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Cutaneous Richter syndrome: a better place to transform?

J. Kluk,[1] M. Moonim,[2] A. Duran,[3] J. Costa Rosa,[4] J. Cabeçadas,[4] R. Alvarez,[5] M. Cravo,[6] S. Whittaker[1] and A. Robson[7]

[1]Skin Tumour Unit and [7]Dermatopathology Department, 2nd Floor, Block C, South Wing, St. John's Institute of Dermatology; and [2]Department of Histopathology, 2nd Floor, North Wing, St Thomas' Hospital, Westminster Bridge Road, London SE1 7EH, U.K.
[3]Department of Haematology, Queen Elizabeth Hospital, Stadium Road, London SE18 4QH, U.K.
[4]Serviço de Anatomia Patológica, [5]Departmento de Hematologia and [6]Serviço de Dermatologia, Instituto Português de Oncologia de Lisboa, Francisco Gentil, Rua Professor Lima Basto, 1099-023 Lisbon, Portugal

Summary

The development of high-grade lymphoma in patients with chronic lymphocytic leukaemia is known as Richter syndrome (RS) and is associated with a grave prognosis, with a mean survival of 8 months despite treatment. Cutaneous RS has been described in a handful of cases and may be associated with a better outcome than the more common extracutaneous variants. We review the literature with particular emphasis on pathogenesis, treatment and survival of RS. We postulate that the absence of B symptoms and a normal lactate dehydrogenase level, presumably reflecting localized or limited disease, and a lower tumour burden, may explain the apparently better survival in some patients with cutaneous RS than with extracutaneous variants.

Correspondence
Justine Kluk.
E-mail: justine.kluk@gstt.nhs.uk

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What's already known about this topic?

- Richter syndrome (RS) denotes the development of high-grade lymphoma in patients with chronic lymphocytic leukaemia and is associated with a grave prognosis.
- Skin involvement is exceptionally rare with <20 cases reported in the literature.

What does this study add?

- We review the literature and present two further examples of RS arising in the skin.
- Cutaneous RS may have a more favourable prognosis than more common extracutaneous variants.

First described in 1928 by Maurice Richter, Richter syndrome (RS) denotes the development of high-grade lymphoma in patients with chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL), and typically heralds an abrupt clinical deterioration and rapid demise, despite aggressive treatment.

Although RS arises in the lymph nodes or bone marrow in most cases, extranodal RS is recognized and may involve the gastrointestinal (GI) tract, central nervous system (CNS), eyes, lungs, kidneys or testes. Skin involvement is exceptionally rare, with < 20 cases reported in the literature. Although some authors have observed a more favourable clinical course with greater survival times in individuals with cutaneous RS compared with extracutaneous RS, firm conclusions cannot be drawn from the small number of cases reported. We present two patients with cutaneous RS seen in our institutions and highlight this entity to the dermatology readership.

Case report

Patient 1

A 79-year-old woman with a 10-year history of CLL (Binet stage A) was referred to the cutaneous lymphoma clinic with

an 18-month history of a skin eruption on her right upper arm. She had been monitored by her local haematology team since her diagnosis of CLL in 2003 and had otherwise been asymptomatic, with a stable leukocyte count of approximately 50×10^9 cells L^{-1} since at least 2007. Her past medical history included hypertension, chronic obstructive pulmonary disease and carcinoma of the right breast treated with mastectomy and axillary lymph node clearance in 2003. In 2012, she underwent surgical excision of a retrosternal goitre. Histopathological examination of six mediastinal lymph nodes resected at the time confirmed infiltration by CLL/SLL. Positron emission tomographic and computed tomographic (PET-CT) scans in 2007 and 2012 demonstrated low-grade uptake within a right cervical lymph node and bilateral external iliac nodes in keeping with CLL.

On presentation to dermatology, the patient was systemically well, with no B symptoms. She described the development of a rash on her right upper arm in 2011 following the administration of a steroid injection. Having initially resolved spontaneously, the rash had subsequently recurred and persisted. Examination revealed multifocal erythematous papules, plaques and tumours on the right upper arm, extending to the inner aspect of the arm and just below the elbow (Fig. 1a). There was no palpable lymphadenopathy or hepatosplenomegaly, and no distant cutaneous involvement. Her leukocyte count was 49·1 ($4–11 \times 10^9$ cells L^{-1}), lymphocyte count was 39·8 ($1·2–3·5 \times 10^9$ cells L^{-1}), neutrophil count was 7·9 ($1·5–7·0 \times 10^9$ cells L^{-1}), platelet count was 141 ($150–400 \times 10^9$ cells L^{-1}), haemoglobin was 14·1 (12·0–15·0 g dL^{-1}), and her lactate dehydrogenase (LDH) was 365

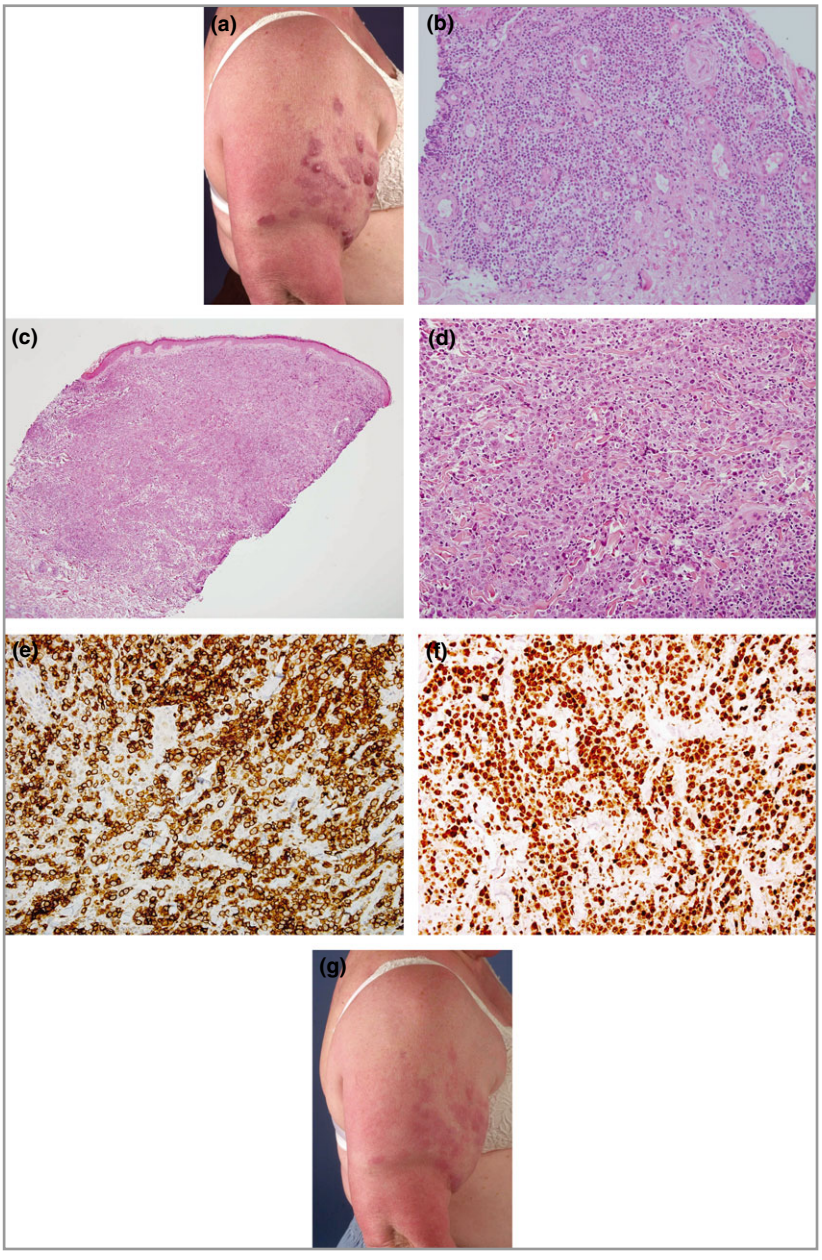

Fig 1. (a) Patient 1 presented with nodules and plaques on the right upper arm. (b) Small-to-medium-sized lymphocytes of chronic lymphocytic leukaemia in the deep dermis and subcutis (haematoxylin and eosin, original magnification ×100). (c) A diffuse dermal infiltrate (haematoxylin and eosin, original magnification ×20). (d) A diffuse population of centroblasts and immunoblasts in the dermis (haematoxylin and eosin, original magnification ×100). (e) Strong expression of CD79a (original magnification ×100). (f) The neoplastic cells strongly expressed MUM1 (original magnification ×100). (g) Partial response to chemotherapy after three cycles of mini R-CHOP.

(240–480 IU L^{-1}). Her immunoglobulin levels were normal, with no paraprotein on serum protein electrophoresis. A staging PET–CT scan confirmed stable appearances compared with previous images with no evidence of a high-grade fluorine-18 fluorodeoxyglucose (FDG)-avid lymphomatous nodal process.

A skin biopsy taken at her local hospital from a representative lesion on the right arm demonstrated a mononuclear cell infiltrate within the deep dermis and subcutis consisting of small-to-medium-sized lymphocytes (Fig. 1b), with a CD20+, CD79a+, CD5+, CD23+, CD10–, MUM1/IRF4– immunophenotype and a low proliferative fraction with Ki-67 (<30%). In contrast, the dermis had a diffuse population of large, atypical blast-like cells with large nuclei and prominent, sometimes multiple, nucleoli, indicative of centroblasts and immunoblasts. These cells had a CD20+, CD79a+, CD5–, CD23–, BCL2+, BCL6+, MUM1+, CD10– phenotype (Fig. 1c–f), and a high growth fraction with Ki-67 (> 95%). Epstein–Barr virus-encoded RNA (EBER) was negative. Only occasional tumour cells expressed p53, with

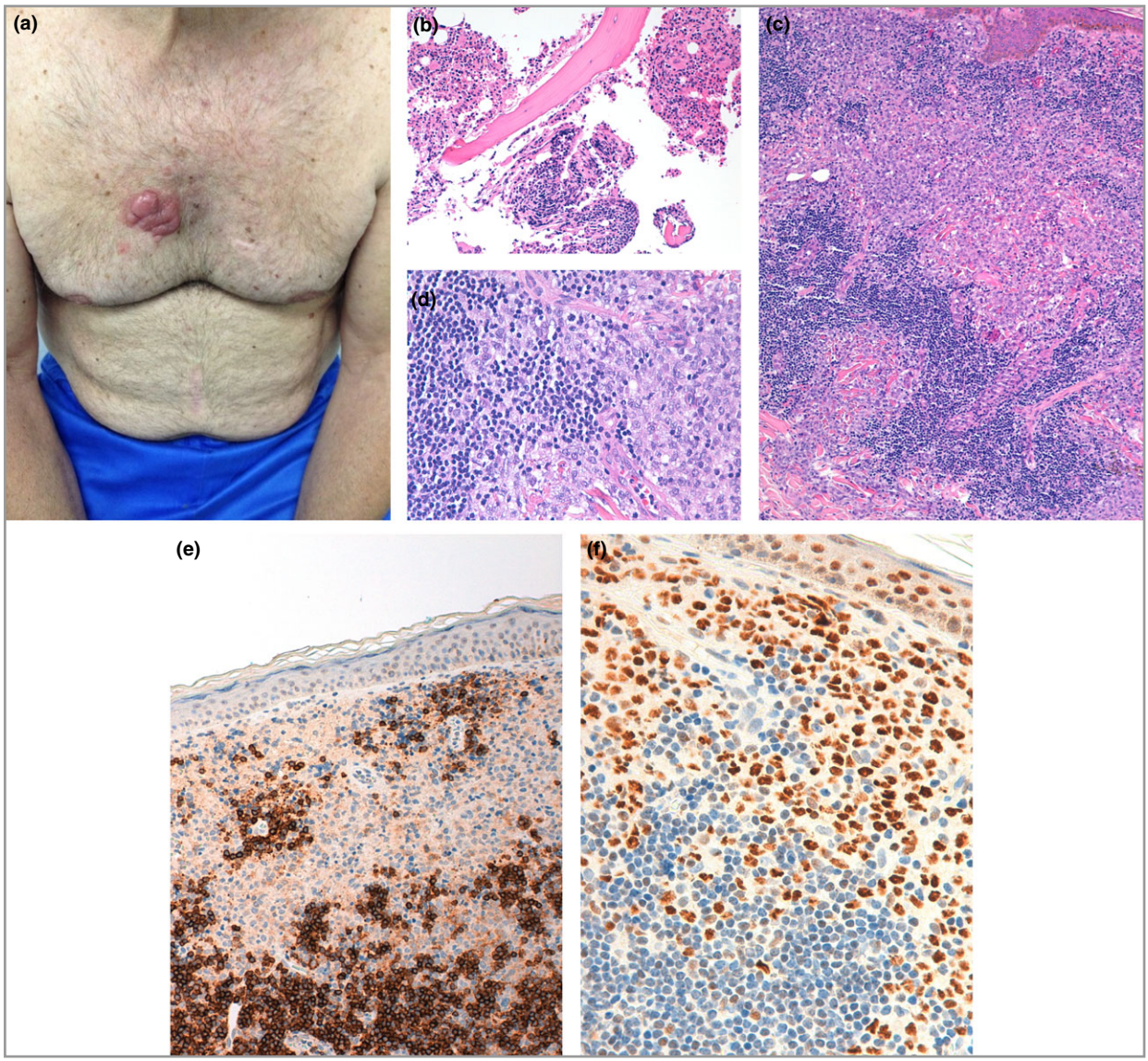

Fig 2. (a) Patient 2 presented with a large tumour on the right anterior chest. (b) Bone marrow trephine with involvement by small lymphoid cells of chronic lymphocytic leukaemia (CLL; original magnification × 100). (c) A diffuse mononuclear infiltrate including small lymphocytes and medium-sized malignant cells (haematoxylin and eosin, original magnification × 40). (d) The lymphocytes of CLL (left) and the high-grade centroblasts (right) are contrasted here (haematoxylin and eosin, original magnification × 200). (e) Expression of CD23 by the smaller lymphocytes of chronic lymphocytic leukaemia (original magnification × 40). (f) The high-grade component is BCL6+ (original magnification × 100). (g) Clonality studies for patient 2 demonstrating clonal IgH and IgK gene rearrangements, which were identical in skin and the bone marrow. (h) Regression after initiation of R-CHOP (rituximab–cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy.

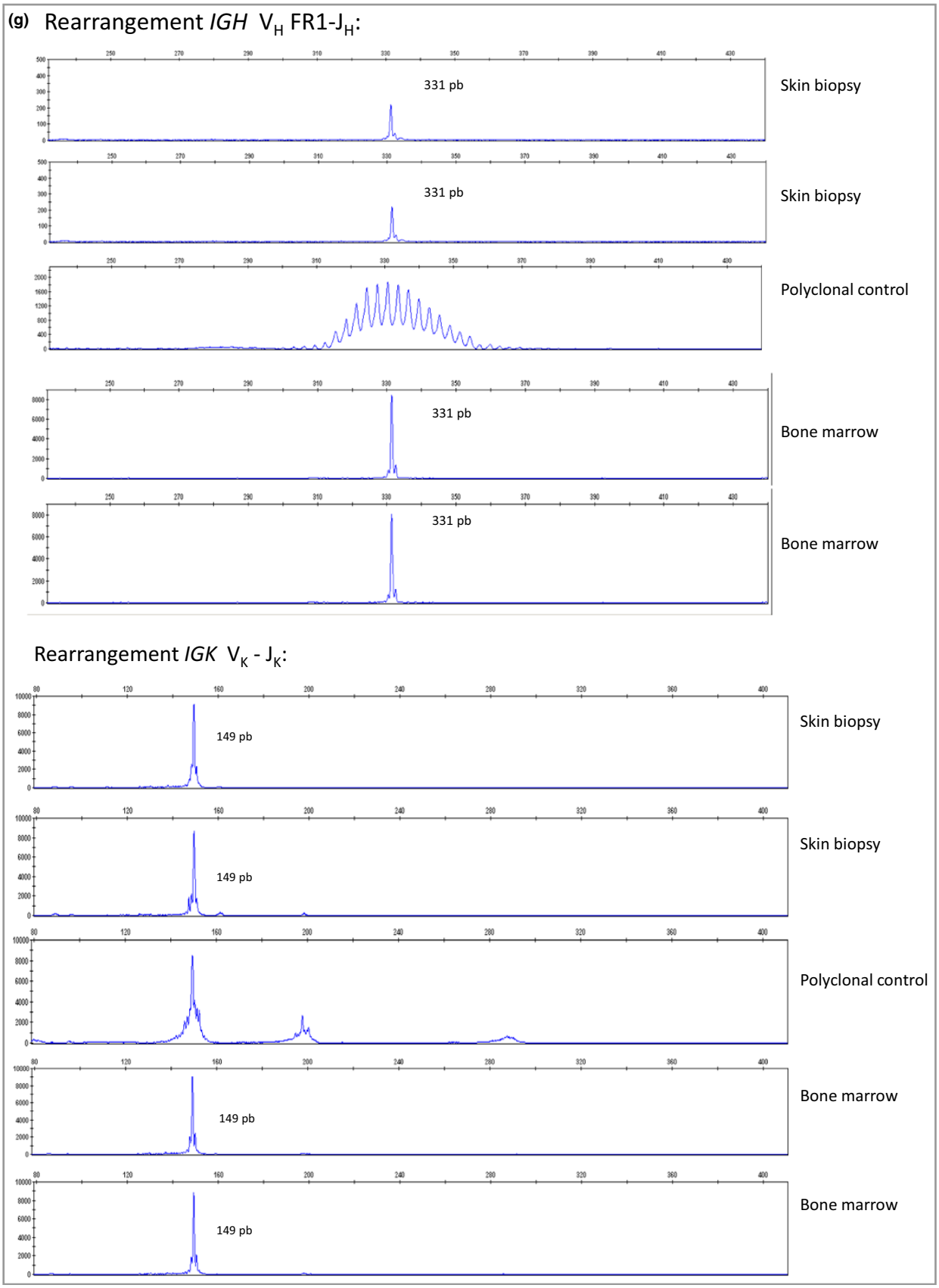

Fig 2. Continued.

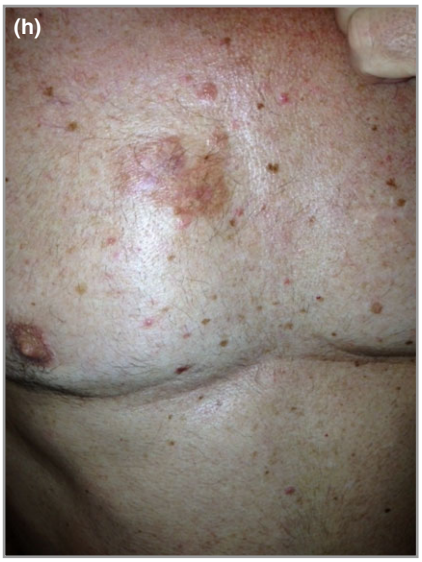

Fig 2. Continued.

no corresponding loss of p21, indicating that a p53 mutation was unlikely. Fluorescent *in situ* hybridization (FISH) analysis showed no evidence of MYC rearrangement and the t(14:18) chromosomal translocation was not detected. In the context of the patient's history of CLL, these findings were felt to represent transformation to cutaneous RS. Molecular genetic analysis demonstrated a clonal IgH gene rearrangement in peripheral blood and a nonidentical IgH clone in the skin. A bone marrow biopsy showed a slightly hypercellular marrow in which there was an extensive infiltrate (80%) of small lymphocytes (CD79a+, CD20+, CD3–, CD5+, cyclin D1–, CD38–), in keeping with CLL.

In view of her age, the patient has recently commenced mini R-CHOP (rituximab–cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy. She is responding to treatment, and the lesions are improving but still prominent after three cycles of chemotherapy (Fig. 1g). Her lymphocyte count has normalized. PET–CT after two cycles of treatment did not show uptake in the right arm. Low-grade uptake was seen in lymph nodes, compatible with her CLL. She may require radiotherapy to the remaining lesions after completing six cycles of chemotherapy.

Patient 2

A 65-year-old man presented with a 3-year history of an enlarging lesion on his chest (Fig. 2a). He was otherwise well, with no B symptoms. His past medical history was unremarkable apart from a previous facial basal cell carcinoma. He was not taking any regular medications. Examination revealed a solitary lobulated erythematous tumour on the right anterior chest with no distant cutaneous lesions and no lymphadenopathy or hepatosplenomegaly.

A full blood count confirmed a leukocyte count of 22·9 (4·0–11·0 $\times$ 10^9 cells L^{-1}) with a lymphocyte count of 13·9 (1·2–3·5 $\times$ 10^9 cells L^{-1}). LDH was 291 (240–480 IU L^{-1}) and β2 microglobulin was normal. Bone marrow biopsy confirmed an interstitial and focally nodular infiltrate of small lymphocytes (CD20+, CD3–, CD23+), and a bone marrow aspirate showed 47% monoclonal B lymphocytes (CD19+, CD20+, CD5+, CD23+, CD10–, CD79b–, CD200+, kappa+, lambda–, CD38–), suggestive of chronic lymphocytic leukaemia (Fig. 2b). A CT scan of the neck, chest, abdomen and pelvis demonstrated a left submandibular lymph node measuring 18 $\times$ 12 mm, a further enlarged node between the portal vein and inferior cava measuring 26 $\times$ 11 mm, and splenomegaly.

A skin biopsy of the tumour demonstrated a cellular infiltrate comprising a dual population (Fig. 2c,d). One population consisted of small cells in keeping with CLL (CD20+, CD23+, CD5+, CD10–, BCL2+, BCL6–, cyclin D1–) (Fig. 2e). MUM1/IRF4 was positive in 10% of the cells, p53 < 5% of cells and Ki67 was negative. The other population consisted of large, markedly atypical cells consistent with diffuse large B-cell lymphoma (CD20+, CD5–, CD23–, CD10+, BCL2–, BCL6+, MUM1/IRF4–, EBER–) (Fig. 2f). p53 was positive in < 5% of the cells and the growth fraction with Ki67 was 50%. FISH analysis showed no evidence of MYC rearrangement, and analysis with a centromeric probe for chromosome 12 performed on isolated nuclei confirmed all small cells to be diploid, with approximately 5% of the large cells showing more than two signals. Molecular genetic analysis confirmed clonal IgH and IgK gene rearrangements, which were identical in the skin and the bone marrow (Fig. 2g).

The patient is currently receiving R-CHOP chemotherapy. Since the initiation of treatment, the cutaneous lesion on his chest has regressed and his lymphocyte count has normalized (Fig. 2h).

Discussion

Chronic lymphocytic leukaemia is characterized by the accumulation of mature monoclonal B cells in the blood, lymph nodes, spleen, liver and bone marrow. It is predominantly a disease of the elderly – patients have an average age of 65 years at diagnosis.[1] Although CLL has a highly variable clinical course, patients may have stable disease for prolonged periods and survival after diagnosis ranges from a few months to decades.[2] Cutaneous infiltration in CLL is uncommon and is not believed to affect adversely prognosis unless leukaemia cutis appears after the diagnosis of CLL or shows blastic transformation.[3]

The development of any high-grade lymphoma in patients with CLL/SLL is known as RS and usually heralds a grave outcome, with a mean survival of 8 months, despite aggressive chemotherapy.[4,5] Richter syndrome occurs in 3–10% of patients with CLL and is characterized by a sudden clinical deterioration with the development of night sweats and fevers (in the absence of infection), weight loss, progressive lymph-

adenopathy, hepatosplenomegaly and an elevation in LDH.[6] The lymph nodes and bone marrow are most frequently affected; however, the lymphomatous clone may invade extranodal sites, and involvement of the GI tract, CNS, eyes, lungs, kidneys, testes, nasopharynx and skin has been described. Diagnosis is confirmed by analysis of an enlarging lymph node or other involved site. In its most common form, histopathological examination of affected organs demonstrates an atypical lymphoid infiltrate composed of large cells with enlarged nuclei, prominent nucleoli and abundant basophilic cytoplasm.[7] The large cells usually display a B-cell immunophenotype (CD20+, CD3–), occasional loss of the 'CLL phenotype' (especially CD5 antigen expression) and clonal IgH gene rearrangements.[8,9] Approximately 80% of diffuse large B-cell lymphoma cases in RS display a postgerminal centre phenotype with MUM1/IRF4 expression. Only a few cases will show a germinal centre variety (CD10 and BCL6 expression). Rarely, Richter's transformation can also present with a Hodgkin variant with Reed Sternberg cells, and expression of CD15 and CD30 by the Reed Sternberg cells, similar to that seen in *de novo* Hodgkin disease.[10]

Cutaneous RS is exceptionally rare. Lesions vary in morphology and distribution, and solitary or multifocal erythematous papules, plaques, nodules and tumours have been described. In a series of 39 patients with RS reported by Robertson *et al.*,[5] cutaneous involvement was identified in two cases but they were not described in detail. Subsequently, there have been a further 10 reports describing 17 patients with cutaneous RS (Tables 1 and 2).[6,8,9,11–17] Of these 17 patients, disease stabilization following chemotherapy with or without radiotherapy was seen in five,[8,9,11,12,17] with survival after treatment of up to 8 years in one case.[11] Length of survival was not documented in the other cases in which remission was achieved. Two of the patients who survived had

Table 1 Patient and tumour characteristics

Study	Cases (n)	CLL grade before RS (Rai)	Lesions (n)	Site of skin involvement	Morphology	Immunophenotype in skin	Clonality
Trump *et al.*[6]	2	NS	Multiple[e]	Scalp/forehead[g] Extremities[h]	Large cell lymphoma[e]	ND	NC
Novice *et al.*[13]	1	NS	Solitary	Lower lip	Large cell lymphoma	ND	Yes
Zarco *et al.*[14]	1	IV	Multiple	Extremities	Large cell lymphoma	λ restricted, Ki67 60%	Yes
Fraitag *et al.*[8]	1	NS	Multiple	Face, chest, fingers	Large cell lymphoma	CD20+, CD30+	Yes
Cerroni *et al.*[15]	2	NS	NS	NS	Large cell lymphoma	NS	NC
Ratnavel *et al.*[16]	1	NS	Multiple	Legs, upper trunk	Large cell lymphoma	CD20+, light chain restriction, MIB1>50%	Yes
Robak *et al.*[17]	1	IV	Solitary	Nose	Large cell lymphoma	IgG κ, CD20+, CD45+, bcl-2+, bcl-6+, EBER+, p53+	No
Yamazaki *et al.*[12]	1	II	Solitary	Upper back	Large cell lymphoma	CD20+, CD45+, Ki67 high in 70% of cells	ND
Duong *et al.*[9]	4	I[a], II[b]	Multiple[f]	Right forearm;[g] right shoulder, left forearm, left flank;[h] nose, forearm, chest;[d] right forearm, trunk[b]	Large cell lymphoma[f]	CD20+;[g] CD20+, CD30+/–;[h] CD20+,CD30+/–, CD138+/–, CD5+/–, MUM1+, EBER+;[d] CD30+, CD45+, MUM1+, EBER+[b]	Yes,[i] no[d]
Yu *et al.*[11]	3	NS,[c] III[d]	Multiple[a]	Face and ears;[g] back;[h] chest[d]	Large cell lymphoma[a]	CD20+, CD79a+, CD43+, CD5 weak+;[g] CD20+, CD79a+, CD43+;[h] CD20+, CD43+, CD30+, EBER+, p53+[d]	ND

CLL, chronic lymphocytic leukaemia; RS, Richter syndrome; NS, not specified; ND, not documented; MIB1, E3 ubiquitin-protein ligase; EBER, Epstein–Barr virus-encoded RNA; MUM1, multiple myeloma oncogene 1; NC, no comparison. [a]Patients 1–3. [b]Patient 4. [c]Patients 1 and 2. [d]Patient 3. [e]Both patients. [f]Patients 1–4. [g]Patient 1. [h]Patient 2. [i]Patients 1, 2 and 4.

Table 2 Disease burden, treatment and survival

Study	Other organs affected by RS at time of diagnosis	B symptoms	LDH	Previous treatment for CLL	Treatment for RS	Time from transformation to death (months)
Trump *et al.*[6]	Spleen affected by CLL 7 years prior to diagnosis of RS[a] Bone involvement at time of RS diagnosis[b]	Night sweats[a] and NS[b]	NS	No previous treatment documented	Not given.[a] Radiotherapy to bone. Intravenous cyclophosphamide, vincristine and prednisolone. Refused further chemotherapy[b]	7[a], 4[b]
Novice *et al.*[13]	Spleen	Weight loss and pyrexia	Elevated: 274	None	Chlorambucil	Unknown. Refused further treatment after 2 months of chemotherapy
Zarco *et al.*[14]	None. Spleen, liver and lymph nodes affected by CLL 5 years prior to diagnosis of RS	NS	NS	Two cycles of CHOP	CHOP, MACOP-B and DHAP. Total body X-irradiation followed by electron beam radiotherapy. IMVP-16 for a later relapse	Approximately 16
Fraitag *et al.*[8]	NS	NS	NS	Chlorambucil	VP-16, cisplatin, methylprednisolone	Disease stabilized after chemotherapy
Cerroni *et al.*[15]	NS	NS	NS	NS	NS	5[a], 8[b]
Ratnavel *et al.*[16]	Lymph node, live and spleen involvement at time of diagnosis	Weight loss and pyrexia	NS	None	Chlorambucil and radiotherapy	4
Robak *et al.*[17]	None. Spleen affected by CLL before diagnosis of RS	NS	Normal[g]	Six cycles of chlorambucil and prednisolone	Four cycles of CHOP followed by radiotherapy	Disease stabilized after chemo- and radiotherapy. Alive at time of publication (approximately 12 months)
Yamazaki *et al.*[12]	None. Spleen and lymph nodes affected by CLL before diagnosis of RS	NS	NS	Chlorambucil	Six cycles of R-CHOP	Disease stabilized after chemotherapy in 2005. Patient alive at time of publication (2009)
Duong *et al.*[9]	Spleen and lymph node involvement at time of diagnosis with RS. Later cerebral lymphoma[c]	NS,[e] asthenia,[d] and asthenia and night sweats[f]	Normal	Chlorambucil,[e] chlorambucil, cyclophosphamide, three cycles of CHOP, three cycles of fludarabine, VP-16 (etoposide) and cisplatin,[d] and chlorambucil, three cycles of fludarabine and cyclophosphamide[f]	Six cycles of CHOP;[a] chlorambucil was continued but later recurrences were treated with radiotherapy and two cycles of RCVP;[b] several chemotherapy regimens poorly effective;[d] CHOP followed by radiotherapy[f]	50,[a] 129,[b] 24,[d] alive at time of publication (approximately 7 months)[f]

Table 2 (continued)

Study	Other organs affected by RS at time of diagnosis	B symptoms	LDH	Previous treatment for CLL	Treatment for RS	Time from transformation to death (months)
Yu *et al.*[11]	Bone marrow,[a] lymph node[b] and lung[d]	NS	NS	No previous treatment documented,[e] six cycles of fludarabine in 2002 and 2005[d]	R-CHOP,[a] two cycles of CHOP,[b] palliative/supportive treatment only[d]	96,[a] 60,[b] <1[d]

RS, Richter syndrome; LDH, lactate dehydrogenase; CLL, chronic lymphocytic leukaemia; NS, not specified; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisolone; MACOP-B, methotrexate with leucovorin rescue, doxorubicin, cyclophosphamide, vincristine, prednisolone and bleomycin; DHAP, dexamethasone, cytarabine and cisplatin; IVMP-16, ifosfamide-VP16213-methotrexate; R-CHOP, rituximab-CHOP; RCVP, rituximab, cyclophosphamide, vincristine and prednisolone. [a]Patient 1. [b]Patient 2. [c]Patient 1. The organs of patients 2–4 were unaffected. [d]Patient 3. [e]Patients 1 and 2. [f]Patient 4. [g]Normal range 100–200.

received R-CHOP chemotherapy,[11,12] and two had received CHOP and radiotherapy.[9,17] Twelve patients died of their disease, with survival between 20 days and 129 months after cutaneous RS was diagnosed (Table 2).[9,11] Patients with prior cutaneous infiltration by small lymphocytes (leukaemia cutis due to CLL) may have an even worse prognosis.[9,11]

The aetiology and pathogenesis of RS are unclear. Analysis of immunoglobulin gene rearrangements indicates that in 70–80% of cases, CLL and RS arise from the same B-cell clone. However, in other cases the development of RS reflects the emergence of a separate and independent large B-cell lymphoma distinct from the original CLL clone.[14,17] The molecular mechanisms involved in transformation to RS are still poorly understood. If the cutaneous lymphoma and leukaemia arise from the same clone, it is considered a transformation. If they arise from distinct clones, the cutaneous disease can be regarded as a secondary cancer arising by chance.[18] Patient 1 had a different clonal IgH gene rearrangement in skin to blood. This could reflect a different lymphoma emerging on the background of previous treatment or disease-related immunosuppression, but equally it could be due to genomic change within the original CLL tumour and reflect an emerging subclone, which happens to have incorporated a genomic event within the IgH locus.

The association of Epstein–Barr virus (EBV) with other B-cell malignancies, such as endemic Burkitt lymphoma and Hodgkin lymphoma, is well established. In a series of 25 patients with noncutaneous RS, EBV was found in 16% of cases.[19] Subsequent series have demonstrated EBV infection in cases of cutaneous and noncutaneous RS, although the precise role of EBV in this setting remains to be established. Interestingly, EBV has been isolated in patients with RS who have received treatment with fludarabine, raising the possibility that the immunosuppressive action of this agent facilitates EBV infection and transformation to RS (Tables 1 and 2).[9,11,20] Furthermore, EBER-positive patients appear to have a shorter survival than non-EBV-infected individuals.[21] EBER positivity was not seen in either of our patients.

Genetic anomalies that may predispose to the development of RS include trisomy 12; deletions or translocations of chromosomes 11q, 13q, 6q and 14q; mutations in p53; and microsatellite instability. It has been proposed that these abnormalities allow proliferation of CLL cells and facilitate the acquisition of new genetic defects leading to Richter transformation. In particular, trisomy 12 has been implicated in disease progression and shorter survival in patients with RS.[22] Mutations of p53 and loss of heterozygosity in 17p, the p53 site, are found in 10–15% of patients with CLL/SLL. An increased frequency of p53 alterations can be observed after large-cell transformation, suggesting that this gene may be implicated in the development of RS.[18,23] p53 was negative in patient 1 and positive in <5% of cells in patient 2.

Univariate analysis has identified a number of risk factors predisposing to the development of RS in patients with CLL. These include lymph node size (≥3 cm), number of involved lymph nodes, Binet stage, LDH level, CD38 expression and immunoglobulin IGHV4-39 rearrangements. Important determinants of subsequent outcome in patients diagnosed with transformation to RS by multivariate analysis include lymph node size, CD38 expression and immunoglobulin IGHV4-39 rearrangements.[24]

Therapeutic options for the management of RS are limited, and there is no consensus on the optimal approach. Strategies include the use of chemotherapeutic regimes that were developed for diffuse large B-cell lymphoma or acute lymphoblastic leukaemia, with response rates of between 5% and 43% and a median survival postchemotherapy of 5–8 months.[4] The combination of rituximab with hyper-CVXD (fractionated cyclophosphamide, vincristine, liposomal doxorubicin, dexamethasone) variants or CHOP induces responses in 47% of patients compared with a 34% response rate with chemotherapy alone, suggesting that there is a benefit to be obtained from chemotherapy and rituximab combination therapies. Other combinations examined include a phase I–II trial of OFAR (oxaliplatin, fludarabine, cytarabine, rituximab), with reported response rates of up to 50% and a median response

duration of 10 months.[25] Furthermore, a study of 148 patients with RS demonstrated that patients who achieve remission after chemotherapy or immunotherapy survive longer if they undergo postremission allogeneic stem cell transplantation, with an estimated 3-year cumulative survival in 75% of patients.[4]

Some authors have observed that patients with cutaneous RS have a better prognosis than those with extracutaneous disease, with an average survival of 5·6 years from diagnosis of RS to death in one study and 6·7 years (range 2·0–11·0) in another compared with 8 month for extracutaneous disease.[4,9,11] In addition, cases of cutaneous RS with systemic involvement (co-existing extracutaneous RS) at the time of diagnosis appear to have worse outcomes (Table 2).[6,15,16.]

Patient 1 was diagnosed with RS almost 2 years after the onset of a skin eruption and had no B symptoms, stable lymphadenopathy and a normal LDH at the time of diagnosis with RS. Similarly, patient 2 was diagnosed with RS 3 years after the appearance of a skin lesion and had no B symptoms and a normal LDH at the time of diagnosis.

The outcome of these two cases remains to be seen; however, the absence of B symptoms and normal LDH may explain, in part, what appears to be a more favourable outcome in cutaneous RS compared with other subtypes in that the presence of B symptoms and an elevated LDH typically reflects a greater disease burden with more extensive internal disease. Cutaneous examples may also come to medical attention earlier in view of the visible nature of skin disease, and we postulate that this may also allow for a more favourable prognosis. However, with so few cases reported it is difficult to draw any firm conclusions. Dermatologists should be aware of this entity in patients with CLL presenting to their clinics.

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