LYMPHOMATOID PAPULOSIS ASSOCIATING MASSIVE EOSINOPHILIA AND FIP1L1-PDGFRα FUSION GENE

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Introduction

Hypereosinophilic syndrome (HES) is a myeloproliferative disorder characterized by a sustained absolute eosinophil count > 1500/μl persisting more than 6 months without identifiable aetiology and eosinophil-mediated organ damage. In some patients with HES the expression of FIP1-Like 1/Platelet Derived Growth Factor Receptor-α (FIP1L1/PDGFRα) fusion protein has been detected. In this subgroup of patients treatment with the tyrosine kinase inhibitor imatinib mesilate appears to be highly effective.

Case Report

A 25-year-old male presented a 2-year history of recurrent crops of papules and ulcerated nodules on the trunk, extremities and oral mucosa which spontaneously resolved after necrotic evolution and left persistent atrophic scars. (Figures 1-3)

A skin biopsy of one of these nodules was performed and showed a wedge-shaped infiltrate of CD4+ anaplastic lymphocytes with marked nuclear pleomorphism, mitoses and some eosinophils. Immunophenotyping analysis showed a CD30+ phenotype consistent with lymphomatoid papulosis type A (LyP). (Figures 4-7) Laboratory tests revealed massive peripheral eosinophilia (7900/mm3), normal IgE levels, elevated tryptase (15.5 ng/ml) and vitamin-B12 serum levels (>2000). Stools for ova and parasites were negative. Other causes of hypereosinophilia were ruled out.

A bone marrow biopsy was hypercellular with marked eosinophilia, atypical spindle-shaped mast cells and increased reticulin fibrosis. CT scan showed splenomegaly and interstitial lung disease. Pulmonary function test demonstrates a restrictive ventilatory defect.Electrocardiogram, echocardiogram and ophthalmologic examination were all normal.

FIP1L1/PDGFRα fusiongene (4q12) was detected by FISH in peripheral blood cells. (Figure 8) Treatment with low dose of imatinib mesilate (100mg/d) was prescribed and a sustained response in both the abnormal haematological profile and LyP lesions was observed (follow-up period 6 months).

Figure 1. Nodule with necrosis in the center on the lower lip

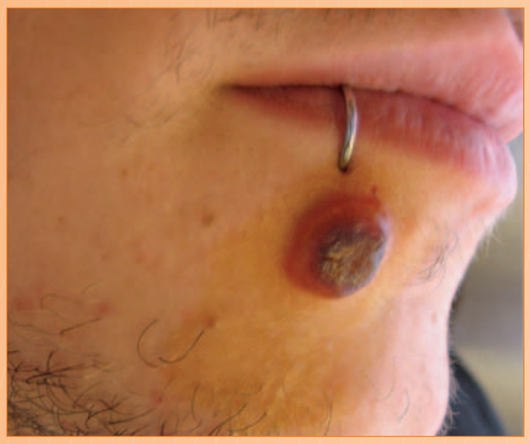

Figure 2. Ulcerated nodule on the tongue

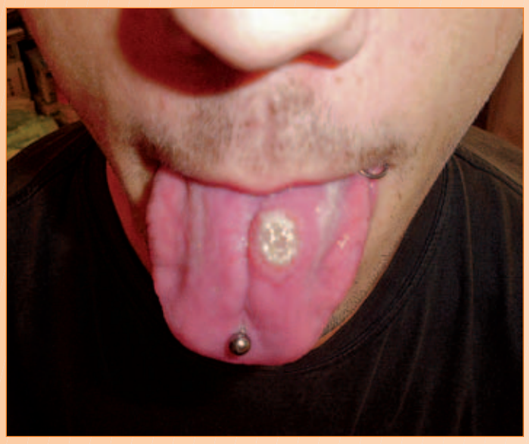

Figure 3. Necrotic papule on the lower leg

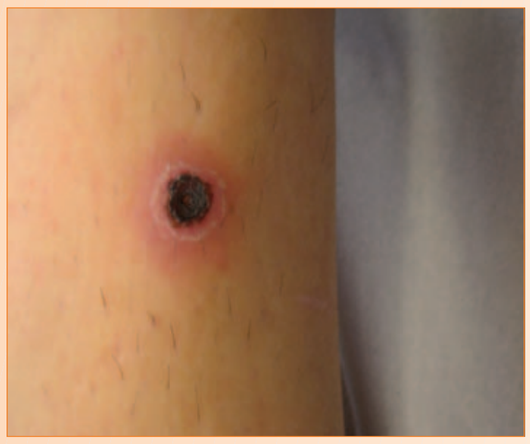

Figure 4. Wedge-shaped infiltrate of atypical lymphocytes (HE 40x)

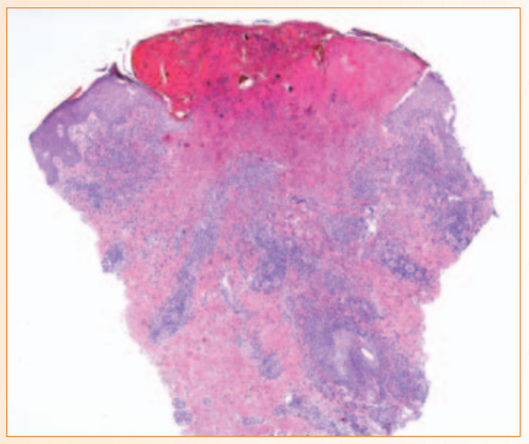

Figure 5-7. Close view showing anaplastic lymphocytes with marked nuclear pleomorphism and eosinophils (HE 400x) (Figure 5). The atypical lymphocites have a CD4+ (Figure 6) and CD30+ (Figure 7) phenotype

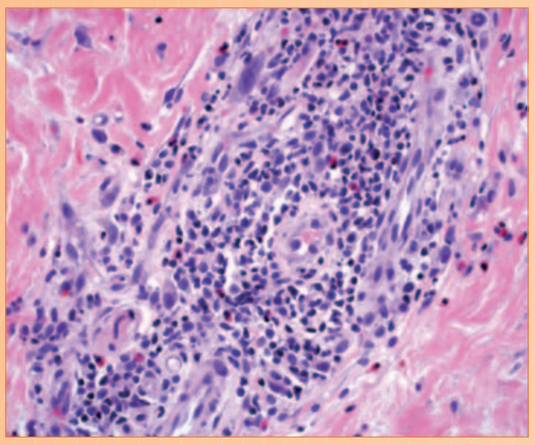

Figure 5

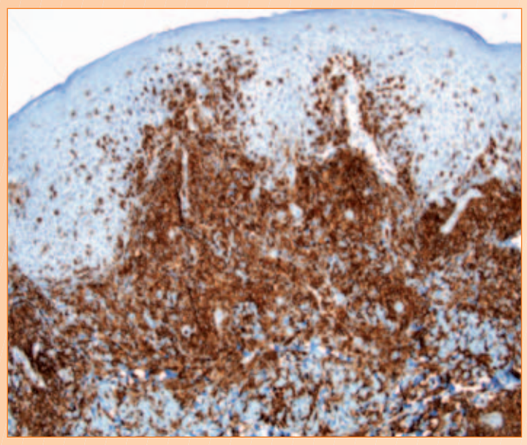

Figure 6

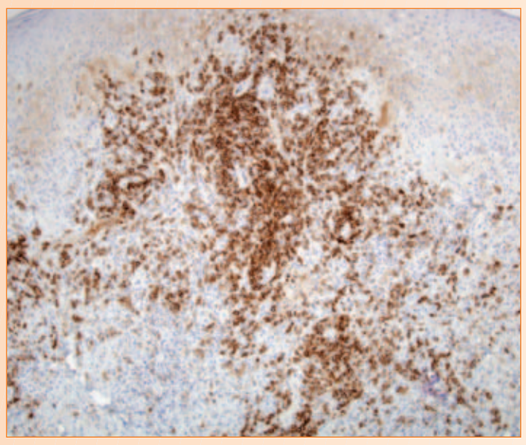

Figure 7

Figure 8. Presence of FIP1L1-PDGFRα fusion gene demonstrated by FISH

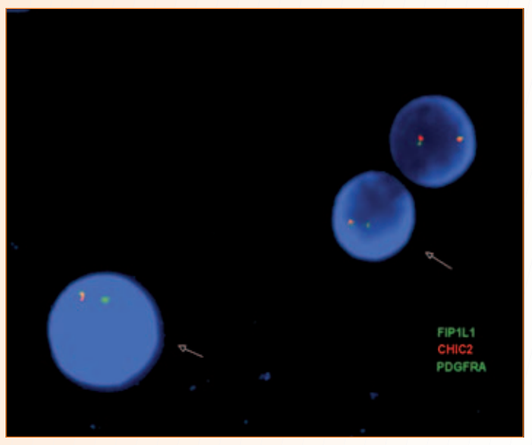

Table 1.Cases of LyP and HES secondary to FIP1L1-PDGFRα

Case	Sex/Age	Clinic presentation	FIP1L1-PDGFRα	Organ damage	Treatment	Follow up	Evolution
McPherson T et al (2006)	M/33	LyP + HES	Present	Myelofibrosis	Imatinib mesilate	9 months	Complete remission
Thuny C et al (2010)	M/51	LyP + CEL	Present	No	Imatinib mesilate	3 months	Complete remission
Present case	M/25	LyP + HES	Present	Splenomegaly, Interstitial lung disease, myelofibrosis	Imatinib mesilate	6 months	Complete remission

CEL: Chronic eosinophilic leukaemia

Discussion

PDGFRα-associated HES occurs more frequently in males (17:1) and is characterized by splenomegaly, elevated serum tryptase and B12 levels, bone marrow evidence of eosinophilia and atypical mast cells, tissue fibrosis, poor prognosis if untreated and spectacular response to imatinib mesilate.

The association of LyP and HES secondary to FIP1L1-PDGFRα has rarely been reported (2 previous reports). In these cases a complete remission of LyP lesions was noted after treatment with low doses of imatinib mesilate. (Table 1) The mechanisms implicated in such association remain obscure. A clonal T-cell population bearing the FIP1L1-PDGFRα has been identified in some HES cases. The possibility that such cells were responsible for induction of LyP lesions in patients with HES could be hypothesised.

References

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