Cutaneous large B-cell lymphoma of the leg: presenting initially as mononeuritis multiplex

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ABSTRACT

We report a rare case of primary B-cell lymphoma of the leg presenting with mononeuropathy multiplex. A 79-year-old Chinese woman who was being investigated for mononeuritis multiplex had an incidental finding of indurated erythematous plaques on the breast and left leg. A skin biopsy from the nodular area on the right breast showed a dense and diffuse infiltrate of atypical cells with large, round, hyperchromatic nuclei with prominent nucleoli. These atypical lymphocytes were CD20+, Bcl-2+ and Mum-1+. A diagnosis of diffuse large B-cell lymphoma, leg type involving the breast and leg with extracutaneous involvement, was made. This case highlights the importance of a full systemic and cutaneous examination in patients presenting with progressive, painful peripheral neuropathy.

Keywords: B-cell lymphoma, lymphoma, mononeuritis multiplex, peripheral neuropathy

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INTRODUCTION

Primary cutaneous diffuse large B-cell lymphoma of the leg type is a primary cutaneous large B-cell lymphoma (PCLBCL) that predominantly affects elderly females. The typical presentation is rapidly growing red or bluish-red tumours on the legs. These lymphomas often disseminate to extracutaneous sites and have an unfavourable prognosis.[1] We report an unusual extracutaneous presentation of this condition.

CASE REPORT

A 79-year-old Chinese woman was being investigated by the neurology service for progressive, painful, asymmetrical mononeuropathy multiplex affecting the right ulnar, left ulnar, median, radial, sural and peroneal nerves of unknown cause. She had presented with a six-month history of weakness and numbness of the right hand and a two-year history of left foot numbness. Her past medical history included right and left Bell's palsy, both of which resolved spontaneously, a meningioma in the frontal midline which was treated conservatively, and a permanent pacemaker for complete heart block. Previous investigations to exclude a vasculitic or autoimmune cause, including ANA, pANCA, cANCA, anti-Ro, anti-La, serum cryoglobulins, hepatitis B and C serology and immunofixation, were negative.

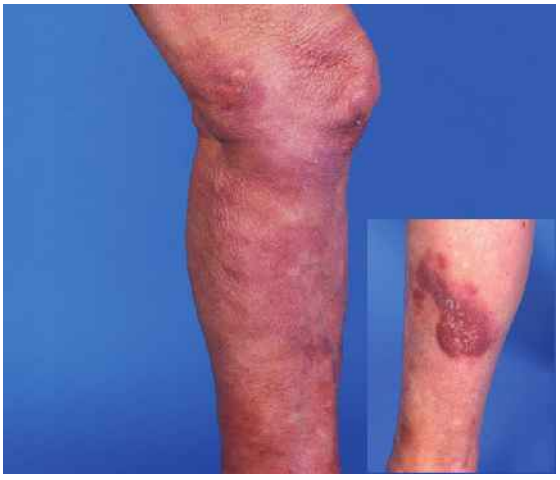

Fig. 1 Photographs show a dusky erythematous plaque on the leg. The inset shows a progression of the lesion a few months after the diagnosis.

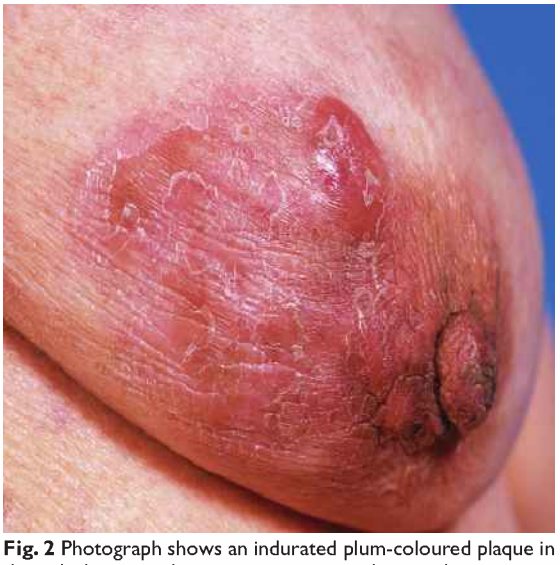

Fig. 2 Photograph shows an indurated plum-coloured plaque in the right breast with tumourous areas at the periphery.

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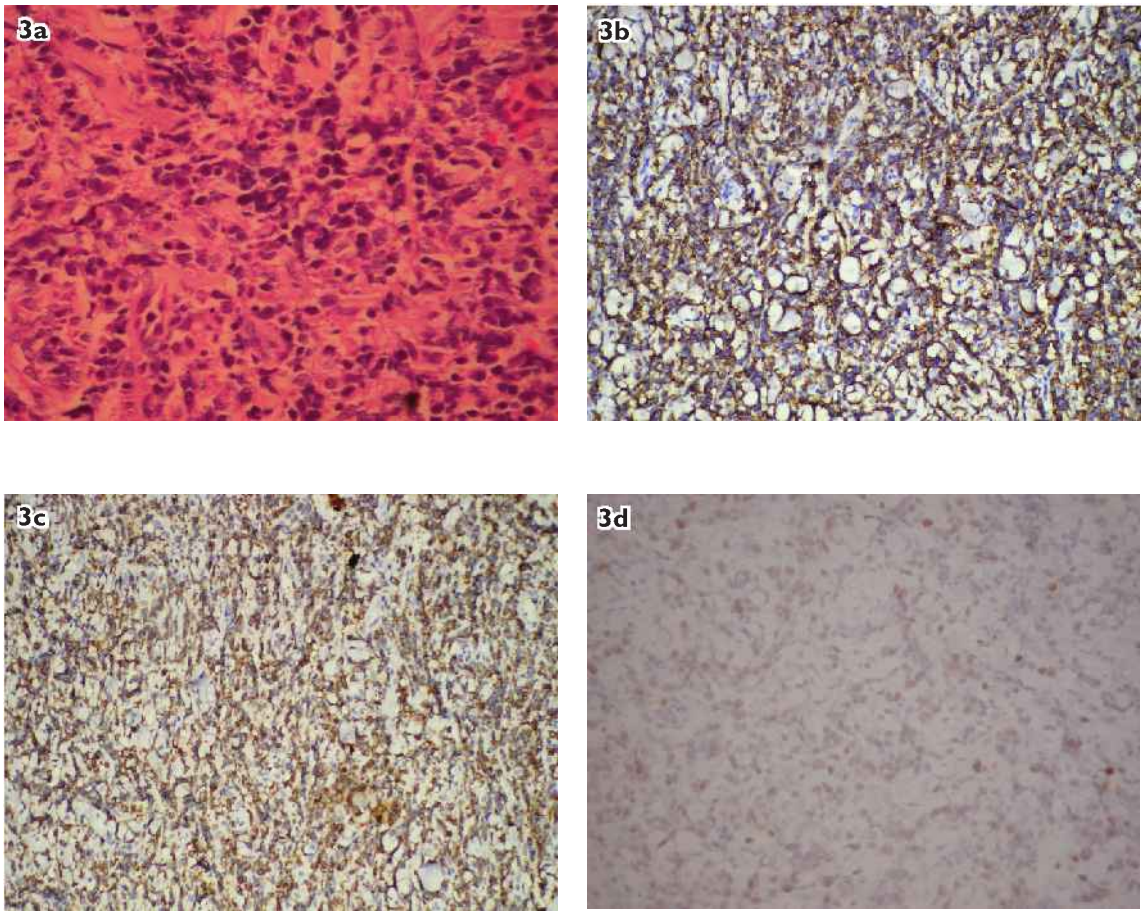

Fig. 3 Photomicrographs show (a) diffuse infiltrate of atypical lymphocytes (Haematoxylin & eosin, × 40); (b) positive CD20 (× 40); (c) strong Bcl-2+ expression by tumour cells (× 20); (d) positive Mum-1 (× 40).

An incidental finding of skin lesions on the left lower limb prompted a referral to a dermatologist. The patient reported that these nodules had been present for three months. She also complained of a previously unexamined lump in her right breast, which had been there for a few months and was gradually increasing in size. There were no systemic complaints of fever or weight loss. Cutaneous examination revealed dusky indurated erythematous plaques over the medial aspect of the left leg in a linear distribution (Fig. 1). In addition, there was a large 5 cm × 4 cm indurated plum-coloured dermal plaque in the right breast with a 2-cm tumourous area at the periphery, which extended to deeper tissue within the breast (Fig. 2).

A skin biopsy from the nodular area on the right breast showed a dense and diffuse infiltrate of atypical cells with large, round, hyperchromatic nuclei, with prominent nucleoli comprising the majority of tumour cells spanning the entire dermis (Fig. 3). A Grenz zone of sparing was also present. Immunohistochemistry staining showed that the atypical lymphocytes were CD20+, Bcl-2+ and Mum-1+. Some reactive CD8+ T cells were also present. Further investigations, including a mammogram and breast ultrasonography, showed multiple solid lesions of the right breast. Computer tomography of the thorax and abdomen showed a malignant mass lesion of the right breast, unilateral axillary lymphadenopathy, with the largest node measuring 1.3 cm × 1.1 cm, and a 1.5-cm para-aortic lymph node in the lower abdomen. A left sural nerve biopsy showed evidence of mononuclear inflammatory cell infiltration at subperineural locations and around small endoneurial and small epineurial blood vessels.

A diagnosis of diffuse large B-cell lymphoma, leg type involving the breast and leg with extracutaneous involvement, was made. The disease was staged at IIIA. She declined further staging investigations. Within three months of initial presentation, the lesions on the left lower limb progressed with more infiltrative plaques (Fig. 1, inset). Following discussion at a family conference, it was decided that she should have palliative chemotherapy treatment with etoposide. She died two months later at a hospice.

DISCUSSION

Primary cutaneous diffuse large B-cell lymphoma of

the leg type is a PCLBCL with a predominance of confluent sheets of centroblasts and immunoblasts, characteristically presenting with skin lesions on the lower legs, predominantly affecting elderly female patients, as in this case.[1] It can rarely present at sites other than the legs, as highlighted here as well. This case report demonstrates an unusual extracutaneous manifestation of PCLBCL, i.e. mononeuropathy multiplex. In a European multicentre study of PCLBCLs, 24% of patients had extracutaneous disease, with 8% restricted to the lymph nodes and 16% developing visceral disease with (6%) or without (10%) lymph node involvement. Sites of visceral dissemination included the central nervous system, bone marrow, bones, lung, small intestine, spleen, testis, kidney, heart, breast, thyroid and brachial plexus. Only one patient (0.7%) had breast involvement.[2]

In our patient, the mechanism of the mononeuropathy multiplex was unclear. The likely cause was a paraneoplastic phenomenon or direct lymphomatous invasion. The presence of paraneoplastic antibodies (e.g. anti-Hu) in the cerebrospinal fluid would be supportive of the former diagnosis. The nerve biopsy did not show any abnormal cells; however, there were atypical cells seen in a muscle biopsy that were in close association with small blood vessels in the epimysium, although not within the vessels. It could have been sampling error that this was not seen in the nerve sample. Thus, we strongly considered neurolymphomatosis as the underlying mechanism for the neuropathy although there was no proof of this. Neurolymphomatosis is generally defined as clinical neuropathy with associated malignant, lymphomatous infiltration of peripheral nerves proven by biopsy or autopsy.[3] It was also possible that there were haematogenous metastases, resulting in local intravascular proliferation or direct pressure with nerve infarcts. Interestingly, a few months before her demise, the patient had leg pain, weakness and numbness, clinically indicating sciatic neuropathy, likely due to lymphoma spread by direct invasion of the lumbosacral plexus.

We believe that this patient was a case of PCLBCL and not a case of nodal lymphoma with metastatic skin disease, for several reasons. She had prominent skin manifestations, with progressive lesions starting initially on the leg and breast. There were no systemic complaints and generalised lymphadenopathy, with only small lymph nodes detected. Nodal lymphoma with metastatic skin disease would have presented as a late-stage disease with more extensive nodal involvement. In addition, there was no evidence of intravascular B-cell lymphoma on the skin biopsy.

In primary B-cell lymphoma of the leg, a diffuse growth pattern with a monomorphous infiltrate, involving the entire dermis histologically, sparing the epidermis with a Grenz zone is seen,[4] as exemplified in this case report. The tumour cells in PCLBCL of the leg express CD19+, CD20+, CD22+, CD79a+ and CD5–, CD10– and CD138–, cyclin D1–.[3] An important feature of this lymphoma is a strong positivity for Bcl-2 protein and MUM-1/IRF4, distinguishing this entity from primary cutaneous follicle centre lymphoma.[4] In contrast to primary cutaneous follicle centre lymphoma, which has an excellent prognosis, the five-year survival of PCLBCL has been quoted to be 55%. The presence of multiple skin lesions at diagnosis is an adverse prognostic factor.[1] Indeed, our patient died within five months of the diagnosis. For therapy, these lymphomas should be treated as systemic diffuse large B-cell lymphomas with anthracycline-based chemotherapy.[1] Radiotherapy is sometimes considered in small, single tumours. The role of rituximab in primary B-cell lymphomas has not been established. We report a rare case of primary B-cell lymphoma of the leg presenting with mononeuropathy multiplex. This case highlights the importance of a full systemic and cutaneous examination in patients presenting with progressive, painful peripheral neuropathy.

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