A Case of Myeloid Sarcoma with Unusually Extensive and Rapidly Progressive Skin Manifestations

Dear Editor,

Myeloid sarcoma (MS) is an uncommon extramedullary tumour of malignant myeloid cells which predominantly occurs concurrently with or after the onset of acute myeloid leukaemia (AML). Careful clinicopathological correlation with comprehensive immunophenotyping of the malignant cells is essential to distinguish myeloid sarcoma from lymphoma with skin involvement. The early recognition of cutaneous MS is important because a late diagnosis is associated with poor prognosis.[1] We report a case of MS with unusually florid and rapidly progressive skin manifestations.

Case Report

A 76-year-old Chinese man with a past medical history of ischaemic heart disease and hypertension presented with a 5-month history of asymptomatic skin tumours over his face, trunk and limbs. They started as multiple non-tender nodules, which initially resolved spontaneously with scarring but subsequently recurred and progressed. Clinically, there were extensive erythematous firm papules, plaques and tumours over the face, trunk and limbs, with no lymphadenopathy noted (Fig. 1). Full blood count revealed leukopenia and thrombocytopenia but no leukaemic blast cells were seen. An excision biopsy taken from the chest showed a grenz zone above a dome-shaped mass in the dermis that extended to the superficial subcutis. There were sheets of atypical cells with abundant eosinophilic cytoplasm and large vesicular nuclei, that exhibited single-filing and dissection of collagen in some areas (Fig. 2). Immunohistochemical staining showed that the atypical cells were strongly positive for lysozyme, leukocyte common antigen (LCA), CD4, CD43 and CD56. They were moderately positive for CD68, and focally positive for myeloperoxidase and chloroacetate esterase. They stained negatively for CD123 and T-cell leukaemia 1 (TCL-1).

At this point, the patient declined further systemic evaluation. His skin lesions eventually became more extensive (Fig. 3) and 3 months after the initial presentation, he finally agreed to a bone marrow examination which showed 20% blasts. The myeloid blast cells stained positive for CD33 and muramidase in addition to focal positivity for CD68 and myeloperoxidase. Cytogenetics of the bone marrow aspirate showed trisomy 8. A repeat skin biopsy demonstrated positivity for CD99 and focal positivity for CD117 and CD68, and negativity for CD3, CD20 and CD34. A final diagnosis of AML with MS was made. He was commenced on chemotherapy comprising etoposide and cytarabine but responded poorly. He was then treated with high dose cytarabine and fludarabine which also failed to control his skin lesions even though a repeat bone marrow aspiration examination showed haematological remission. After failing oral methotrexate and mercaptopurine, electron beam therapy was attempted to ameliorate his cutaneous lesions which were enlarging and ulcerating. He responded partially but subsequently passed away after developing intracranial haemorrhage from suspected brain metastases 6 months from the time of diagnosis.

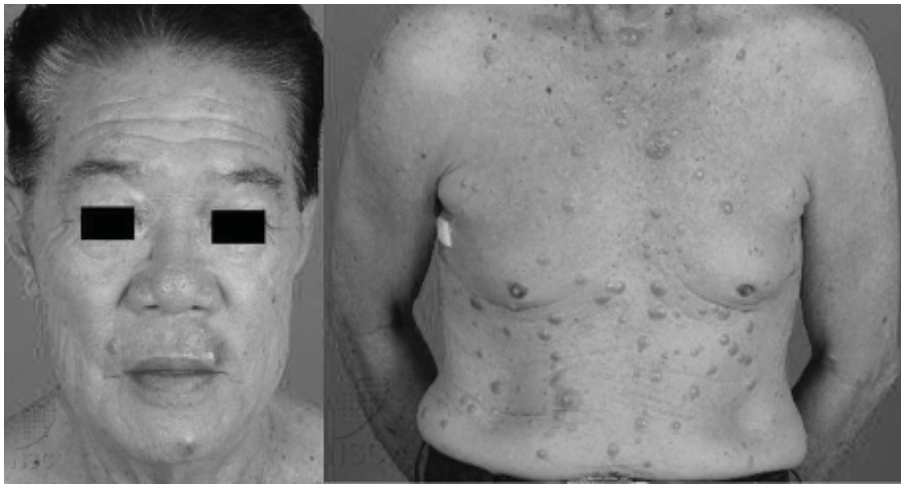

Fig. 1. Multiple erythematous papules, plaques and tumours over the face and trunk at presentation.

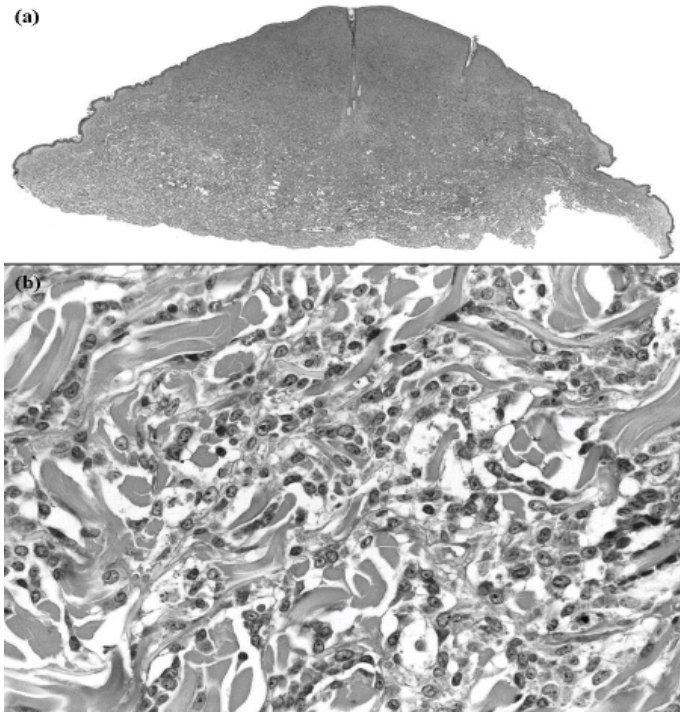

Fig. 2a. Excision biopsy of a skin nodule showing a dense infiltrate within the dermis with a grenz zone. H and E stain, x 20. Fig. 2b. The infiltrate consists of atypical cells with abundant eosinophilic cytoplasm and vesicular nuclei with increased mitotic figures. These cells exhibit single-filing and dissect between collagen bundles. H and E stain, x 400.

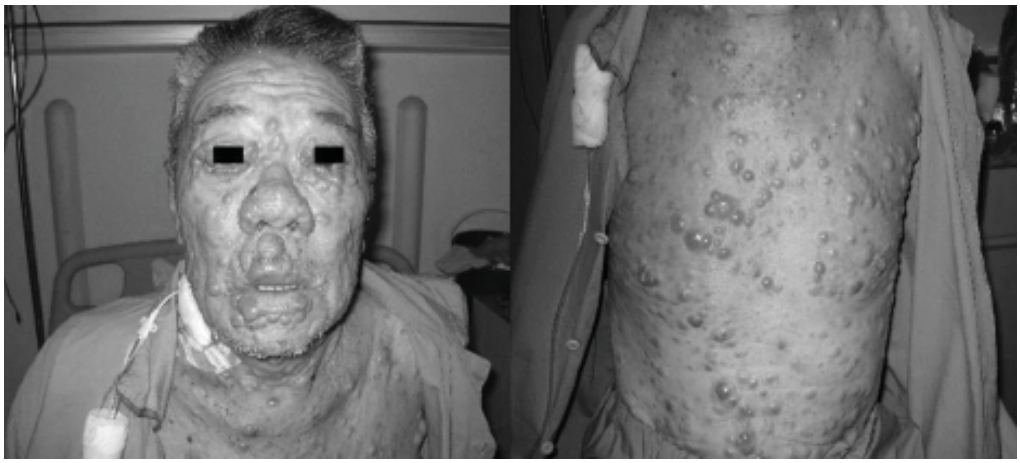

Fig. 3. Extensive enlarging plaques and tumours over the face and trunk 3 months post-presentation.

Discussion

Formerly termed as granulocytic sarcoma, MS occurs in 1.4% of patients with AML.[2] It typically presents as a localised extramedullary tumour of immature myeloid cells that can occur in various sites including the skin, visceral organs, bone, lymph nodes and oral cavity.[3] Rarely, MS may present as multiple skin nodules.[4]

Due to its rare occurrence, MS poses a diagnostic challenge in the absence of peripheral blood and bone marrow disease. Before the use of immunohistochemical stains, Byrd et al reported that 46% of cases of extramedullary leukaemia were initially misdiagnosed as lymphoma.[5] In addition to clinical and histopathologic findings, immunohistochemical studies are particularly important to distinguish MS from lymphoma. Myeloid cell markers include myeloperoxidase, chloroacetate esterase, lysozyme and CD43, and their presence may vary with the degree of tumour differentiation. The most sensitive myeloid markers are lysozyme and CD43, staining positive for the majority of tumour cells in both well-differentiated and poorly differentiated MS.[6] As demonstrated in this patient, other immunohistochemical markers useful for diagnosis include CD56, CD68 and CD117 which are frequently positive in MS. In terms of cytogenetic abnormalities, trisomy 8 and inv(16) are most

commonly associated with MS. The main differential diagnosis considered was blastic plasmacytoid dendritic cell neoplasm (BPDCN). The differentiation of BPDCN from MS is often challenging as both tumours can share a similar clinical presentation and can express CD4 and CD56. However, BPDCN is usually positive for CD123 and TCL-1 in the absence of lineage-specific markers for T-cells, B-cells or myelomonocytic cells,[7] which was not seen in this case.

The early and accurate diagnosis of MS is crucial as the disease favours an aggressive course with rapid transformation to acute leukaemia. Our patient's survival was 6 months from the time of diagnosis, and underscores the rapid progression and poor prognosis of this disease. In a Japanese study of 32 patients with MS who did not receive chemotherapy, 88% transformed to acute non-lymphoblastic leukaemia within 11 months from diagnosis.[8] Several studies have demonstrated that early treatment of MS with intensive chemotherapy is associated with a lower probability of malignant transformation and with prolonged survival.[9] Tsimberidou et al[2] reported a median survival of 20 months from diagnosis after treatment with chemotherapy and/or radiotherapy. Another study by Tsimberidou et al[10] comparing the treatment of MS and AML with anti-AML chemotherapy (cytarabine plus idarubicin or fludarabine as induction remission therapy) showed a higher complete response rate of 69% and superior survival in patients with MS, proving that such therapy is effective in MS. The 2-year event-free survival and overall survival rates were reported as 32% and 18% respectively. In our patient, chemotherapy was started after he was diagnosed with AML from the bone marrow biopsy. He responded poorly and subsequent treatment with electron beam therapy was largely palliative. This clearly underlines the importance of maintaining a high clinical index of suspicion in the early identification of MS as early administration of AML-type chemotherapy before leukaemic transformation may reduce the risk of systemic progression and mortality.

Our patient represents a rare case of cutaneous MS with an unusually florid clinical presentation of rapidly progressive extensive cutaneous tumours and an atypical relapsing-remitting course before treatment was commenced. Expedient histopathologic and immunohistochemical studies are crucial in confirming the diagnosis. It is prudent for clinicians to recognise this entity as early treatment with chemotherapy may confer a better outcome.

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