CASE REPORT

Pemphigus vulgaris: a multidisciplinary approach to management

Christopher Vinall, Lucy Stevens, Paul McArdle

Department of Oral & Maxillofacial Surgery, Derriford Hospital, Plymouth, UK

Correspondence to
Christopher Vinall,
vinallc@tcd.ie

SUMMARY

Pemphigus vulgaris (PV) is a rare but potentially life-threatening autoimmune disease affecting the mucosa and the skin. The disease is caused by circulating antibodies to desmosomes (important adhesion proteins linking cells together). Disruption of these intercellular connections results in a loss of cohesion between cells (acantholysis). The clinical result of this process is the development of multiple blisters that easily rupture, leaving behind painful sloughing eroded areas of mucosa and/or skin. We report a case of severe PV in a 56-year-old man presenting with widespread, painful, eroded mucocutaneous lesions. The severity of the disease demanded a range of medical and surgical specialties to successfully manage the problem. This paper highlights the importance of an early multidisciplinary team approach to improve the outcome of patients suffering with this disease.

BACKGROUND

Cell adhesion in the outer layer of skin and mucosa (stratified squamous epithelium) is important to maintain tissue integrity and form a protective barrier against the external environment. Desmosomes are specific protein complexes (made up of two types of calcium-dependent protein called desmoglein and desmocollin) responsible for maintaining cell-to-cell adhesion in this layer.

Pemphigus vulgaris (PV) is a potentially life-threatening autoimmune disease affecting the skin and/or mucosa. The incidence of PV is 0.1–0.5 cases/100 000 people/year¹ with an equal predilection for both genders. The mean age of onset is 50–60 years.² PV can be associated with other autoimmune disorders, particularly rheumatoid arthritis and lupus erythematosus.³ The disease is characterised by the loss of cellular adhesion due to the formation of IgG autoantibodies against desmoglein 1 and/or 3. Types 1 and 3 desmogleins are found within skin whereas mucosa contains only the type 3 variant. The severity and site of the disease will depend on whether types 1 and 3 desmogleins are affected. Patients with high-serum antidesmoglein 3 antibodies but low-antidesmoglein 1 antibodies will have only mucosal involvement. This is because the function of desmoglein 1 is preserved preventing the development of skin lesions.⁴ Loss of cell-to-cell adhesion results in the development of intraepithelial blisters that rupture following minimal trauma, leaving behind painful sloughing eroded areas of skin and/or mucosa.

Diagnosis requires biopsy of the perilesional tissue for histopathology to show acantholysis and direct immunofluorescence to demonstrate the presence of IgG antibody along the cell surface within the intercellular space.⁵

The oral cavity is often the first site affected and can predate widespread mucocutaneous involvement by several months. We present a case of a 56-year-old man who required hospital admission for several weeks following a life threatening exacerbation of previously undiagnosed PV.

CASE PRESENTATION

A previously fit and well 56-year-old man attended his general practitioner (GP) following a 4-month history of intermittent painful oral blisters (buccal mucosa and lips). The lesions would present for up to a week before healing and then representing a few weeks later. On the fourth month the patient noticed similar lesions on his torso and limbs prompting an appointment with his GP. The history of blisters affecting the skin and oral mucosa raised concerns of a possible autoimmune vesiculobullous disease, prompting an urgent referral to the dermatology department.

Figure 1 Eroded areas of skin affecting torso and limbs.

CrossMark

To cite: Vinall C, Stevens L, McArdle P. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-200479

Figure 2 Eroded areas of skin affecting torso and limbs.

In between waiting for an appointment with the dermatology team, the patient suffered a severe flare up of the disease requiring urgent admission to hospital. This resulted in widespread mucocutaneous blisters affecting the torso, limbs and oral mucosa. These lesions broke down following minimal contact leaving behind painful eroded areas of skin and oral mucosa (figures 1–3). The severity of the disease led to the following life-threatening issues:

- ▶ Dehydration and electrolyte imbalance secondary to excess fluid loss from the skin wounds;
- ▶ Sepsis secondary to infection of the exposed wounds.

The initial assessment of the patient was performed in the emergency department and the following immediate action taken:

Figure 3 Eroded areas of oral mucosa.

- ▶ Urinary catheterisation and resuscitation with intravenous fluids to correct the circulatory and electrolyte imbalance.
- ▶ Early management of sepsis with intravenous antibiotics as advised by the microbiology team.
- ▶ Control of acute pain with opioid analgesia.

Following stabilisation the patient was admitted under the joint care of the medical and dermatology teams. A problem list was formulated (table 1) to address the ongoing issues and provide a definitive management plan.

INVESTIGATIONS

Perilesional incisional biopsies were taken from both the oral mucosa and skin. The specimens were sent to the lab for urgent histopathology and direct immunofluorescence. Histopathology confirmed acantholysis in the epidermis with intraepidermal blistering. Direct immunofluorescence showed intercellular deposition of IgG in the epidermis. Both these findings confirmed a diagnosis of PV.

Indirect immunofluorescence was also performed and confirmed the presence of anti-intercellular substance antibodies. Indirect immunofluorescence is not the gold standard, but does support a possible diagnosis of pemphigus while awaiting confirmation from histopathology and direct immunofluorescence.

DIFFERENTIAL DIAGNOSIS

Pemphigus (vulgaris, erythematosus, paraneoplastic), bullous pemphigoid, impetigo, lichen planus and erythema multiforme.

TREATMENT

An appropriate ongoing intravenous fluid regimen was started under the guidance of the medical team to manage the acute renal injury.

While awaiting the definitive diagnosis, the patient was started on corticosteroid therapy (prednisolone 60 mg once daily). Prophylaxis for osteoporosis (alendronate 70 mg weekly) and peptic ulceration (omeprazole 20 mg once daily) were prescribed with the prednisolone.

A steroid mouthrinse (betnesol), diluted chlorhexidine mouthwash and an oral analgesic spray (benzydamine) were prescribed (four times daily) under the direction of the maxillofacial team to manage the oral lesions. This resulted in a dramatic improvement in the patient's oral symptoms within 2 days.

Table 1

Problem	Specialty advising management
▶ Awaiting definitive diagnosis	Dermatology Histopathology
▶ Inadequate nutrition Secondary to painful oral lesions	Dietitian Oral and maxillofacial surgery
▶ Acute renal injury Secondary to hypovolaemia (dehydration)	Acute medicine
▶ Inadequate pain management Oral and skin lesions	Acute pain team Oral and maxillofacial surgery
▶ No protective dressings for erosive skin wounds	Plastic surgery
▶ Ongoing management of sepsis	Microbiology
▶ Rehabilitation following recovery	Physiotherapy Occupational therapy

Prior to admission the bullous skin lesions would breakdown leaving painful eroded areas of skin with a similar appearance to the type of wounds found on burn victims. Early assessment by the plastic surgery team resulted in the placement of appropriate dressings to protect the skin wounds and relieve the patient's distress.

Within 2 days of admission the patient was able to manage a soft diet. An appropriate nutritional plan was prescribed by the dietitian.

On confirming the diagnosis by histopathology and direct immunofluorescence the patient was prescribed mycophenolate mofetil (steroid sparing immunosuppressant) at a dose of 1 g twice daily in addition to prednisolone.

OUTCOME AND FOLLOW-UP

The patient made a slow but gradual recovery over the next 4 weeks. The patient had been bedbound for the majority of the hospital admission. The physiotherapy/occupational therapy teams had been instrumental in providing appropriate rehabilitation and ensuring a safe discharge to his home environment.

Six months since discharge from hospital the patient continues to be reviewed regularly by the dermatology team. He is still prescribed mycophenolate mofetil, and is on a tapering dose of prednisolone (currently 10 mg once daily). He has fortunately not suffered a recurrence of the disease.

DISCUSSION

Pemphigus (derived from the Greek 'pemphix' meaning bubble or blister⁶) is the term given to a group of autoimmune vesiculobullous diseases characterised by intraepithelial acantholysis leading to epithelial and/or mucosal blistering. PV is the commonest variant of the disease.

Up to 70% of patients present with oral involvement long before skin lesions appear (up to 1 year¹). Common sites of oral involvement include the buccal, palatal, ventral tongue and labial mucosa.^{7 8 9-13} Other mucosal sites that can be affected by the disease are the oropharynx, oesophagus, conjunctiva, nasal, larynx, urethra, vulva and cervix.¹⁴⁻¹⁹

Owing to the friable nature of the involved skin/mucosa, it is preferable to biopsy tissue a short distance from clinically evident disease⁵ (perilesional tissue). Separate tissue specimens should be sent for histopathology to show suprabasal acantholysis and direct immunofluorescence to demonstrate IgG antibody and activated complement (C-3) in the intercellular space.²⁰ The oral mucosa is the optimum site for biopsy to show suprabasal acantholysis.⁴

Prior to the advent of corticosteroid therapy in the 1950s, the disease was in most cases fatal within 5 years.⁴ Systemic corticosteroids (prednisolone) rapidly brought the disease under control and up until recently have been the mainstay of treatment.¹² However when used as a single agent patients often relapse when the corticosteroid is tapered. Complications associated with the long-term use of corticosteroids led to a move towards immunosuppressants with a steroid-sparing effect. Plasmapheresis in combination with steroid-sparing immunosuppressants (azathioprine, cyclophosphamide) have been successful in controlling the disease.²¹⁻²³ However, the unfavourable side effect profile of these drugs (pancytopenia, hepatotoxicity) has led to the development of newer immunosuppressants such as mycophenolate mofetil that are better tolerated by patients. This drug has been shown to significantly reduce relapse of the disease when corticosteroids are tapered.²⁴

Learning points

- ▶ Oral lesions are often the first manifestations of the disease and can predate cutaneous lesions by up to a year.
- ▶ Early referral by the physician/dentist to the dermatology/oral and maxillofacial surgery department is necessary to ensure a prompt diagnosis before the onset of the more severe form of the disease.
- ▶ Patients presenting with severe pemphigus vulgaris will have multiple life-threatening issues. It is important to recognise these early and involve the appropriate medical/surgical specialty to ensure a rapid and comfortable path to recovery for the patient.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Said S, Golitz L. Vesiculobullous eruptions of the oral cavity. *Otolaryngol Clin North Am* 2011;44:133-60.
- 2 Knudson RM. The management of mucous membrane pemphigoid and pemphigus. *Dermatol Ther* 2010;23:268-80.
- 3 Anon. Pemphigus: current concepts. *Ann Intern Med* 1980;92:396-405.
- 4 Edgin W, Pratt TC, Grimwood RE, et al. Pemphigus vulgaris and paraneoplastic pemphigus. *Oral Maxillofac Surg Clin North Am* 2008;20:577-84.
- 5 Sciubba JJ. Autoimmune oral mucosal diseases: clinical, etiologic, diagnostic, and treatment considerations. *Dent Clin North Am* 2011;55:89-103.
- 6 Lira da Silva AV. Pemphigus vulgaris: a therapeutic option for disease control. *Gen Dent* 2008;56:700-3.
- 7 Lamey PJ, Rees TD, Binnie WH, et al. Oral presentation of pemphigus vulgaris and its response to systemic steroid therapy. *Oral Surg Oral Med Oral Pathol* 1992;74:54-7.
- 8 Pisanty S, Sharav Y, Kaufman E, et al. Pemphigus vulgaris: incidence in Jews of different ethnic groups according to age, sex and initial lesion. *Oral Surg Oral Med Oral Pathol* 1974;38:382-7.
- 9 Zagarelli D, Zagarelli E. Intraoral pemphigus vulgaris. *Oral Surg Oral Med Oral Pathol* 1977;44:384-93.
- 10 Shah RM, Billmoria KF. Oral pemphigus vulgaris. Clinico-pathological followup of 34 cases. *J Oral Med* 1983;38:170-3.
- 11 Kanwar AJ, Dhar S. Oral pemphigus vulgaris. *Pediat Dermatol* 1995;12:195-7.
- 12 Scully C, Paes De Almeida O, Porter SR, et al. Pemphigus vulgaris: the manifestations and long term management of 55 patients with oral lesions. *Br J Dermatol* 1999;140:84-9.
- 13 Scully C, Callacombe SJ. Pemphigus vulgaris: an update on etiopathogenesis, oral manifestations and managements. *Crit Rev Oral Biol Med* 2002;13:397-408.
- 14 Hodak E, Kremer I, David M, et al. Conjunctival involvement in pemphigus vulgaris: a clinical, histopathological and immunofluorescence study. *Br J Dermatol* 1990;123:615-20.
- 15 Hale EK, Bystryn JC. Laryngeal and nasal involvement in pemphigus vulgaris. *J Am Acad Dermatol* 2001;44:609-11.
- 16 Lurie R, Trattner A, David M, et al. Esophageal involvement in pemphigus vulgaris: report of two cases and review of the literature. *Dermatologica* 1990;181:233-6.
- 17 Trattner A, Lurie R, Leiser A, et al. Esophageal involvement in pemphigus vulgaris: a clinical, histologic, and immunopathologic study. *J Am Acad Dermatol* 1991;24:223-6.
- 18 Marren P, Wojnarowska F, Venning V, et al. Vulvar involvement in autoimmune bullous diseases. *J Reprod Med* 1993;38:101-7.
- 19 Sagher F, Bercovici B, Romem R. Nikolsky sign on cervix uteri in pemphigus. *Br J Dermatol* 1974;90:407-11.
- 20 Etlin DA. Pemphigus. *Dent Clin North Am* 2005;49:107-25.
- 21 Mazzi G, Raineri A, Zanoli FA, et al. Plasmapheresis therapy in pemphigus vulgaris and bullous pemphigoid. *Transfus Apher Sci* 2003;28:13-18.
- 22 Roujeau JC, Andre C, Joneau Fabre M, et al. Plasma exchange in pemphigus. Uncontrolled study of ten patients. *Arch Dermatol* 1983;119:215-21.
- 23 Blaszczyk M, Chorzelski TP, Jablonska S, et al. Indications for future studies on the treatment of pemphigus with plasmapheresis. *Arch Dermatol* 1989;125:843-4.
- 24 Erik AH, Knop J. Mycophenolate is effective in the treatment of pemphigus vulgaris. *Arch Dermatol* 1999;135:54-6.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow