Singapore Med J 2012; 53(9) : e198

Diffuse large B-cell lymphoma presenting with extensive cutaneous infiltration

Norashikin Shamsudin[1], MRCP, AdvMDerm, *Choong Chor Chang*[2], MRCP, AdvMDerm

ABSTRACT We report a case of systemic diffuse large B-cell lymphoma presenting with extensive infiltration of the skin. A 56-year-old woman presented with a two-month history of pruritic erythematous plaques and nodules over the neck, trunk and upper limbs. She also had night sweats, weight loss, lethargy and reduced effort tolerance. Systemic examination revealed a pale, ill appearance with hepatosplenomegaly and lymphadenopathy. Blood investigations showed pancytopenia (haemoglobin 6.3 g/dL, total white cell count 3.0 × 10^9/L, platelet count 138 × 10^9/L) with a few suspicious mononuclear cells and a mildly elevated lactate dehydrogenase level (478 U/L). Skin biopsy demonstrated diffuse sheets and nodular infiltrates of CD20 and CD79a positive neoplastic cells in the dermis and subcutis. Computed tomography revealed multiple cervical, axillary, mediastinal, para-aortic and mesenteric lymph nodes. Bone marrow aspiration and trephine biopsy confirmed marrow involvement by non-Hodgkin's lymphoma. The patient was treated with chemotherapy, which resulted in resolution of the skin lesions.

Keywords: cutaneous infiltration, cutaneous lymphoma, secondary lymphoma
Singapore Med J 2012; 53(9): e198–e200

INTRODUCTION

Systemic lymphoma could metastasise to the skin, often as a late presentation of non-Hodgkin's lymphoma. In contrast to primary skin lymphomas, which are predominantly of T-cell origin, secondary skin lymphomas are less common and are mainly made up of B-cell tumours. These are typically subtypes of non-Hodgkin's lymphoma, such as systemic diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma. We report a case of systemic DLBCL presenting with extensive infiltration of the skin.

CASE REPORT

A 56-year-old Malay woman presented in June 2009 with a two-month history of multiple extremely pruritic erythematous plaques and nodules (over the trunk, and upper and lower limbs), associated with bilateral lower limb swelling. She also complained of recurrent fever, night sweats, weight loss, lethargy and reduced effort tolerance.

Physical examination revealed a pale and ill appearance with extensive erythematous, infiltrated plaques and nodules involving the neck, chest, back and upper limbs (Fig. 1). There were urticarial lesions on the thighs and back with positive dermatographism as well as pitting oedema of the lower limbs. On systemic examination, the patient had hepatosplenomegaly as well as cervical and inguinal lymphadenopathy. Other systems were unremarkable. At this juncture, our provisional diagnosis was systemic lymphoma with cutaneous secondaries, with differential diagnoses of chronic lymphocytic leukaemia with leukaemia cutis, urticarial vasculitis secondary to underlying connective tissue disorder, and lepromatous leprosy.

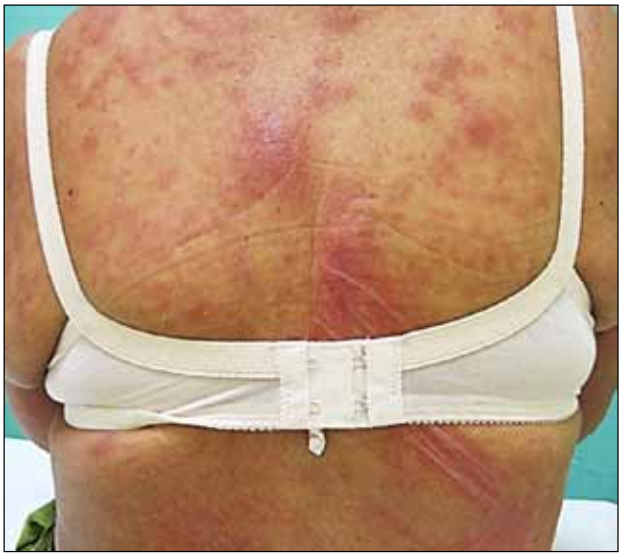

Fig. 1 Photograph shows extensive erythematous skin infiltrates and urticarial lesions with positive dermatographism on the back.

Full blood count showed pancytopenia (haemoglobin 6.3 g/dL, total white cell count 3.0 × 10^9/L, platelet count 138 × 10^9/L). A few suspicious mononuclear cells were seen in the peripheral blood film, suggesting possible myelo- or lympho-proliferative disorder. There was hypoalbuminaemia (23 g/L), hyperbilirubinaemia (28.6 µmol/L) and a mildly elevated lactate dehydrogenase level (478 U/L). Urinalysis revealed 2+ proteinuria. Ultrasonography of the abdomen confirmed the

[1]Department of Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Selangor, [2]Department of Dermatology, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia
Correspondence: Dr Norashikin Shamsudin, Associate Professor, Department of Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM, Serdang, Selangor, Malaysia. aliffarhan@yahoo.com

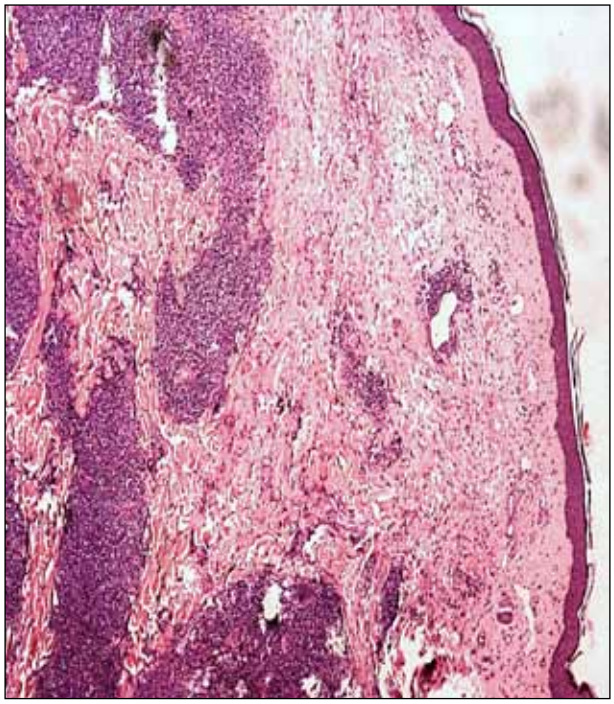

Fig. 2 Photomicrograph shows tumour cells infiltrating the dermis, forming a Grenz zone at the upper dermis (Haematoxylin & eosin, × 2.5).

presence of an enlarged liver and spleen. Staging computed tomography (CT) revealed multiple cervical, axillary, mediastinal, para-aortic and mesenteric lymph nodes as well as pleural effusion and ascites.

Skin biopsy of a chest lesion demonstrated diffuse sheets and nodular infiltrates of neoplastic cells in the dermis and subcutis, forming a Grenz zone in the upper dermis (Fig. 2). The tumour cells were medium-sized with vesicular and irregular nuclei, and mitosis was present (Fig. 3). Some of these cells invaded the subcutis, forming a honeycomb growth pattern. These neoplastic cells were strongly positive for CD20 and CD79a immunohistochemical stains, suggesting a B-cell lineage. Bone marrow aspiration and trephine biopsy showed infiltration of large lymphoid cells with immature nuclei. A final diagnosis of Stage-IV DLBCL with cutaneous infiltration was made. The patient initially completed five cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) in February 2010, to which she responded partially, and her treatment was subsequently changed to HyperCVAD (methotrexate, cytarabine, vincristine and dexamethasone). She completed two courses of these in April 2010 and a repeat CT showed complete resolution of the lymphadenopathy. Her skin lesions also gradually resolved with chemotherapy. She was scheduled for autologous stem cell transplantation (ASCT) in June 2010, but she subsequently defaulted follow-up at the dermatology clinic.

DISCUSSION

This report illustrates a case of systemic DLBCL in which cutaneous lesions were the presenting feature and the diagnosis was clinched by skin biopsy. Subsequent investigation revealed

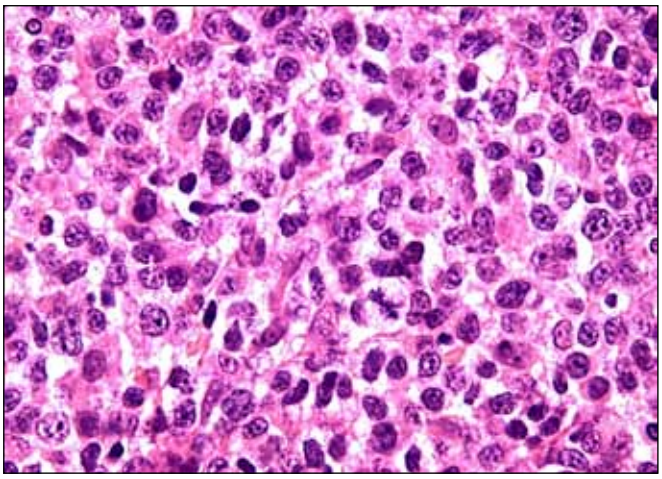

Fig. 3 Photomicrograph shows medium-sized tumour cells with vesicular and irregular nuclei and prominent nucleoli (Haematoxylin & eosin, × 40).

disseminated disease at the time of diagnosis. Our patient presented with extensive lesions involving almost the whole body in a short span of time. She also had constitutional upset and 'B' symptoms such as fever, night sweats and weight loss, which do not usually occur in patients with primary cutaneous lymphomas. The presence of pallor, generalised lymphadenopathy and hepatosplenomegaly further raised the suspicion of an underlying systemic disease. The skin biopsy identified these lesions as neoplastic infiltrates of B-cell origin. Subsequent bone marrow biopsy confirmed bone marrow involvement of the disease.

Secondary skin involvement from systemic non-Hodgkin's lymphoma is not uncommon. A study in Stanford University showed that secondary lymphomas, or lymphomas that involve both nodal sites and the skin at presentation, appeared to represent approximately 25% of all cutaneous lymphomas.[1] 65.8% of these secondary lymphomas were of B-cell origin, composed mainly of DLBCL (26.8%) and follicular lymphoma (21.4%). In contrast to primary cutaneous lymphomas, secondary cutaneous lymphomas show B-cell predominance. The histologies of primary and secondary cutaneous lymphomas are similar, but their clinical behaviours and prognoses are distinctively different.[2] Primary cutaneous lymphoma tends to be more indolent and has a better prognosis.

DLBCL is the most common type of nodal or systemic non-Hodgkin's lymphoma and is heterogeneous clinically, morphologically and molecularly.[3,4] All cases show a diffuse growth of predominantly large tumour cells, the size being defined as at least twice as large as a normal lymphocyte or with a nuclear size equal to or greater than that of a normal macrophage.[4] The nuclei have vesicular chromatin, prominent nucleoli and basophilic cytoplasm.[5] Not surprisingly, it is one of the most common types of lymphoma to metastasise. Skin involvement confers an unfavourable prognosis for patients, as this is an extranodal site and immediately categorises patients into Ann Arbor Stage IV. Both primary and secondary DLBCL commonly involve the head and neck regions or the extremities,

but trunk involvement may be more characteristic of secondary disease, as in our patient.[1] Although clinically aggressive, DLBCL is potentially curable. The treatment of DLBCL depends on the stage of the disease. Patients with disseminated disease (Stage III or IV) are given 6–8 cycles of R-CHOP (anti-CD20 antibody rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisolone), which results in complete remission in up to 60%–70% of patients, with cure rates of approximately 35%.[6] No long-term toxicity appears to be associated with the R-CHOP combination, making this the standard of care in DLBCL.[3] Rituximab has dramatically improved the outcome in advanced stage DLBCL. Its combination with CHOP chemotherapy has shown overall survival benefit in patients from all risk groups.[3] A French study previously demonstrated that the overall 5-year survival rates in patients treated with CHOP and R-CHOP were approximately 50% and 60%, respectively.[3] Other attempts to improve the response to CHOP involve consolidation with high-dose therapy and ASCT. Several studies evaluating ASCT as consolidation therapy after CHOP-based chemotherapy have suggested benefit in patients with aggressive lymphoma.[3]

ACKNOWLEDGEMENTS

The authors thank Dr Ngan Kah Wai, Department of Pathology, Serdang Hospital, Dr Alan Teh Kee Hean, Consultant Haematologist, Sime Darby Medical Centre, Subang Jaya and Dr Mohd Munzir Skhori, Department of Haematology, Ampang Hospital, for their invaluable help and support.

REFERENCES

1. DA Arber. Secondary lymphomas of the skin. Companion Meeting Handouts, Society for Hematopathology [online]. Available at: www.pathologyportal.org/95th/pdf/companion21h5.pdf. Accessed October 2, 2010.
2. Storz MN, van de Rijn M, Kim YH, et al. Gene expression profiles of cutaneous B cell lymphoma. J Invest Dermatol 2003; 120:865-70.
3. Friedberg JW, Fisher RI. Diffuse large B-cell lymphoma. Hematol Oncol Clin North Am 2008; 22:941-52, ix.
4. Dong HY. Aggressive B-cell Lymphomas: Diffuse Large B-cell Lymphoma and Burkitt Lymphoma. In: Jones D, ed. Neoplastic Hematopathology: Contemporary Hematology. New Jersey: Humana Press, 2010: 303-22.
5. JM Connors, ED Hsi, and FM Foss. Lymphoma of the Skin. American Society of Hematology Education Program Handbook [online]. Available at: asheducationbook.hematologylibrary.org/. Accessed October 8, 2010.
6. Munker R, Marion J, Ye G, Dreyling MH. The non-Hodgkin's lymphomas. In: Munker R, Hiller E, Glass J, Paquette R, eds. Modern Hematology: Biology and Clinical Management. 2nd ed. New Jersey: Humana Press, 2007: 237-70.