A retrospective study of mortality of pemphigus patients in a tertiary care hospital

Sir,

Pemphigus vulgaris (PV), an autoimmune vesiculo-bullous disorder, which primarily affects the skin, scalp, and mucous membranes, is potentially a fatal disease. The primary objective of this study was to find the case fatality rate in PV patients and our secondary objective was to elucidate the co-morbidities and antecedent complications which contributed to the death of the patient.

This is a 13-year (2000-2012) retrospective descriptive study done in the department of Dermatology and Venereology, Medical College Trivandrum by obtaining data from the case records of the Medical Records Library. All clinically diagnosed cases of pemphigus confirmed by skin biopsy and direct immunofluorescence and who died during the study period were included in the study. The salient demographic, clinical, treatment, and mortality details are given in Table 1.

In the present study, there were 18 deaths from a total of 235 pemphigus patients in a 13 year study period, thus accounting for a case fatality rate of 7.65%. Various other mortality studies range from 4 to 88 deaths.[1-5] The mortality figures of pemphigus

Table 1: Demographic, clinical features, treatment, and complications of the patients (*n*=18)

Age/sex years	Duration	Co-morbidities	Area of skin affected (%)	Oral/ scalp lesions	Type of pemphigus	Treatment given	Other salient clinical and treatment features	Antecedent causes leading to death
36/M	7 months	Nil	36	Yes	PV	Steroids	Irregular treatment	Bronchopneumonia
52/M	2 years	DM, HT	90	Yes	PV	DCP	Irregular treatment	Septicemia
52/M	1 month	Nil	30	Yes	PV	Steroids	Stopped steroid treatment	Renal failure
45/F	12 years	DM	90	Oral alone	PV	Steroids+DCP	Irregular treatment	TB, hepatitis, thrombocytopenia
42/M	1 year	DM	90	No	PV	Steroids	Nil	Gram negative septicemia
61/M	3 months	Nil	63	Yes	PV	Steroids+DCP	Nil	Perforation of peptic ulcer
63/M	2 years	Nil	90	Scalp alone	PF	Steroids+C	Nil	Perforation of peptic ulcer
65/M	1 year	DM	36	Yes	PF	Steroids	Irregular treatment	Septicemia
55/F	2 years	Nil	27	Yes	PV	Steroids	Oral candidiasis	Septicemia, ulcer perforation
70/F	9 years	Nil	90	Yes	PV	Steroids	Irregular treatment	Bronchopneumonia
24/F	1.5 years	Nil	90	No	PV	Steroids DCP, IVIG	Oral candidiasis	MRSA septicemia
53/F	1.25 years	DM	45	Yes	PV	Steroids, DCP, IVIG	Oral candidiasis	MRSA septicemia, acute pancreatitis
40/F	1 year	Nil	90	Yes	PV	Steroids	Nil	Pneumonia
44/F	1 year	DM, HT	27	Yes	PV	Steroids	Irregular treatment, oral candidiasis	Renal failure, hyponatrenemia
46/F	1 month	Nil	72	Yes	PV	Steroids	Oral candidiasis, myiasis	Renal failure, septicemia
24/M	1.5 years	HT	90	Yes	PV	Steroids	Irregular treatment, oral candidiasis	Septicemia, pneumonia
56/F	2.5 years	DM	27	Yes	PV	Steroids	Oral candidiasis	MRSA septicemia, ketoacidosis
65/M	1 year	DM, HT	90	Yes	PV	Steroids	Irregular treatment, oral candidiasis	Septicemia

PV: Pemphigus vulgaris, PF: Pemphigus foliaceus, DM: Diabetes mellitus, HT: Hypertension, DCP: Dexamethasone-cyclophosphamide pulse, C: Cyclophosphamide, IVIG: Intravenous immunoglobulin, MRSA: Methicillin-resistant Staphylococcus aureus

in India compared to their Western counterparts is much less. This could be due to racial factors.[1] PV was the commonest type of pemphigus to cause mortality in this study (88.8%). This is in conformance with other similar studies.[2-4] The majority of deaths in this study occurred in patients with age more than 50 years (55.5%), similar to other studies. Older age group patients are also more prone for co-morbidities like diabetes and hypertension, which in turn may contribute to the mortality, especially steroid-induced worsening of diabetes and hypertension.[1-4] In the present study, 50% of the cases had more than 90% body surface involvement. This indicates that when the body surface involvement is extensive, there is a greater chance for mortality. Erosions involving extensive areas of the body in effect, damages the primary barrier function of the skin, making the patients more prone for infections which in turn may lead to septicemia and bronchopneumonia, causing death. Moreover, Savin JA *et al.*, in his study has demonstrated that blister fluid in pemphigus are rich in protein, sodium, potassium, and chlorides and their loss when the blisters ruptures leads to severe electrolyte imbalance which in turn contributes to mortality.[2] The present study showed that mortality occurred more in patients who had scalp and oral lesions (77.7%), as seen in other studies [Figures 1 and 2]. The oral and scalp lesions in PV are the last to heal and are sometimes even resistant to therapy. This may necessitate prolongation of steroid therapy or even up-dosing the therapy to gain remission. Unfortunately, this may contribute to therapy induced complications leading to mortality.[2-5] However, Kalra *et al.*, has cautioned that concomitant oral herpes and oral cytomegalovirus (CMV) infections may delay the healing of oral pemphigus lesions and early diagnosis and treatment of these infections is

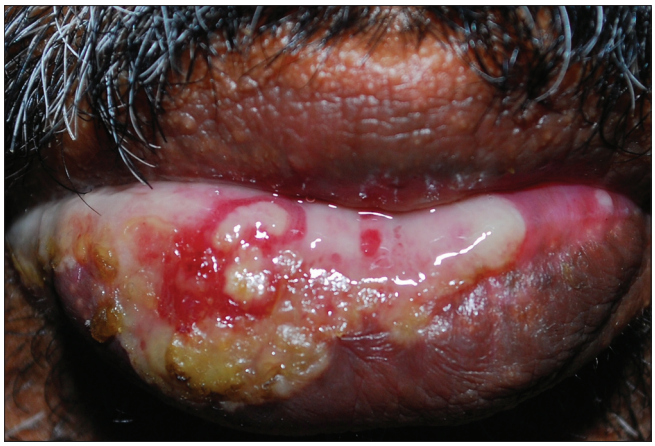

Figure 1: Recalcitrant oral lesions of pemphigus with concomitant oral herpes

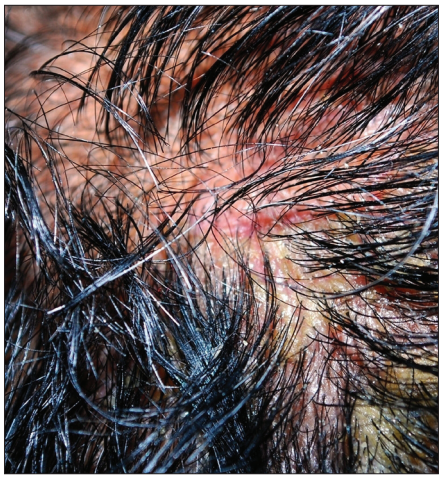

Figure 2: Recalcitrant scalp lesions of pemphigus

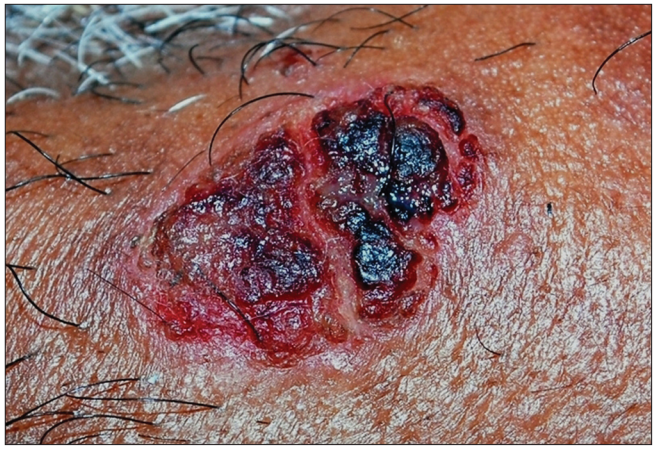

Figure 3: Crusted plaque of pemphigus colonized with MRSA

mandatory. In the present study, 94.4% of the patients were on systemic steroids at the time of death. Death also occurred in 5 cases of patients who were on dexamethasone-cyclophosphamide pulse (DCP) therapy. In most of the other studies, steroid-induced complications contributed significantly to the mortality of the patients.[1-5] Prompt and judicious treatment alone is not sufficient, as the present study showed that 50% of the patients who had died were irregular on treatment (missed therapy for more than 1 month). In the present study, 88.8% of the patients died due to disease process and therapy-induced complications, septicemia accounting for 55.5%, followed by respiratory tract infection and peptic ulcer perforation. Septicemia was the commonest cause of death in most mortality studies of pemphigus.[2-4] *Staphylococcus aureus* was the commonest pathogen isolated in this study and in three cases Methicillin-resistant *Staphylococcus aureus* (MRSA) [Figure 3] was cultured. MRSA infection has very high mortality in immunosuppressed patients. In a resource poor country like India, steroids may be the only available option for most pemphigus patients in the foreseeable future, as expensive alternatives like Intravenous immunoglobulin (IVIG) and the anti CD20 monoclonal antibody, rituximab may be beyond most patients. When treating with steroids alone, judicious acumen should be employed keeping in mind the aforementioned facts.

Retrospective studies have inherent weakness and not comparing patients with favorable outcome, is this study's limitation. Long duration of disease, extensive areas of skin involvement, oral and scalp lesions, and co-morbidities like diabetes contributed significantly to mortality. Irregular treatment and prolonged monotherapy with systemic steroids were other factors causing mortality. Disease process and therapy induced complications like septicemia, pneumonia, and peptic ulcer perforation were the commonest causes of death.

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