Erythema annulare centrifugum associated with chronic lymphocytic leukaemia

DOI: 10.1111/j.1365-2133.2007.08125.x

SIR, Many conditions have been described as causing or being associated with erythema annulare centrifugum (EAC).1 We describe a patient in whom the simultaneous diagnoses of EAC and chronic lymphocytic leukaemia (CLL) were made, an association not previously reported.

A 74-year-old woman presented to the Department of Dermatology with a 3-week history of pruritic skin lesions affecting her upper back, upper arms, buttocks and thighs. On examination, there were several annular and arcuate erythematous plaques with central clearing and no scales (Fig. 1), consistent with an annular erythema.

She was concurrently referred with a lymphocytosis and diagnosed as having stage A(0) CLL, which did not require active treatment. The white cell count was 16.2 × 10⁹ L⁻¹ (normal 4.0–11.0 × 10⁹) with a lymphocytosis of 7.5 × 10⁹ L⁻¹ (normal 1.0–4.0 × 10⁹). The leukaemic cells expressed an immunophenotype consistent with CLL (CD19+/CD5+, CD23+ and weak surface immunoglobulin) but unexpectedly expressed CD20 and FMC7 strongly. Interphase fluorescent in situ hybridization studies showed trisomy 12 as the sole abnormality in 24% of cells.

The concurrent presentation of an annular erythema and CLL in this patient prompted suspicion that they might be linked. Cutaneous lesions in patients with leukaemia can be nonleukaemic (or ‘nonspecific’) such as caused by infections, drug reactions, vasculitis or secondary to a haemorrhagic

Fig 1. Annular, well-circumscribed erythematous plaque with raised edges and central clearing.

Fig 2. Skin biopsy showed a superficial perivascular infiltrate (a) composed predominantly of lymphocytes with occasional eosinophils (b). Haematoxylin and eosin; original magnification: (a) × 4; (b) × 40.
More rarely, neoplastic lymphocytes are found within the skin and these lesions are known as leukaemia cutis (or 'specific' lesions). In the context of CLL, both cutaneous findings in general and specific leukaemic cutaneous infiltrates have been reviewed.

An initial skin biopsy in our case showed a moderately intense superficial perivascular infiltrate composed predominantly of lymphocytes with several eosinophils. The epidermis showed focal spongiosis containing occasional eosinophils. A second biopsy showed similar changes but with minimal spongiosis, a more closely clustered arrangement of the infiltrate around superficial blood vessels and very few eosinophils (Fig. 2). No fungi were seen in periodic acid–Schiff-stained sections. Direct immunofluorescence on perilesional skin, taken to screen for early bullous pemphigoid, was negative. Immunochemistry demonstrated that the infiltrate was predominantly CD3 and CD5 positive, confirming a predominance of T cells, and CD23 negative, thus excluding leukaemia cutis. Interestingly, the first biopsy coincided with a peripheral blood eosinophilia of $2\times10^3$ L$^{-1}$ (normal 0·04–0·4 × 10$^3$), but this was resolved by the time of her second biopsy, and prior to treatment.

Having ruled out more specific categories of annular erythema (erythema chronicum migrans, erythema gyratum repens, erythema marginatum), and those associated with anti-SSA (anti-Ro) and anti-SSB (anti-La) antibodies, a diagnosis of EAC was made. The pathological findings favour what has been controversially termed 'superficial' EAC in which the dermal infiltrate is superficial, spongiosis is found in 80% of cases and eosinophils are observed in around one third of cases. Our patient’s skin lesions did not respond to potent topical steroids but to a reducing course of oral prednisolone starting at 30 mg daily.

EAC has been associated with drugs and a wide variety of disorders including infections, endocrine and immunological disorders, haematological and other neoplastic disorders. Annular erythemas have been described as the clinical presentation of bullous pemphigoid and hyper eosinophilic dermatitis in two patients with CLL, but to our knowledge, EAC per se has not been described in association with CLL. Although this association may be coincidental, the close temporal association prompts us to speculate that EAC in this case was a nonspecific manifestation of CLL.

References

1. Kim KJ, Chang SE, Choi JH et al. Clinicopathologic analysis of 66 cases of erythema annulare centrifugum. J Dermatol 2002; 29: 61–7.

2. Desch JK, Smoller BR. The spectrum of cutaneous disease in leukaemias. J Cutan Pathol 1993; 20: 407–10.

3. Agnew KL, Ruchlemer R, Catovsky D et al. Cutaneous findings in chronic lymphocytic leukaemia. Br J Dermatol 2003; 150: 1129–35.

4. Cerroni L, Zenahlk P, Höfler G et al. Specific cutaneous infiltrates of B-cell chronic lymphocytic leukaemia: a clinicopathologic and prognostic study of 42 patients. Am J Surg Pathol 1996; 20: 1000–10.

5. Oelère LS, Harris D, Rustin MH. Urticarial annular erythema: a new manifestation of Sjögren’s syndrome. Clin Exp Dermatol 1993; 18: 50–1.

6. Weyers W, Diaz-Cascajo C, Weyers I. Erythema annulare centrifugum: results of a clinicopathologic study of 73 patients. Am J Dermatopathol 2003; 25: 451–62.

7. Arseen M, Pembroke AC, Black MM et al. Eosinophilic spongiosis in association with bullous pemphigoid and chronic lymphocytic leukaemia. Br J Dermatol 2000; 143: 421–4.

8. Miljkovic J, Barntenjev I. Hyper eosinophilic dermatitis-like erythema annulare centrifugum in a patient with chronic lymphocytic leukaemia. J Eur Acad Dermatol Venereol 2005; 19: 328–31.

Conflicts of interest: none declared.

Erythema annulare centrifugum revealing chronic lymphocytic leukaemia

Sn, A 42-year-old woman presented with a 5-month history of annular skin eruptions. Skin lesions involved all four limbs and consisted of nonscaling erythematous, slightly papular lesions forming concentric rings (Fig. 1). The patient complained of mild pruritus and asthenia without weight loss. Physical examination was otherwise unremarkable, without palpable nodes or spleen. Blood analysis revealed lymphocytosis at $5\times10^9$ L$^{-1}$ (normal 1·5–4·0 × 10$^9$), with a normal erythrocyte and platelet count. Blood and bone marrow immunophenotyping showed that most of the lymphocytes were CD20, CD19, CD5 and CD23 positive, leading to the diagnosis of chronic lymphocytic leukaemia (CLL). Polymerase chain reaction (PCR) analysis showed a main B-cell clone in the blood. Fluorescent in situ hybridization study of blood lymphocytes showed a chromosome 13 deletion. Chest, abdominal and pelvic X-ray was normal and the CLL was classified as Binet stage A.

Skin biopsy revealed a deep dermal perivascular infiltrate of small nonatypical lymphocytes, without vasculitis, and only a few interstitial lymphocytes (Fig. 2a). The epidermis was normal. The underlying subcutaneous fat was not involved. The infiltrate was composed of T lymphocytes, stained by anti-CD3 antibody (Fig. 2b), and a minority of B lymphocytes as revealed by anti-CD20 staining (Fig. 2c). Only a few B lymphocytes expressed CD23 antigen (Fig. 2d), which is characteristic of CLL lymphocytes. CD5 was difficult to analyse because of the staining of T lymphocytes. PCR study of the skin biopsy showed a polyclonal profile within a very weak B-cell clone.

Departments of Dermatology and
Pathology, Leicester Royal Infirmary,
Leicester LE1 5WW, U.K.
*MIC Toxicology Unit,
University of Leicester, Leicester, U.K.
Correspondence: Karen Harman.
E-mail: karenharman@doctors.org.uk

I. Helbling
R. Walewska*
M. S. Dyer*
M. Bamford†
K. E. Harman

References

1 Kim KJ, Chang SE, Choi JH et al. Clinicopathologic analysis of 66 cases of erythema annulare centrifugum. J Dermatol 2002; 29: 61–7.

2 Desch JK, Smoller BR. The spectrum of cutaneous disease in leukaemias. J Cutan Pathol 1993; 20: 407–10.

3 Agnew KL, Ruchlemer R, Catovsky D et al. Cutaneous findings in chronic lymphocytic leukaemia. Br J Dermatol 2003; 150: 1129–35.

4 Cerroni L, Zenahlk P, Höfler G et al. Specific cutaneous infiltrates of B-cell chronic lymphocytic leukaemia: a clinicopathologic and prognostic study of 42 patients. Am J Surg Pathol 1996; 20: 1000–10.

5 Oelère LS, Harris D, Rustin MH. Urticarial annular erythema: a new manifestation of Sjögren’s syndrome. Clin Exp Dermatol 1993; 18: 50–1.

6 Weyers W, Diaz-Cascajo C, Weyers I. Erythema annulare centrifugum: results of a clinicopathologic study of 73 patients. Am J Dermatopathol 2003; 25: 451–62.

7 Arseen M, Pembroke AC, Black MM et al. Eosinophilic spongiosis in association with bullous pemphigoid and chronic lymphocytic leukaemia. Br J Dermatol 2000; 143: 421–4.

8 Miljkovic J, Barntenjev I. Hyper eosinophilic dermatitis-like erythema annulare centrifugum in a patient with chronic lymphocytic leukaemia. J Eur Acad Dermatol Venereol 2005; 19: 328–31.

Conflicts of interest: none declared.

Erythema annulare centrifugum revealing chronic lymphocytic leukaemia

DOI: 10.1111/j.1365-2133.2007.08132.x

Sn, A 42-year-old woman presented with a 5-month history of annular skin eruptions. Skin lesions involved all four limbs and consisted of nonscaling erythematous, slightly papular lesions forming concentric rings (Fig. 1). The patient complained of mild pruritus and asthenia without weight loss. Physical examination was otherwise unremarkable, without palpable nodes or spleen. Blood analysis revealed lymphocytosis at $5\times10^9$ L$^{-1}$ (normal 1·5–4·0 × 10$^9$), with a normal erythrocyte and platelet count. Blood and bone marrow immunophenotyping showed that most of the lymphocytes were CD20, CD19, CD5 and CD23 positive, leading to the diagnosis of chronic lymphocytic leukaemia (CLL). Polymerase chain reaction (PCR) analysis showed a main B-cell clone in the blood. Fluorescent in situ hybridization study of blood lymphocytes showed a chromosome 13 deletion. Chest, abdominal and pelvic X-ray was normal and the CLL was classified as Binet stage A.

Skin biopsy revealed a deep dermal perivascular infiltrate of small nonatypical lymphocytes, without vasculitis, and only a few interstitial lymphocytes (Fig. 2a). The epidermis was normal. The underlying subcutaneous fat was not involved. The infiltrate was composed of T lymphocytes, stained by anti-CD3 antibody (Fig. 2b), and a minority of B lymphocytes as revealed by anti-CD20 staining (Fig. 2c). Only a few B lymphocytes expressed CD23 antigen (Fig. 2d), which is characteristic of CLL lymphocytes. CD5 was difficult to analyse because of the staining of T lymphocytes. PCR study of the skin biopsy showed a polyclonal profile within a very weak B-cell clone.