

DR ERIN WEI (Orcid ID : 0000-0002-2637-8963)

Article type : Research Letter

Post-traumatic stress disorder in patients with autoimmune blistering diseases

E. X. Wei^{1*}, S. J. Li^{1*}, A. Mostaghimi¹

***equal contribution**

Author Affiliations: ¹Brigham and Women's Hospital, Department of Dermatology, Harvard Medical School, Boston, MA

Corresponding Author: Erin X Wei MD, Brigham and Women's Hospital, Department of Dermatology, Harvard Medical School, Boston, MA **Email:** xewei@bwh.harvard.edu

Word Count: 748

Funding/Support: This study was supported by the International Pemphigus and Pemphigoid Foundation (IPPF)

Conflict of Interest Disclosures: The authors have no conflict of interest to disclose

Statement on prior presentations: This work was presented at the 2019 American Academy of Dermatology Meeting, Washington, DC

Reprint Request to: xewei@bwh.harvard.edu

Keywords: autoimmune bullous diseases, pemphigus, bullous pemphigoid, post-traumatic stress disorders

This article has been accepted for publication and 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/BJD.18548](https://doi.org/10.1111/BJD.18548)

This article is protected by copyright. All rights reserved

Post-Traumatic Stress Disorder (PTSD) can develop when an individual has an experience that threatens their psychological or physical integrity.¹ PTSD has been observed in patients with sudden-onset, life-altering or life-threatening health conditions ranging from cancer and asthma^{2,3} to Stevens-Johnson Syndrome,⁴ but has not been evaluated in chronic, relapsing inflammatory dermatologic diseases such as autoimmune bullous disease. PTSD may also directly impact immune function and a wide range of immune based disorders; previous studies of PTSD patients have reported a higher prevalence of autoimmune disorders, such as psoriasis.⁵

A diagnosis of autoimmune bullous disease (AIBD) often elicits a sense of apprehension and loss of control. The initial treatment phase frequently requires a combination of powerful immunosuppressive medications with an array of potential side-effects. Many patients experience acute limitations of their activities of daily living from their disease. In-office visits, frequent blood draws, daily medication administrations, wound care and dressing changes, as well as in-hospital and/or home infusions are time consuming, disruptive to work and life, and can be both directly and indirectly financially costly. Among patients who respond to treatment, the unpredictable relapsing and remitting nature of AIBD can result in long-term uncertainty.

These aspects of AIBD may result in anxiety that persists long after physical symptoms have improved. In clinical practice, many AIBD patients' biggest concern is that disease remission will be interrupted by acute episodes of recurrence and requirement for re-initiation of therapy. Many patients scrutinize every new skin lesion, itchy eyes, and oral sores during remission as signs of recurrent disease. There is a practice gap in the source of ongoing secondary psychological morbidity that is outside of the scope of current evaluations and its effect on the quality of life in patients with AIBD.

This study aims to evaluate the prevalence of PTSD among patients with AIBD.

In a single-center, IRB-approved cross-sectional study, the PTSD Checklist for DSM-5 (PCL-5), a 20-item validated patient-reported screening tool for PTSD⁶ was administered to 50 consecutive AIBD patients in outpatient clinics at Brigham & Women's Hospital.

Of 50 patients, 24 (48%) had pemphigus, 13 (26%) had bullous pemphigoid (BP), and 11 (22%) had mucous membrane pemphigoid (MMP) with the remainder a mix of other AIBD diagnosis (Table 1). Forty-three patients (86%) were undergoing treatment and 7 patients (14%) were in remission (defined as no new lesions and off all medications for > 2 months). Sixteen percent (8/50) screened positively for PTSD, with an average score of 42 ± 4.28 on the PCL-5 (Table 1). Feelings of intrusion (Cluster B) and avoidance (Cluster C) were predominant symptoms (Table 1). BP had the highest average PCL-5 score (19.0), followed by pemphigus (15.0) and MMP (15.0).

According to these results, one out of six AIBD patients met criteria for provisional diagnosis of PTSD, which is comparable to the prevalence of PTSD after a cancer diagnosis,⁷ and almost triple the lifetime prevalence of PTSD (6.8%) in the general population⁸. BP had the highest average PCL-5 score. Given the sudden and potentially traumatic nature of AIBD onset and its unpredictable remission and relapse, it would not be surprising if some patients develop PTSD. This may be especially true in BP given the often diffuse and persistent itching, and variability in treatment response often seen in that disorder.

Patients with AIBD suffering from PTSD can have long-term symptoms, including anxiety, hyperarousal and avoidance, with negative consequences in their personal, social, and professional interactions. Importantly, these symptoms may exist beyond the duration of disease activity even if patients do not meet formal criteria. These findings should raise awareness for this unseen aspect of their disease.

This study must be considered within the context of its study design, as the number of patients with non-BP and PV AIBD was limited. Recruitment in clinic may lead to selection bias that could either include more patients worried about their condition and therefore at higher risk of PTSD or conversely missed patients with PTSD who are health-care avoidant. Furthermore, as a cross-sectional study without pretreatment data on a patient's mental health, we cannot conclude a causal relationship between PTSD and AIBD at this time.

Future study is needed to evaluate risk factors for PTSD in AIBD and to quantify the overall burden of disease for this population. Simultaneously, given the potential for significant impact of PTSD on patients, early intervention and management in those who show signs of PTSD should be evaluated. Physicians should be aware of the lingering psychological effect of the disease and offer psychological support when appropriate.

References

1. American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders. 5th edn. Washington DA.
2. Kwakkenbos L, Coyne JC, Thombs BD. Prevalence of posttraumatic stress disorder (PTSD) in women with breast cancer. *J Psychosom Res.* 2014;76(6):485-486.
3. Chung MC, Rudd H, Wall N. Posttraumatic stress disorder following asthma attack (post-asthma attack PTSD) and psychiatric co-morbidity: the impact of alexithymia and coping. *Psychiatry Res.* 2012;197(3):246-252.
4. Hefez L, Zaghbib K, Sbidian E, et al. Post-traumatic stress disorder in Stevens-Johnson syndrome and toxic epidermal necrolysis: prevalence and risk factors. A prospective study of 31 patients. *Br J Dermatol.* 2019;180(5):1206-1213.
5. Boscarino JA. Posttraumatic stress disorder and physical illness: results from clinical and epidemiologic studies. *Annals of the New York Academy of Sciences.* 2004;1032:141-153.
6. Weathers FW, Litz BT, Keane TM, et al. The PTSD Checklist for DSM-5 (PCL-5). Available at: <https://www.ptsd.va.gov> (last accessed 19, August 2019).
7. Abbey G, Thompson SB, Hickish T, et al. A meta-analysis of prevalence rates and moderating factors for cancer-related post-traumatic stress disorder. *Psychooncology.* 2015;24(4):371-381.

8. Harvard Medical School NCSN, August 21. Data Table 1: Lifetime prevalence DSM-IV/WMH-CIDI disorders by sex and cohort. Available at <https://www.hcp.med.harvard.edu/ncs/index.php> (last accessed 19, August 2019).

Abbreviations:

PTSD: post-traumatic stress disorder

AIBD: autoimmune bullous disease

PV: pemphigus vulgaris

BP: bullous pemphigoid

MMP: mucous membrane pemphigoid

Table 1: PCL-5* Score by Disease-type

Demographic characteristics					
	Pemphigus (n=24)	Bullous Pemphigoid (n=13)	Mucous Membrane Pemphigoid (n=11)	Other (n=2)	Overall (n=50)
Male n (%)	12 (50%)	4 (31%)	3 (27%)	1 (50%)	20 (40%)
Age mean (SD)	61.0 (9.2)	77.6 (9.0)	65.5 (5.7)	55.0 (7.1)	66.1 (10.9)
PCL-5 score mean (SD)	15.0 (12.6)	19.0 (16.6)	15.0 (13.8)	12.0 (11.3)	16.0 (13.7)
PCL5 score >33	3/24 (13%), 42.7 (2.08)	3/13 (23%), 44 (5.29)	2/11 (18%), 38 (4.24)	0/2 (0%)	8/50 (16%), 42 (4.28)
PCL-5 Cluster scores per disease type; Mean (SD) Proportion of answers ranging “moderately – extremely” in each cluster					
Intrusion (B)	5.54 (4.12) 33.3% (5.15)	5.38 (4.59) 32.3% (3.11)	3.27 (4.05) 21.8% (1.52)	1.50 (2.12) 10% (0.45)	4.84 (4.23) 29.6% (9.98)
Avoidance	1.83 (1.95)	1.69 (1.70)	2.27 (2.8)	1.00 (1.41)	1.86 (2.05)

(C)	27.1% (3.54)	26.9% (0.71)	36.4% (0)	0% (0)	28% (4.24)
Cognition and Mood	3.83 (4.98)	6.69 (6.42)	4.27 (5.92)	4.00 (5.66)	4.68 (5.57)
(D)	16.7% (1.29)	31.9% (2.07)	15.6% (0.95)	21.4% (0.53)	20.57% (3.2)
Arousal and Reactivity	3.83 (3.67)	5.54 (5.88)	5 (3.61)	5.50 (2.12)	4.6 (4.26)
(E)	16.7% (3.29)	35.9% (1.26)	25.8% (1.47)	25% (0.55)	22.33% (6.94)

*PCL-5 score of 33 is generally used as the standard cut-off score for diagnosis of PTSD⁶