprine, methotrexate, cyclophos-phamide, gold salts and dapsone are used in combination with corticosteroids. Plasmap-heresis and photopheresis have also been tried.[12,13]

Cutaneous lesion respond to treatment while oral ulcerations are refractory especially in PNP associated with a malignancy. Topical or systemic corticosteroids offer partial relief for oral ulcerations. Secondary candidal infection may require treatment with oral triazole drugs such as fluconazole or nystatin oral pastilles.[5,7]

In most cases, the prognosis for PNP is poor. Patients generally succumb to sepsis, multi organ failure, gastro intestinal bleeding and respiratory failure.

Conclusion

Though for decades, isolated case reports have described the association of malignancy and a vesiculobullous disease mostly pemphigus vulgaris, now a definite entity called as paraneoplastic pemphigus have been established. Neoplasia associated pemphigus is a multisystem disorder that may first appear as oral erosions and ulceration. As the oral lesion may appear in patients with occult malignancy, the oral physician plays a key role in the identification of patients with this disorder so that a timely diagnosis can be made and proper therapy instituted.

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