OPEN ACCESS Freely available online

Lupus: Open Access

Commentary

# Bullous Pemphigoid Associated with Neurological Disease: A Distinct Clinical Subtype

**Jonny Sain***

*Department of Dermatology, Clínica Universidad de Navarra, Madrid, Spain*

## DESCRIPTION

Bullous Pemphigoid (BP) is a chronic autoimmune sub epidermal blistering disease that primarily affects the elderly. It typically manifests as tense bullae on erythematous or normal-appearing skin, often accompanied by severe itching. While the pathogenesis of BP involves autoantibodies against hemidesmosomal proteins BP180 and BP230, growing evidence suggests a significant association between BP and neurological disorders, including Alzheimer's disease, vascular dementia, Parkinson's disease and multiple sclerosis.

A recent 20-year retrospective analysis at a specialized autoimmune blistering disease center evaluated 257 BP cases. Among them, 102 patients (approximately 40%) had a documented neurological comorbidity. The most frequently observed conditions were Alzheimer's disease, senile dementia and vascular dementia. This strong co-occurrence supports the hypothesis that bullous pemphigoid associated with neurological disease (BP-N) may constitute a clinically distinct subtype.

Clinically, BP-N patients demonstrated significantly elevated peripheral eosinophil counts and prominent eosinophilic infiltration in histological skin samples. Furthermore, they exhibited higher titers of circulating anti-BP180 IgG antibodies, a well-recognized biomarker of disease activity. Eosinophilia both in the bloodstream and tissues associated with more intense inflammation and often correlates with disease severity in BP. These immunological findings indicate a potentially more robust or dysregulated autoimmune response in BP-N patients.

Importantly, the data also revealed a notable prognostic difference. Of the 102 BP-N patients, 78 had died during the observation period, suggesting a higher mortality rate compared to BP patients without neurological conditions. Whether this elevated mortality is due to BP disease severity, the neurological disease itself, or their combined effect remains unclear. Nonetheless, this association raises the clinical relevance of early identification and potentially more aggressive treatment for patients with BP-N.

### Pathogenesis, implications and future direction

The immunological and clinical differences observed between BP and BP-N patients suggest possible differences in pathogenesis. Both BP180 and BP230 antigens are expressed not only in the skin but also within the Central Nervous System (CNS). In neurodegenerative diseases, damage to the blood-brain barrier, chronic inflammation and neuronal death may lead to the release or modification of neuronal isoforms of these proteins. This could prompt an autoimmune response, ultimately manifesting as cutaneous disease.

One prevailing theory is that neuro inflammation acts as a trigger for autoimmune skin involvement via molecular mimicry or epitope spreading. In such a model, neural exposure of BP antigens during neurodegeneration could break immune tolerance, leading to systemic antibody production that targets both CNS and cutaneous tissues. This "neuro cutaneous axis" provides a compelling explanation for the temporal and biological link between neurodegeneration and the subsequent development of BP.

Recognition of BP-N as a potential distinct entity carries important clinical implications. Physicians should maintain a high index of suspicion for underlying neurological disease in elderly patients presenting with BP, especially when laboratory markers show elevated eosinophils or BP180 titers. These patients may benefit from closer monitoring, more proactive immunosuppressive therapy and integrated care between dermatology and neurology specialists.

From a therapeutic perspective, BP-N patients may respond differently to standard treatments. Current guidelines do not differentiate between BP subtypes; however, the enhanced immune activation seen in BP-N may require tailored approaches. Further research should investigate whether BP-N patients benefit from early introduction of steroid-sparing immune suppressants, biologics, or adjunct therapies targeting eosinophilic pathways.

**Correspondence to:** Jonny Sain, Department of Dermatology, Clínica Universidad de Navarra, Madrid, Spain. Email: jonny@gmail.com

**Received:** 22-Jan-2025, Manuscript No. LOA- 25-37752; **Editor assigned:** 24-Jan-2025, PreQC No. LOA- 25-37752 (PQ); **Reviewed:** 7-Feb-2025, QC No. LOA- 25-37752; **Revised:** 14-Feb-2025, Manuscript No. LOA- 25-37752 (R); **Published:** 21-Feb-2025, DOI: 10.35248/2684-1630.25.10.328

**Citation:** Sain J (2025). Bullous Pemphigoid Associated with Neurological Disease: A Distinct Clinical Subtype. Lupus: Open Access.10:328.

Despite increased interest, standardized criteria for diagnosing BP-N are lacking. The majority of studies to date have been retrospective and vary in terms of diagnostic rigor for both BP and neurological conditions. Future prospective, multicenter studies are needed to confirm the distinct clinical course of BP-N and establish evidence-based diagnostic and therapeutic guidelines.

Additionally, investigation into predictive biomarker such as specific patterns of antibody isotypes, cytokine profiles, or imaging changes could facilitate earlier diagnosis and stratification of BP patients at risk for neurological comorbidities. Elucidating the molecular interplay between the CNS and cutaneous immune responses could also uncover novel targets for therapy, potentially improving long-term outcomes.

## CONCLUSION

Bullous pemphigoid associated with neurological disease represents a clinically and immunologically distinct variant characterized by higher eosinophilic activity, elevated anti-BP180 IgG antibody titers and increased mortality. These findings highlight the importance of a multidisciplinary approach and more vigilant disease monitoring in affected individuals. While the pathophysiological mechanisms linking neurological disease and BP remain under investigation, neuroinflammation and shared antigenic targets likely contribute to this association. Future research must focus on refining diagnostic tools, therapeutic strategies and prognostic indicators to optimize care for patients within this unique BP-N subset.