

2. Enjolras O, Wassef M, Chapot R. *Color atlas of vascular tumors and vascular malformations*. New York: Cambridge University Press, 2007.
 3. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg* 1982; 69: 412-22.
 4. Hermans DJ, Boezeman JB, Van de Kerkhof PC, *et al*. Differences between ulcerated and nonulcerated hemangiomas, a retrospective study of 465 cases. *Eur J Dermatol* 2009; 19: 152-6.
 5. Raffetto JD, Khalil RA. Mechanisms of varicose vein formation: valve dysfunction and wall dilation. *Phlebology* 2008; 23: 85-98.
- doi:10.1684/ejd.2010.0965

Urticarial vasculitis and asymptomatic acquired C1 esterase inhibitor deficiency revealing an angioimmunoblastic T cell lymphoma

A 60-year-old woman presented with a recurrent asymptomatic eruption of the legs that had lasted for 6 months. There was neither angioedema nor remarkable medical history. General examination revealed nothing more than a few urticarial papules on the inferior limbs. Histopathological examination of a skin biopsy showed lymphocytic and polymorphonuclear perivascular infiltrates without any alteration of vascular walls and no atypical cells. The clinical presentation and histopathological data, though not specific, were consistent with an urticarial vasculitis. Echocardiography, chest X-ray, and ultrasound scan of the abdomen and pelvis were normal. Full blood count and renal function were normal, ESR and serum C-reactive protein were low, serum lactate dehydrogenase and serum protein electrophoresis and immunofixation were normal (no hypergamma globulinemia (gamma globulins: 9.9 g/dL; normal range 8-13.5 g/dL) or monoclonal gammopathy). Prothrombin time was 100% and albuminemia was normal (45.5 g/dL). Anti-nuclear antibodies were positive (1600), with no specificity; anti-dsDNA antibodies were negative. Serologies of syphilis, hepatitis B, hepatitis C and HIV were negative. Beta2-microglobulinemia was slightly increased (3.3 mg/L); CH50, C4 and C1q levels were significantly decreased, whereas C3 was normal (CH50: 13.7 UH50/mL, normal range 42-61 UH50/mL; C4 < 0.045 g/L, normal range 0.1-0.4 g/L; C1q: 0.035 g/L, normal > 0.1 g/L); C1 esterase inhibitor (C1INH) level was decreased (C1INH activity: 0,12 (normal > 0,7) (chromogenic technic - Technochrom C1-Inh; Technoclone, Vienne, Autriche)); C1INH antigen: 0.09 (normal > 0.24 g/L) (radial immunodiffusion assay - NOR Partigen C1-Inhibitor Simens)); Anti-C1INH antibodies were negative (IgG, IgA and IgM < 10 UA/mL). Such results were in favour of an acquired C1INH deficiency. The patient was therefore referred to haematologists. A TEP scan and surgical biopsy of a hypermetabolic inguinal adenopathy led to the diagnosis of an angioimmunoblastic T cell lymphoma (*figure 1*).

Acquired C1INH deficiency was classically considered to be related to activation of the classical pathway of the complement (type 1, mainly associated with B-cell lymphoproliferation) or neutralisation by antiC1INH autoanti-

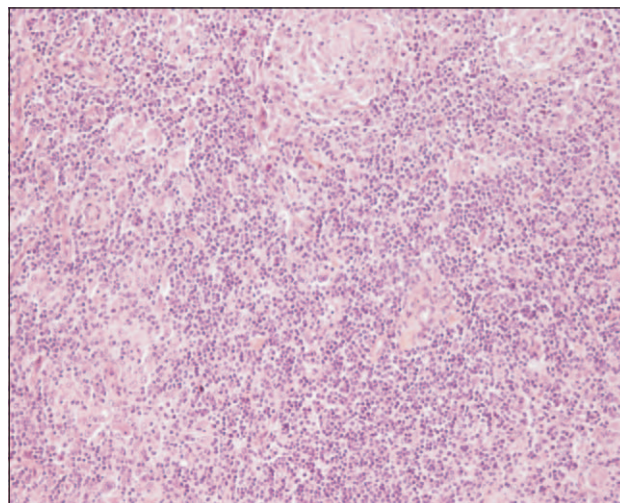


Figure 1. HPS, obj×10: The lymph node architecture is effaced. The node is infiltrated by polymorphous lymphocytes; there are abundant vessels and epithelioid cells. These features led to evoke AITL, further confirmed by immunohistochemistry.

bodies (type 2, mainly associated with monoclonal gammopathy of undetermined significance (MGUS) and autoimmune conditions). It has now been shown that the reality is not so clear cut and the frequent coexistence of true B cell lymphoproliferations, non malignant B cell proliferations and autoimmune phenomena has led to the current concept that increased C1INH consumption and C1INH neutralisation are frequently associated. Alterations in the control of B cell proliferation seems to be the common denominator [1, 2]. Since C1INH contributes to down-regulating bradykinin levels, its deficiency causes episodic angioedema, a rare clinical condition characterized by recurrent, localized, non-demarcated, non-pruritic subcutaneous swellings, which appear rapidly and resolve within hours to days. It can be potentially life threatening when affecting the upper-airways. Asymptomatic acquired C1INH deficiency is rare but has occasionally been found when systematically looked for in patients with lymphoproliferative disorders [3]; it has also been reported in association with autoimmune conditions [4]; thus it may be significantly underdiagnosed.

Angio-immunoblastic T-cell lymphoma (AITL) is a peripheral T-cell lymphoma, usually with a poor prognosis. The diagnosis requires a biopsy and histological examination of a pathologic lymph node (changes in peripheral blood and on bone marrow examination are usually non-specific). Various skin manifestations can be observed: transient morbilliform eruptions, infiltrated plaques, purpuric, urticarial or prurigo-like lesions. Even when clinical and histological features are non-specific, skin lesions often seem to be clonally related to the nodal T-cell proliferation. Patients sometimes also have various symptomatic autoimmune manifestations [5].

The association of these 2 rare conditions, which has never been reported to our knowledge, seems more than fortuitous. It seems that LAI can be added to the list of malignancies that can potentially be associated with acquired C1INH deficiency. ■

Acknowledgements. Financial source: none. Conflict of interest: none.

¹Dermatology Department,
HCL Lyon Sud 69495 Pierre Bénite,
France

²Haematology Department,
HCL Lyon Sud 69495 Pierre Bénite,
France

³University of Lyon,
Department of Immunology;
INSERM U851; HCL Lyon-Sud,
F-69495 Pierre-Benite, France

⁴Pathology department, HCL
Lyon Sud, 69495 Pierre Bénite,
France

⁵Biological Immunology Department,
Hôpital Européen Georges Pompidou,
Paris, France

⁶Dermatopathology Department,
HCL Lyon Sud 69495 Pierre Bénite,
France

<sebastien.debarbieux@chu-lyon.fr>

Clelia MOULIN¹

Sébastien

DEBARBIEUX¹

**Sophie DUCASTELLE-
LEPRETRE²**

Nicole FABIEN³

Lauriane DEPAEPE⁴

**Cécile VEYSEYRE-
BALTER³**

**Véronique FREMEAUX-
BACCHI⁵**

Sylvie ISAAC⁴

Brigitte BALME⁶

Luc THOMAS¹

1. Cicardi M, Zingale LC, Pappalardo E, Folcioni A, Agostoni A. Autoantibodies and lymphoproliferative diseases in acquired C1-inhibitor deficiencies. *Medicine* 2003; 82: 274-81 (Baltimore).

2. Cugno M, Castelli R, Cicardi M. Angioedema due to acquired C1 inhibitor deficiency: a bridging condition between autoimmunity and lymphoproliferation. *Autoimmunity Reviews* 2008; 8: 156-9.

3. Bibi-Trikki T, Eclache V, Frilay Y, et al. Acquired C1 inhibitor deficiency associated with lymphoproliferative disorders: four cases. *Rev Med Interne* 2004; 25: 667-72.

4. Barilla-Labarca ML, Giofrè D, Zanichelli A, Cicardi M, Atkinson JP. Acquired C1 esterase inhibitor deficiency in two patients presenting with a lupus-like syndrome and anticardiolipin antibodies. *Arthritis Rheum* 2002; 47: 223-6.

5. Dogan A, Attygalle AD, Kyriakou C. Angioimmunoblastic T-cell lymphoma. *Br J Haematol* 2003; 121: 681-91.

doi:10.1684/ejd.2010.0963

Pemphigus vulgaris of the pompholyx type

Pemphigus may present with a striking variety of clinical phenotypes. Here we report an 86-year old man who complained for six months about extensive blisters, dyshidrotic bullae and pustules limited to both plantae, and intense pruritus (figures 1A, B). Histopathology revealed eosinophilic and neutrophilic spongiosis (figures 1C, D). Direct immunofluorescence microscopy of perilesional skin showed intercellular deposition of IgG (figure 1E). Indirect immunofluorescence analysis on monkey oesophagus showed a positive intercellular staining pattern (figure 1F) and was negative on rat bladder. ELISA showed IgG against Dsg3, consistent with PV, while IgG autoantibodies against Dsg1, bullous pemphigoid (BP)180, BP230 and collagen type VII were not detectable. Moreover, an allergy work-up showed a positive patch test with fragrance mix (++), and parabene mix (+). In light of the limited involvement of PV, treatment with dapsone and topical steroids was initiated and relevant contact allergens, *i.e.* fragrance and parabene mix, were avoided, leading to complete remission within 3 weeks. When dapsone

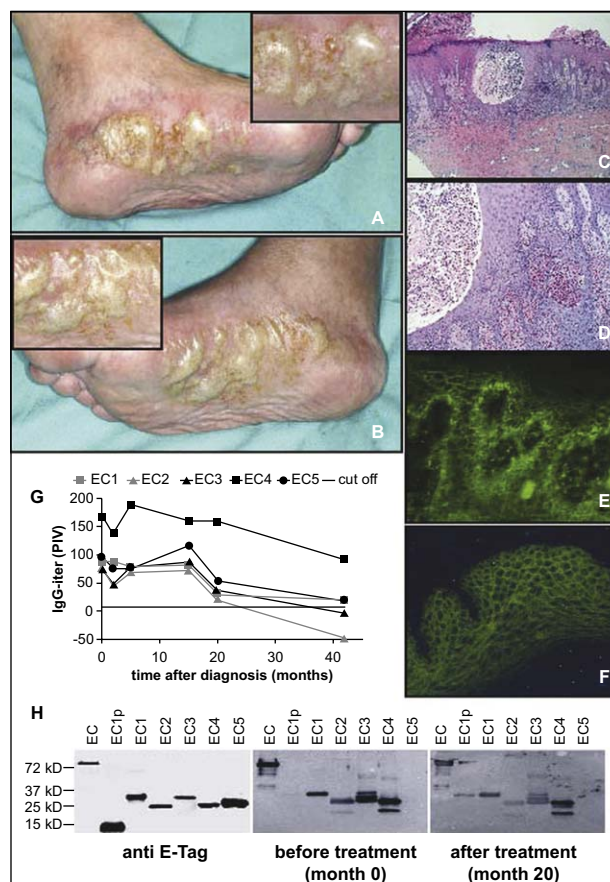


Figure 1. Pemphigus vulgaris restricted to the plantae. On the soles of the right (A) and on the left (B) medial side of the plantae, multiple tense and some flaccid yellow, serous, fluid-filled vesicles and bullae of variable sizes are formed with surrounding erythema. Inset shows small partly confluent vesicles demonstrating the pompholyx aspect. C) Histological examination of a Haematoxylin & Eosin stained biopsy in scanning magnification (40×) revealed an acanthotic epidermis, enhanced papillary plexus, and an intraepidermal blister. A dense superficial and deep perivascular and interstitial inflammatory infiltrate is seen. D) Higher magnification (100×) demonstrates eosinophilic and neutrophilic spongiosis. E) Direct immunofluorescence examination magnification (40×) of perilesional skin showed intercellular deposits of IgG. F) Indirect immunofluorescence examination (40×) of the patient's serum using monkey esophagus as a substrate shows intercellular binding of serum IgG autoantibodies. G) IgG titers against the subdomains of Dsg3 (EC1, EC2, EC3, EC4 and EC5). H) Immunoblot analyses show IgG reactivity before treatment (month 0, middle panel) and at the time of complete remission (month 20, right panel). Shown is the reactivity and molecular weight of the different recombinant proteins with a second antibody against the E-Tag (left panel). The middle panel depicts reactivity of our patient with EC (73,2 kD), EC1p (15,8 kD), EC1 (26,6 kD), EC2 (24,4 kD), EC3 (27,7 kD), EC4 (24,3 kD), or EC5 (24,3 kD) of Dsg3 prior to therapy. The patient's sera showed IgG reactivity against the entire Dsg3 ectodomain and the EC1, EC2, EC3, EC4, but not EC5 subregions of the Dsg3 ectodomain throughout the entire observation period.