

# Relapsed lymphoma mimicking venous ulcer: A case report

Wan Syameen Afira Wan Ahmad Kamal, AdvMDerm<sup>1</sup>, Azura Mohd Affandi, AdvMDerm<sup>2</sup>, Anisha Bhullar, AdvMDerm<sup>3</sup>, Wan Syazween Liyana Wan Ahmad Kamal, MRCP<sup>4</sup>

<sup>1</sup>Department of Dermatology, Faculty of Medicine, Universiti Teknologi MARA, Selangor, Malaysia, <sup>2</sup>Hospital Kuala Lumpur, Kuala Lumpur, Malaysia, <sup>3</sup>Universiti Putra Malaysia, Serdang, Selangor, Malaysia, <sup>4</sup>Hospital Tuanku Fauziah, Pusat Bandar Kangar, Perlis, Malaysia.

## SUMMARY

**Lymphoma presenting with ulceration is not typical. We report a case of relapsed DLBCL in a 73-year-old man presenting with a chronic non-healing leg ulcer. He has underlying varicose veins with recurrent venous ulcers. This patient was diagnosed to have DLBCL six years earlier when he presented with recurrent epistaxis originating from a left nasal cavity nodule. Complete resolution was achieved after eight cycles of R-CHOP and intrathecal methotrexate. For this current problem, this patient was treated with rituximab combined with chemotherapy which resulted in healing of the ulcer.**

## CASE REPORT

We report a case of non-healing leg ulcers in a 73-year-old Chinese man with underlying varicose veins and stasis dermatitis associated with recurrent venous ulcers for 15 years. At the age of 65 years old, this gentleman developed recurrent episodes of epistaxis originating from a left nasal cavity nodule. Biopsy of the nodule revealed diffuse large B cell lymphoma (DLBCL) (CD 20, CD79- alpha positive, CK and MNF 116 negative). The initial computed tomography (CT) scan of the neck, thorax and abdomen revealed submental and right inguinal lymphadenopathy. He was treated with eight cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone) and intrathecal methotrexate. A repeat CT scan a year later showed complete resolution of lymphoma. Concurrently, this gentleman was also still suffering from recurrent episodes of venous ulcers which resolved after a few weeks with appropriate dressing, compression and antibiotics. He had venous stripping done by the vascular team. Six years after the diagnosis of lymphoma, he complained of persistent non-healing painful lower limb ulcers for three months. He had no epistaxis nor other systemic symptoms.

Examination revealed a large, sloughy well-defined tender ulcer with necrotic tissue on the left shin measuring 10x5cm and two smaller, less sloughy ulcers with granulation tissue on the right medial malleolus and anterior ankle (Figure 1 and 2). He has venous varicosities on bilateral lower limbs with swollen left inguinal lymph nodes. The peripheral pulses were normal. Other examination including the head and neck examination was normal. As the ulcers did not improve

with appropriate antibiotics, wound debridement and dressing, a skin biopsy was performed on all the ulcers.

Histopathological examination of the largest ulcer on the left leg revealed diffuse infiltration by neoplastic lymphoid cells which were positive to CD20, CD79 and negative to CD3; consistent with relapsed DLBCL. Ki67 was approximately 75%. Immunohistochemical study showed double expressor lymphoma. No malignancy was reported in the tissue samples of the smaller ulcers on the right lower limb. The cultures from skin swab and biopsy samples grew a mixture of gram negative and gram-positive organisms.

This patient was treated with rituximab immunotherapy combined with etoposide and then gemcitabine, alongside broad-spectrum antibiotics coverage. He is currently on 6 mercaptopurine 50mg daily and methotrexate 5mg weekly. He was not subjected to radiotherapy as the left leg ulcer had healed well, leaving a hypopigmented scar. The venous ulcers on the right leg also healed with scarring.

## DISCUSSION

Ulceration as a clinical presentation of lymphoma itself is an atypical phenomenon, but the diagnosis becomes more difficult when it masquerades as a chronic venous ulcer, in the background of varicose veins and stasis dermatitis. 4.4% of these apparently benign lesions have been found to have a malignant aetiology.<sup>1</sup> DLBCL typically arises in lymph nodes; however, initial extranodal sites are identified in about 30-40% of cases. Any organ system may be affected, although involvement of the gastrointestinal system is most common.

Primary cutaneous diffuse large B-cell lymphoma (PCLBCL), leg type, is a unique entity more common in elderly females with a relatively aggressive behaviour. In contrast to PCLBCL, our case however showcased a relapsed lymphoma rather than a primary lesion. Interestingly although Non-Hodgkin lymphomas generally relapse in the same sites, the nasal cavity which was the primarily involved site was normal in our patient. The outcome of relapsed DLBCL largely depends on several factors such as time interval of relapse after diagnosis, prior rituximab treatment, fitness and chemosensitivity of the patient, eligibility for stem cell transplantation and the International Prognostic Index (IPI)

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*Corresponding Author: Wan Syameen Afira Wan Ahmad Kamal*

*Email: syameen.afira@gmail.com*



Fig. 1: Sloughy Ulcer with Necrotic Tissue on Left Shin.

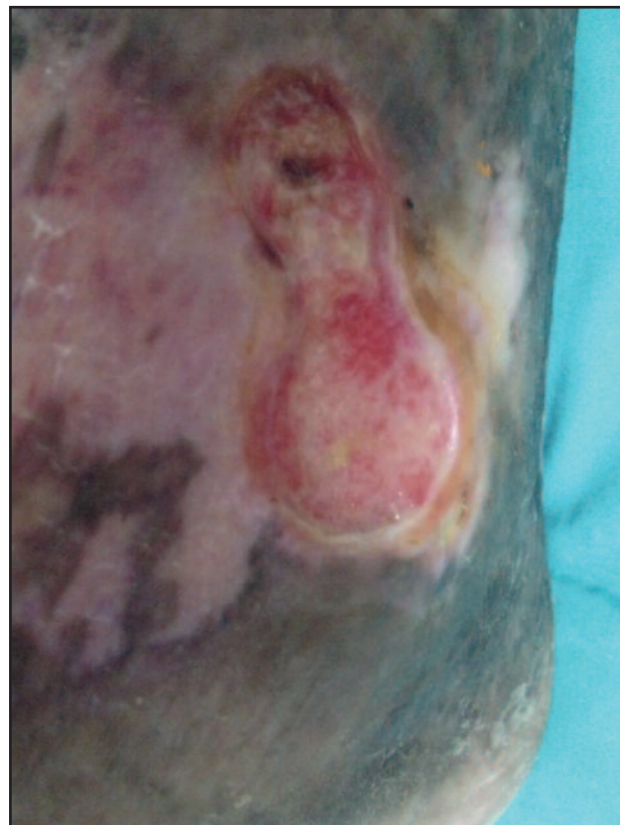


Fig. 2: Smaller Ulcer on the Right Medial Malleolus.

score at relapse.<sup>3</sup> Our patient also exhibited a double expressor lymphoma whereby there is an overexpression of c-MYC and BCL-2 on immunohistochemistry examination. In several independent studies, this co-expression of c-MYC and BCL-2 was associated with a lower complete response rate and shorter progression-free and overall survival.<sup>4</sup>

In the literature, there are reports of cases who relapsed with CD20- skin involvement after rituximab therapy.<sup>5</sup> Our case differs from these reports as our patient had a CD20+ relapse after eight cycles of R-CHOP regimen. There has also been another report of extensive CD20+ cutaneous relapse without initial cutaneous involvement, which suggests that there might be a resistant disease to rituximab which tends to involve the skin.

In conclusion, a suspicion for lymphoproliferative disorders should be borne in mind when presented with unusual or non-healing skin lesions even if there is clinical basis for a more benign aetiology, such as venous disease. An early

biopsy sooner would result in appropriate oncological treatment, and perhaps a better outcome.

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