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LYMPHOCYTIC VARIANT HYPEREOSINOPHILIC SYNDROME OVERLAPS WITH ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA: A CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

Introduction: Lymphocytic-variant of hypereosinophilic syndrome (L-HES) is a clonal T-cell disorder driven by an aberrant Th2 response, typically featuring CD3- CD4+ T-cell expansion, eosinophil-mediated tissue injury, most commonly skin lesions, and lymphadenopathy. Angioimmunoblastic T-cell lymphoma (AITL) is an aggressive peripheral T-cell lymphoma of follicular helper T-cell origin; it can present with similar clinical features such as lymphadenopathy, rash and eosinophilia. Histological and immunophenotypic features may also be common in both diseases, thus creating a diagnostic overlap.

Case description: We report the case of a 53-year-old man with a medical history of allergic rhinitis who developed a diffuse, persistent maculopapular rash with pruritis. Physical examination revealed inguinal lymphadenopathy without organomegaly, laboratory investigations demonstrated marked eosinophilia, and hypergammaglobulinemia, while additional testing excluded any infectious or autoimmune aetiologies. Lymphocytic immunophenotyping on peripheral blood and skin biopsy revealed a high proportion of CD3-CD4+ cells exhibiting a classic TH2 phenotype, consistent with L-HES. However, lymph node histology demonstrated architectural remodelling with intrafollicular infiltration by atypical T lymphocytes showing a T-cell follicular helper phenotype, findings indicative of AITL. The coexistence of L-HES and AITL was established. The patient underwent polychemotherapy, resulting in rapid clinical improvement of skin lesions with sustained remission at 6 months of follow up.

Conclusion: L-HES and AITL may coexist, or L-HES may precede overt lymphoma, suggesting clonal evolution within a shared biological spectrum. This case highlights diagnostic pitfalls and emphasizes the need for integrated clinical, pathological, flow cytometric and molecular evaluation.

KEYWORDS

Eosinophilia, adenomegaly, lymphoproliferation, flow cytometry

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LEARNING POINTS

- Lymphocytic-variant of hypereosinophilic syndrome (L-HES) may precede or be associated with T malignant lymphoproliferation.
- Physician awareness of L-HES conditions presenting with tumoral syndrome is necessary to rule out malignant lymphoproliferation.
- Histological samples and biological investigations are mandatory to distinguish L-HES from angioimmunoblastic T-cell lymphoma.

INTRODUCTION

Lymphocytic-variant of hypereosinophilic syndrome (L-HES) is a chronic clonal T-cell disorder defined by the presence of a Th2 T-cell subset overproducing interleukin-5 (IL-5), resulting in blood and tissue eosinophilia and multisystem involvement. Clinical manifestations most often affect the skin, lungs joints, and less commonly the heart and gastrointestinal tract. Although the abnormal T-cell population may be clinically silent, it can display various immunophenotypes, among which three predominate in L-HES: CD3-CD4+, CD3+CD4+CD7-, and CD3+CD4-CD8- TCR αβ, with the CD3+CD4- phenotype being the most frequent[1]. This pattern has also been reported in angioimmunoblastic T-cell lymphoma (AITL), an aggressive T-cell follicular helper (TFH)-derived lymphoma associated with heterogeneous clinical features and autoimmune manifestations such as autoimmune haemolytic anaemia, immune thrombocytopenia, and autoantibody production[2]. These two entities share similar clinical and biological features, including eosinophilia, skin involvement, lymphadenopathy, and hypergammaglobulinemia[1]. Their overlap may delay diagnosis and obscure the presence of an underlying lymphoma. Although progression from L-HES to T-cell lymphoma has been reported in previous studies[1], concomitant diagnosis of both conditions has rarely been described. Herein, we report the case of a 53-year-old man with concomitant L-HES and AITL. We describe the clinical, histopathological, and immunophenotypic characteristics of this uncommon association, and explore its diagnostic and pathological implications through a literature review.

CASE DESCRIPTION

A 53-year-old man with a history of allergic rhinitis presented to the emergency department with a diffuse pruritic maculopapular rash. The patient reported a persistent eruption without fever or other general symptoms. On physical examination, he was afebrile, body temperature of 36.7°C, blood pressure of 134/86 mmHg, heart rate of 89 beats per minute, and respiratory rate of 16 breaths per minute. Cardiopulmonary auscultation was normal. Dermatological examination revealed an extensive pruritic maculopapular rash involving the trunk, back, and lower limbs *(Fig. 1)*. Lymph node examination revealed bilateral inguinal lymphadenopathy, while the remaining lymph node regions were free. The rest of physical examination was unremarkable. Complete cell blood count showed marked leucocytosis with a white blood cell count at 11.2 g/l (normal range 4.5-10 g/l), eosinophils at 3.5 $\times 10^9$/l (normal range 0-0.5 $\times 10^9$/l), neutrophils at 5.49$\times 10^9$/l (normal range 1.8–7.5 $\times 10^9$/l), lymphocytes at 1.86 $\times 10^9$/l (normal range 1-4 $\times 10^9$/l), and monocytes at 1.33 $\times 10^9$/l (normal range 0.2-1 $\times 10^9$/l). Haemoglobin was 15.2 g/dl (normal range 12-17.5 g/dl) and platelet count was 295 $\times 10^9$/l (normal range 150-400 $\times 10^9$/l). Serum electrolytes, renal function, C-reactive protein and liver tests were normal. Serum electrophoresis showed polyclonal hypergammaglobulinemia at 21 g/l (normal range 7-16 g/l). Hepatitis B, C and human immunodeficiency virus serologies were negative. Immunological assessment (antinuclear antibody and antineutrophil cytoplasmic antibody) was negative. Lymphocyte immunophenotyping revealed a high proportion of CD3-CD4+ cells with a classic TH2 phenotype (CCR4+CCR6-CXCR3-CRTH2) consistent with L-HES *(Fig. 2)*. Eighteen fluorodeoxyglucose positron emission tomography scan with whole-body computed tomography showed bilateral hypermetabolic inguinal nodes (SUV 4.85-5.5) restricted to inguinal/pelvic



Figure 1. *Diffuse maculopapular rash involving the anterior trunk, predominantly the abdomen and bilateral flanks.*

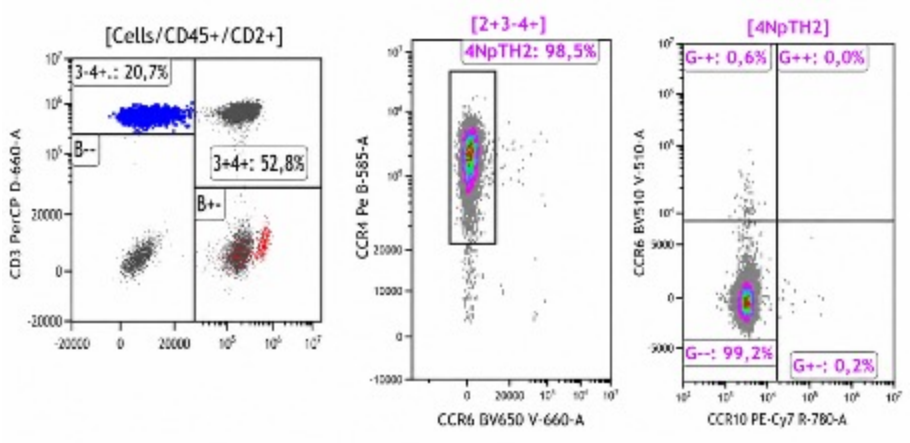


Figure 2. Flow cytometric analysis of CD45+ / CD2+ cells showing an expanded CD3−CD4+population. The secondary panel is consistent with a Th2 phenotype, characterized by CCR4 expression and absence of CCR6 and CCR10.

regions without hepatosplenomegaly *(Fig. 3)*. Skin biopsy showed a predominantly interstitial T-cell lymphocytic infiltrate involving the dermis and hypodermis, composed mainly of small, atypical lymphocytes with eosinophils, *(Fig. 4)*. Immunophenotyping revealed a dermal and per-adnexal T-cell infiltrates with CD3 -, CD4+, and partial loss of CD2/CD7. Complementary immunochemistry showed expression of several TFH markers, particularly PD1, CD10, CXCL13, ICOS, and BCL6. These findings are highly suggestive of TFH lymphoma. Lymph node biopsy showed a remodelled architecture with intrafollicular infiltration by atypical T lymphocytes. These T cells were CD4-positive and CD8-negative, and some expressed CD30. Epstein-Barr virus (EBV)-encoded ribonucleic acid was positive, consistent with EBV reactivation. Anti-CD20 immunostaining demonstrated interfollicular immunoblastic hyperplasia. Flow cytometric analysis revealed a CD3-low, CD4-positive, CD10-positive T-cell population. T-cell receptor (TCR) gene rearrangement was positive *(Fig. 5)*. The diagnosis of AITL in a patient with a L-HES clinical presentation was considered. The management consisted of polychemotherapy (cyclophosphamide, doxorubicin, vincristine, and methylprednisolone). Complete resolution of the cutaneous manifestations was achieved within 4 weeks, and the patient remained in sustained clinical and haematological remission after 6 months of regular follow-up.

DISCUSSION

L-HES is a chronic clonal T-cell disorder characterized by expansion of CD3-CD4+ T cells that exhibit a Th2 cytokine profile with overproduction of IL-5, resulting in peripheral eosinophilia and tissue eosinophilic infiltration[1]. These aberrant lymphocytes show strong expression of CD2 and CD5, partial or complete loss of CD7, and absence of surface CD3 despite cytoplasmic CD3ε retention, defining a distinctive immunophenotypic signature[3]. In our case, the inaugural presentation consisted of a generalized pruritic rash without systemic symptoms, and lymphadenopathy. In the French Cohort of L-HES, cutaneous involvement was reported in up to 81% of patients including urticaria, angioedema, purpura, and pruritus, followed by lymph node enlargement in 36% of cases. Other manifestations such as inflammatory arthralgia, synovitis, myositis or fasciitis, and gastrointestinal symptoms have also been described, all of which are consistent with a systemic inflammatory process, although these extracutaneous features appear to be relatively uncommon[4]. These features overlap with those observed in AITL, an aggressive TFH-derived neoplasm, which accounts for approximately 18% of peripheral T-cell lymphomas, though its incidence is likely underestimated due to diagnostic challenges[2]. AITL typically presents with an acute or subacute onset, most characterized by lymphadenopathy, which is nearly constant; fever, night sweats, and weight loss occur in over 68% of patients, while splenomegaly and/or hepatomegaly are observed in more than50% of patients. Cutaneous involvement is frequent with pruritus reported in 6–32% of patients, skin eruption may occur in 33-49% of patients. A wide range of additional manifestations, including ear nose and throat,

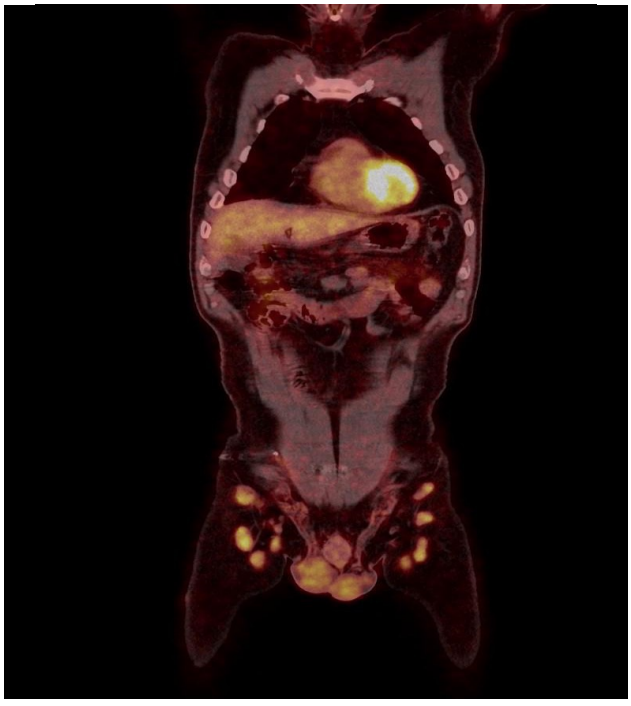


Figure 3. Coronal positron emission tomography/computed tomography fusion image demonstrating bilateral hypermetabolic inguinal and pelvic lymphadenopathy.

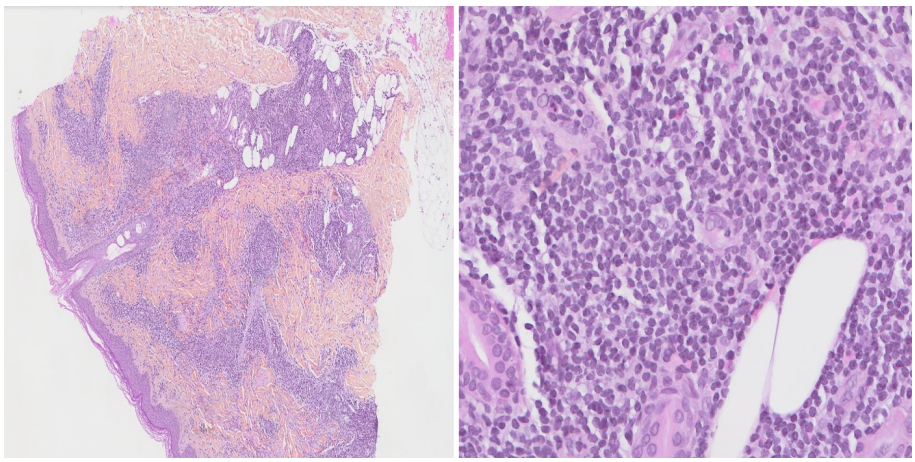


Figure 4. High-power view of hematoxylin and eosin staining showing a dermal infiltrate composed of small to medium sized lymphocytes with mild cytologic atypia, admixed with numerous eosinophils.

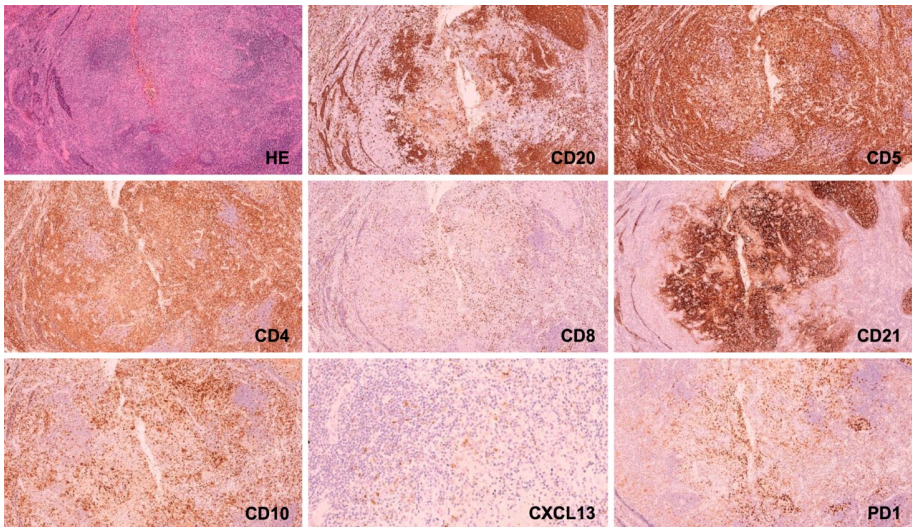


Figure 5. Effacement of the nodal architecture by a neoplastic T-cell infiltrate showing a T-follicular helper cell phenotype. Residual CD20⁺ B-cell follicles are disrupted and permeated by CD5⁺ CD8⁻ neoplastic T cells, accompanied by expansion of the follicular dendritic cell (CD21) network and expression of the T-follicular helper cell markers CD10, CXCL13, and PD-1.

Authors	Numbers of patients	Country	Mean age (years)	Sex (M/F)	Main clinical manifestations	CD3-CD4+ cells: detection site (%)	TCR gamma rearrangement site	Clinical outcome
Serke et al.[6]	5	Canada	55.6	5/0	NS	PB (0.7-10)	PB, BM	Died
Lee et al.[8]	2	Korea	65	NS	Lymphadenopathy, splenomegaly, fever	PB, LN (2-4)	Negative	Died
Chen et al.[7]	9	USA	52	4/5	NS	PB, LN, BM (0.1-55)	LN, PB, BM	Died
Stacchini et al.[9]	6	Italy	71	3/3	Fever, General symptoms	LN (8-50)	LN	Died
Baseggio et al.[10]	7	France	61	6/1	Lymphadenopathy, splenomegaly, pruritus	PB, LN (NS)	PB, LN	Died
Lefèvre et al.[3]	4	France	56	3/1	NS	PB, LN, BM (NS)	LN, PB	Died
Roufosse et al.[1]	1	Belgium	49	0/1	Fatigue, fever, angioedema	BM aspirate, PB (19% in LN)	NS	Died
Our case	1	France	53	1/0	Skin rash, lymphadenopathy	PB, LN (17% in LN)	LN, skin biopsy	Ongoing chemotherapy

Table 1. Summary of clinical and immuno-hematological findings of all reported cases of AITL associated with CD3-CD4+ L-HES. Abbreviations: NS, not specified; PB, peripheral blood; BM, bone marrow; LN, lymph node.

neurological, rheumatological, pulmonary, and renal involvement, may also occur and can occasionally be the initial presentation[2]. These common clinical manifestations may be misleading at first. Histologically, AITL and L-HES can exhibit polymorphous lymphoid infiltrates rich in eosinophils and plasma cells, which may initially suggest a reactive rather than neoplastic process[5]. CD3-CD4+ T cells are found in both diseases: small, uniform, indolent lymphocytes in L-HES, and in AITL as part of the neoplastic TFH infiltrate lymphocytes showing loss of CD3 and CD7 in AITL[6,7]. Moreover, expression of TFH markers such as PD-1, CXCL13, and ICOS can be detected in both conditions. Both disorders may show TCR-γ clonal rearrangement, but AITL is typically accompanied by additional TFH-related somatic mutations such as TET2, DNMT3A, or RHOA G17V not routinely found in benign L-HES clones[2].

The association between L-HES and AITL remains exceedingly rare. A literature review showed 35 cases of CD3- CD4+population associated with AITL. In most cases, L-HES precedes the diagnosis of AITL with a mean delay of 20 months (4 months to 2 years). The main clinical presentation was skin rash, lymphadenopathy, impaired general condition with eosinophilia. Despite appropriate chemotherapy, all reported patients died. *Table 1* summarizes the clinical and immuno-haematological findings of all reported cases of AILT and CD3-CD4+ L-HES. In contrast to the published data, our patient simultaneously developed L-HES and AITL. He received appropriate chemotherapy with a favourable outcome. Our case demonstrates that hyper eosinophilic symptoms associated with expanded CD3- CD4+ T cells with positive TCR rearrangement is not enough to establish a diagnosis of L-HES; therefore, a prompt careful exclusion of AITL is necessary, especially when associated with lymphadenopathy and/or unexplained systemic inflammation[3]. Additional molecular studies are mandatory to distinguish the two conditions. We suggest further investigations with histological confrontation by biopsy and molecular investigations in order not to miss a T malignant lymphoproliferation. In fact, L-HES clone may undergo somatic mutations (RHOA G17V and IDH2 R172) into TFH leading to AIT.

REFERENCES

1. Roufosse F, De Leval L, Van Krieken H, Van Deuren M. Lymphocytic variant hypereosinophilic syndrome progressing to angioimmunoblastic T-cell lymphoma. *Leuk Lymphoma* 2015;**56**:1891–1894. doi: 10.3109/10428194.2014.976823
2. Lachenal F. Lymphomes T angio-immunoblastiques. *Presse Médicale* 2007;**36**:1655–1662. doi: 10.1016/j.lpm.2007.06.001
3. Lefevre G, Copin MC, Roumier C, Aubert H, Avenel-Audran M, Grardel N, et al. CD3-CD4+ lymphoid variant of hypereosinophilic syndrome: nodal and extranodal histopathological and immunophenotypic features of a peripheral indolent clonal T-cell lymphoproliferative disorder. *Haematologica* 2015;haematol.2014.118042. doi: 10.3324/haematol.2014.118042
4. Lefèvre G, Bleuse S, Puyade M, Moulis G, Néel A, Abisror N, et al. Hypereosinophilia and Hypereosinophilic Syndromes: First Findings From a Nationwide Multicenter Cohort. *Allergy* 2025;**80**:1100–1110. doi: 10.1111/all.16463
5. De Leval L, Gisselbrecht C, Gaulard P. Advances in the understanding and management of angioimmunoblastic T-cell lymphoma. *Br J Haematol* 2010;**148**:673–689. doi: 10.1111/j.1365-2141.2009.08003.x
6. Serke S, Van Lessen A, Hummel M, Szczepek A, Huhn D, Stein H. Circulating CD4+ T lymphocytes with intracellular but no surface CD3 antigen in five of seven patients consecutively diagnosed with angioimmunoblastic T-cell lymphoma. *Cytometry* 2000;**42**:180–187. doi: 10.1002/1097-0320(20000615)42:3<180::AID-CYTO4>3.0.CO;2-0
7. Chen W, Kesler MV, Karandikar NJ, McKenna RW, Kroft SH. Flow cytometric features of angioimmunoblastic T-cell lymphoma. *Cytometry B Clin Cytom* 2006;**70B**:142–148. doi: 10.1002/cyto.b.20107
8. Lee S, Rüdiger T, Odenwald T, Roth S, Starostik P, Müller-Hermelink HK. Angioimmunoblastic T cell lymphoma is derived from mature T-helper cells with varying expression and loss of detectable CD4. *Int J Cancer* 2003;**103**:12–20. doi :10.1002/ijc.10758
9. Stacchini A, Demurtas A, Aliberti S, Di Celle PF, Godio L, Palestro G, et al. The Usefulness of Flow Cytometric CD10 Detection in the Differential Diagnosis of Peripheral T-Cell Lymphomas. *Am J Clin Pathol* 2007;**128**:854–864. doi: 10.1309/MC7QRGPTV0LRR98X
10. Baseggio L, Traverse-Glehen A, Berger F, Ffrench M, Jallades L, Morel D, et al. CD10 and ICOS expression by multiparametric flow cytometry in angioimmunoblastic T-cell lymphoma. *Mod Pathol* 2011;**24**:993–1003. doi: 10.1038/modpathol.2011.53