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Title:
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Date:
2019-01-01

Citation:
Yang, G. Q. Q., Yap, T., Martyres, R., Varigos, G. A. & Scardamaglia, L. (2019). The impact of human herpesvirus detection in pemphigus vulgaris. Australasian Journal of Dermatology, 60 (3), pp.e259-e261. https://doi.org/10.1111/ajd.12977.

Persistent Link:
https://hdl.handle.net/11343/285019

The impact of human herpesvirus detection in pemphigus vulgaris

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Acknowledgements: The authors would like to thank the doctors and staff of The Royal Melbourne Hospital Department of Dermatology Outpatient Clinic.

Running title: Herpesvirus detection in pemphigus.

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ajd.12977

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Article type : Research Letter

The impact of human herpesvirus detection in pemphigus vulgaris

Pemphigus vulgaris is a rare immunobullous condition characterised by blistering of the skin and mucosa. Immunomodulating therapies are the primary treatment for pemphigus vulgaris and individuals may be susceptible to opportunistic infection.

While identified as possible triggering factors for pemphigus vulgaris, human herpesviruses are also a frequent complication of immunosuppression. Case reports indicate that the presence of human herpesviruses, particularly herpes simplex virus (HSV) and cytomegalovirus, in patients with pemphigus vulgaris can lead to delayed healing and poorer outcomes[1-3].

The medical records of 27 patients with a diagnosis of pemphigus vulgaris at The Royal Melbourne Hospital were reviewed to assess treatment outcomes and associations between pemphigus vulgaris and human herpesviruses. A Disease Severity Score was assigned to each clinical encounter based on history and clinical examination[4].

Thirty-two flocked nylon swabs for PCR detection of human herpesvirus were collected from 14 patients according to clinical indication, such as recalcitrant lesions, during their course of care (Figure 1). Eleven swabs were positive across 5 patients. HSV was detected in 5 patients and cytomegalovirus was detected in 2 patients. One patient had both cytomegalovirus and Epstein-Barr

virus isolated from the same swab. Four patients received prophylactic valaciclovir (0.5–2 grams/day) during their course of care (mean=15.6 months).

Twenty-four of 32 swabs were taken when the Disease Severity Score was 2 or 3 (Figure 2). No human herpesvirus was detected in patients with a score of 0. The chi-squared test for trend was not statistically significant (p=0.11).

Seven positive swabs were obtained whilst the patient was on mycophenolate mofetil (MMF). Among those, 5 were on maximal therapy (>3 grams/day) compared to 8 of 14 for a negative result. This association was not significant (p>0.66).

All patients treated for greater than 12 months (n=24) achieved a complete clinical remission. Four of 5 patients with positive swabs achieved complete remission with mean of 8.5 months compared to 16.7 months in those who were negative or never swabbed (p=0.18). The remaining patient had been treated for less than 12 months.

Further, the 4 patients treated for greater than 12 months who had a positive swab and subsequent antiviral treatment did not experience relapse during the study period (mean=18.1 months). Comparison of relapse rate between those who received (n=4) or did not receive (n=20) prophylactic valaciclovir was statistically significant (p=0.003). Comparison between those who received prophylaxis with those who were never swabbed was also significant (p=0.009).

In our cohort, 19% of patients had positive herpesvirus detection by swab in keeping with rates reported in the literature[5,6]. Interestingly, patients with positive viral swabs had lower times to first complete remission than those who had negative swabs or no swabs at all. All patients who had positive swabs were treated with the appropriate antiviral therapy. It is unclear if this played a role in the shorter time to first complete remission, however, as the numbers are too small to draw any significant conclusions. In addition, the 4 patients who received prophylactic valacyclovir remained disease free once complete remission was achieved. Should herpesviruses delay achieving remission or contribute to relapses of disease, it would support the prophylactic use of antiviral therapy. Stratification of individuals in which this is more appropriate is not clear. It may be that serum evidence of prior exposure should comprise a pre-immunosuppression screen.

Case reports have highlighted detection of herpesviruses in recalcitrant lesions, where subsequent antiviral therapy induced remission[7-9]. Further, a report described salivary viral presence predicted a more aggressive disease course intractable to conventional therapy[10]. Given pemphigus vulgaris is a multifactorial disease, in individuals where herpesviruses detection is associated with recalcitrant lesions, antiviral treatment may remit the progression of disease.

The proportion of positive versus negative viral swabs did not differ when compared to the dose of MMF. A trend exists for positive swabs with disease activity, however, immunosuppression does not appear to be associated. Thus, presence of herpesviruses in our cohort could be more strongly related to persistent mucosal ulceration than therapeutic immunosuppression.

Viral associations did not affect overall clinical outcomes but may be more significant on an individual level as those under antiviral prophylaxis had lower rates of relapse. These trends have been found in the largest reported cohort of pemphigus vulgaris patients in Australia. Further studies inspecting viral detection rates in individuals with and without mucosal ulceration who are and are not therapeutically immunocompromised are warranted. Although data of small cohort studies must be respectfully interpreted with caution, in a disease as rare as pemphigus vulgaris, such data can be clinically valuable.

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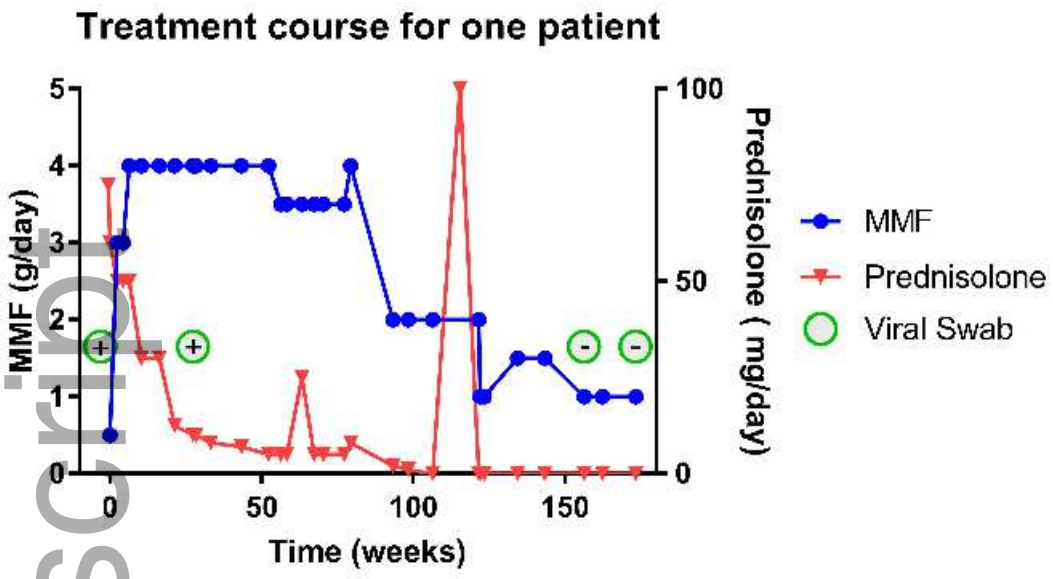
Figure legends

Figure 1: Treatment course of one patient. Treatment timeline for one patient showing wean of corticosteroid (prednisolone) and introduction and wean of mycophenolate mofetil (MMF) as well as viral swabs (+: positive viral swab, -: negative viral swab) where clinically indicated.

Figure 2: Viral Detection vs Disease Activity. Comparison of viral swab detection and distribution versus Disease Severity Score at time of swab. Thirty-two swabs were taken from 14 patients. The majority of positive swabs were taken when disease was severe (Disease Severity Score 2 or 3).



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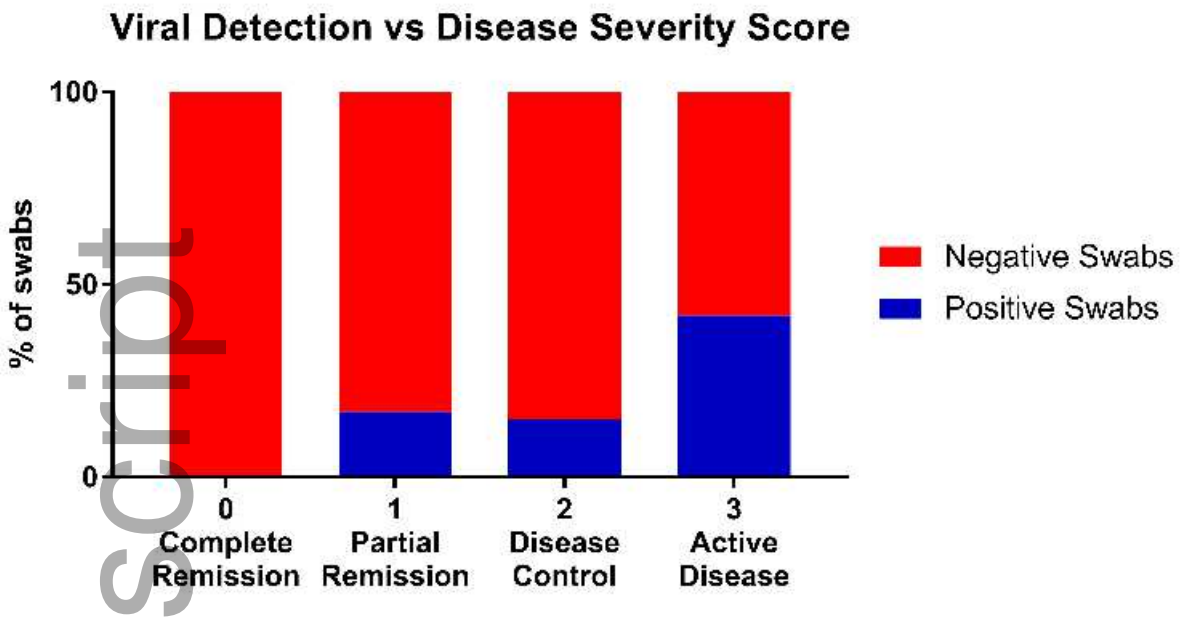

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