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To the Editor. We read with interest the manuscript published by Atzmony et al, concerning the association between bullous pemphigoid (BP) and malignancies.[1] As known, numerous studies have tried to investigate the link between BP and cancer. Besides the temporal association, some clinical evidences such as skin lesions improvement while on cancer-targeting procedures and the lack of recurrence after tumour excision are thought to support this relationship. Conversely, experimental studies providing plausible explanations about cancer-induced production of anti-basement membrane zone autoantibodies are still lacking. Moreover, revision studies have yielded contrasting results, because devoid of systematic approach.[1] Thus, the issue remains open to speculation as yet.

Interestingly, analysing the data of one cohort and four cross-sectional studies, Atzmony et al found a possible association between BP and hematoproliferative diseases, but not with overall malignancies.[1]

It is our opinion that the results by Atzmony et al might be influenced by an overestimated incidence of BP in hematologic patients, due to its clinico-pathologic, and sometimes immunopathologic, overlap with eosinophilic dermatoses of haematologic malignancies (EDHM). The latter refer to a heterogeneous spectrum of cutaneous manifestations occurring in patients with underlying hematologic cancer, mostly B-cells chronic lymphocytic leukaemia (B-CLL). Clinically, EDHM may present with urticarial papules, plaques, or nodules mimicking the pre-bullous phase of BP. Even blistering eruptions have been often reported.[2,3,4] Histopathologically, dermo-epidermal detachment and eosinophil-rich dermal inflammatory infiltrates are classically detected in both diseases.[4] Finally, EDHM may show confounding immunopathologic features, as reported in a study by Bottoni et al, in which six B-CLL patients with insect bite-like reactions had positive anti-BP180 antibodies on immunoblotting test,[5] and in a case by our group, in which a B-CLL patient with EDHM had linear deposition of Immunoglobulin M and C3 at direct immunofluorescence test.[4] Indeed, EDHM and BP appear challenging to distinguish, leading to potential diagnostic pitfalls. However, their distinction is crucial for many reasons: i) patients with idiopathic eosinophilic dermatoses has to be closely monitored because of the further risk of developing

hematologic malignancies, compared to idiopathic BP; ii) EDHM follow a waxing and waning behaviour despite both dermatologic and hematologic treatments; iii) the treatment of the two conditions is different.

To conclude, although BP may occur as a paraneoplastic event in patients with hematoproliferative diseases, clinicians should keep in mind EDHM in the diagnostic work-up of hematologic patients experiencing BP-like blistering eruptions.

References

1. Atzmony L, Mimouni I, Reiter O, et al. Association of bullous pemphigoid with malignancy: A systematic review and meta-analysis. J Am Acad Dermatol. 2017;77:691-699.
2. Bairey O, Goldschmidt N, Ruchlemer R et al. Insect-bite-like reaction in patients with chronic lymphocytic leukemia: a study from the Israeli Chronic Lymphocytic Leukemia Study Group. Eur J Haematol. 2012;89:491–6.
3. Rosen LB, Frank BL, Rywlin AM. A characteristic vesiculo-bullous eruption in patients with chronic lymphocytic leukemia. J Am Acad Dermatol. 1986;15:943–50.
4. Maglie R, Antiga E, Vannucchi M, et al. Bullous eruption in a patient with B-cells chronic lymphocytic leukaemia: a diagnostic challenge. Int J Dermatol. DOI: 10.1111/ijd.13807
5. Bottoni U, Mauro FR, Cozzani E, Innocenzi D. Bullous lesions in chronic lymphocytic leukaemia: pemphigoid or insect bites? Acta Derm Venereol. 2006;86:74-6.

116 **ABBREVIATIONS**

117 Bullous pemphigoid: BP.

118 Eosinophilic dermatoses of hematologic malignancies: EDHM.

119 B-cells chronic lymphocytic leukemia: B-CLL.