Rare cutaneous manifestation of B-cell chronic lymphocytic leukaemia involving the toes

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Introduction

B cell chronic lymphocytic leukaemia (B-CLL) is a disease that most commonly occurs in adults with a median age of 72. Affecting males predominantly, it has an incidence of 4.1/100,000 cases in the population, making B-CLL one of the most common hematological malignancies.[1]

Skin manifestations in patients with B-CLL can be divided into specific and non-specific forms. Specific skin lesions are caused by direct infiltration of the skin by malignant cells, most commonly affecting the head and neck, represented as nodules or papules, that can be localized or disseminated.[2] These should be distinguished from secondary skin changes such as those resulting from infections and pruritus.[3] Patients diagnosed with B-CLL have an 8- fold increased risk of developing secondary cutaneous cancer compared to age and sex matched population. [4]

Case presentation

We present the case of an eighty-year-old female with a two-month history of erythema, swelling and pain affecting all her toes which limited her walking and prevented her from fitting her shoes comfortably.

She had a history of chronic lymphocytic laeukemia diagnosed twenty years previously that had remained stable under observation without active treatment. Her only regular medication was pravastatin which she had been taking long term. She had no history of prior dermatological conditions.

On examination she had markedly abnormal toes, with erythema, irregular oedema and scale of all her toes, primarily her first and second digits bilaterally. (Figure 1) Also noted were trumpet and pincer nails secondary to nail bed inflammation. An antalgic gait was evident due to the pain caused by inflammation. She had long standing onychomycosis, previously unresponsive to systemic anti-fungal medications as prescribed by her family physician. Feet were warm to touch, dorsalis pedis was palpable bilaterally, and there was no clinical evidence of peripheral vascular disease, ankle oedema or venous insufficiency. Examination of her fingers and fingernails, along with full skin examination was normal. She had no palpable lymphadenopathy.

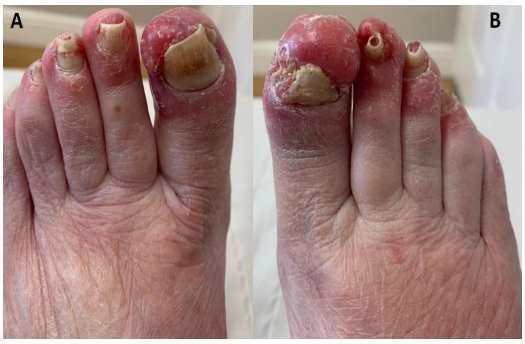

Figure 1. A) Left foot. B) Right foot. Both showing erythema and oedema of the toes and nail beds, leading to nail deformities.

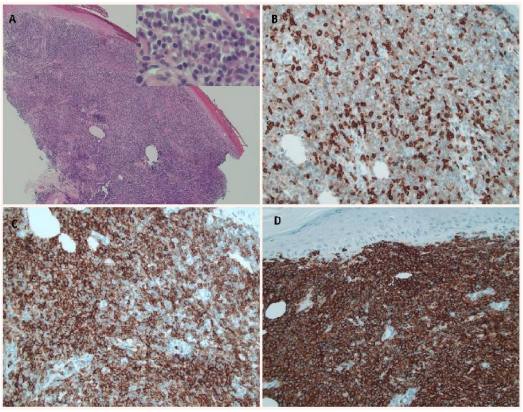

Figure 2. A) Haematoxylin and Eosin stain of skin biopsy of the toe, original maginification x40 and x400 in right upper corner. B) CD 5 stain. C) CD 23 stain. D) CD 20 stain. Original magnification x200 [B, C and D].

Treatment

The patient was treated by her haematologist with:

- Three cycles of chlorambucil;
- Prednisolone;
- Obinutuzumab

Leading to an improvement of signs and symptoms. WCC decreaes to 12.4 x10^9/L and lymphocyte count dropped to 6.7 x10^9/L.
Her nails were medically debrided with 25% urea under occlusion topically.

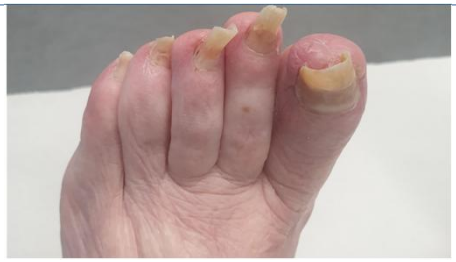

Figure 3. Left foot post treatment

Investigations

A skin biopsy of the right toe was carried out, Histologic evaluation showed a diffuse infiltrate of lymphocytes involving the full thickness of the dermis. The majority of the lymphocytes were comprised of CD20+ cells with a mitotic index of 20 - 30%.

On review of histological slides (Figure 2) there was a diffuse infiltrate of lymphoid cells occupying the dermis of the skin biopsy. The overlying epidermis is uninvolved, with no evidence of epidermotropism. On higher power, the infiltrate is composed of small mature lymphoid cells with a monotonous appearance.

By immunohistochemistry, the neoplastic lymphoid cells stain positive for the B-cell marker CD20. They demonstrate co-expression of CD23 and BCL2, with weak co-expression of CD5. CD10, cyclin-D1 and MUM1 are negative in neoplastic B-cells. CD3 and CD5 highlight interspersed, scattered T-cells. Overall, the morphology and immunophenotype are consistent with cutaneous involvement by chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL).

Discussion

Identifying skin lesions secondary to CLL remains challenging due to the diversity of clinical presentations. [5]

CLL manifesting in the toes has only been reported once previously in the literature. The case described is a 57-year-old male with CLL that presented with erythematous hypertrophic changes of the ears, eyebrows, tip of the nose, toes and fingers. [6]

B-CLL does not commonly lead to direct infiltration of the skin and when it occurs, it has been previously described in the literature that it mostly consists of T-Cells which demonstrates their epidermotropism, however in our case the cells have kept their B-Cell characteristics. The pathogenesis of this event has not been elucidated but it has been suggested that this relocation of cells through the dermis is carried by the CAM-1/LFA-1 interaction. [7]

In our patient's case we did not feel her signs were attributable to the bystander effect alone, and her response to treatment made this less likely.

References

(1) Hallek M. Chronic lymphocytic leukemia: 2020 update on diagnosis, risk stratification and treatment. Am J Hematol. 2019 Nov;94(11):1266-1287.
(2) Jasim, Z., Cooke, N., Somerville, J. and Hay, R. Chronic lymphocytic leukaemia skin infiltrates affecting prominent parts of the face and the scalp. British Journal of Dermatology 2006; 154: 981-982.
(3) Morozova EA, Olisova OY, Nikitin EA. Cutaneous manifestations of B-cell chronic lymphocytic leukemia. Int J Hematol. 2020 Oct;112(4):459-465.
(4) Robak, T. Second Malignancies and Richter's Syndrome in Patients with Chronic Lymphocytic Leukemia. Hematology 2004; 9(5-6), 387–400.
(5) Watson, K.M.T., Mufti, G., Salisbury, J.R., du Vivier, A.W.P. and Creamer, D. Spectrum of clinical presentation, treatment and prognosis in a series of eight patients with leukaemia cutis. Clinical and Experimental Dermatology 2006; 31: 218-221.
(6) Lu C, Li L, Qiao Q, Liu G, Fang L. Cutaneous manifestations in a patient with chronic lymphocytic leukemia involving the head, neck and distal extremities. Exp Ther Med. 2015;9(3):877-879.
(7) Várkonyi J, Zalatnai A, Timár J, Matolcsi A, Falus A, Bencsáth M, László V, Pócsik E, Kotlán B, Császár A. Secondary cutaneous infiltration in B cell chronic lymphocytic leukemia. Acta Haematol. 2000;103(2):116-21.

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