

CASE REPORT

Cutaneous involvement of multiple myeloma

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Abstract

Cutaneous multiple myeloma (MM) is a rare disease. It can be primary or secondary in origin. The secondary type is further classified into specific and nonspecific types. The specific type is uncommon and is known as a secondary cutaneous plasmacytoma. We report a case of secondary cutaneous plasmacytoma in a 58-year-old man who had a history of plasma cell tumour of the lung and multiple myeloma. He achieved complete remission after the completion of chemotherapy and autologous stem cell transplant (ASCT). However, five months later, he developed multiple erythematous nodules on the whole body. Skin biopsy revealed diffuse neoplastic cells infiltrate in the reticular dermis with sparing of the upper papillary dermis and epidermis. The neoplastic cells were monotonous and homogenous with variable degrees of cytological atypia. Occasional cells showed distinctive plasma cell features. Plasma cell lineage was confirmed with CD138. The cells were immunoreactive to Kappa. Ki-67 was greater than 90%. They were non-immunoreactive to CD45, CD3, CD20, CD79 alpha and CK AE1/AE3. The findings were consistent with secondary cutaneous plasmacytoma. Our case illustrates that MM may present with nonspecific dermatological manifestations. As specific cutaneous involvement of MM is very uncommon; a high degree of clinical suspicion, detailed medical history and histopathological examination are required to arrive at an early diagnosis.

Keywords: Cutaneous multiple myeloma, plasmacytoma, erythematous nodules, plasma cells

INTRODUCTION

Multiple myeloma (MM) is a rare cancer, representing 1% of all malignancies. It is characterised by abnormal monoclonal proliferation of plasma cells in the bone marrow and is associated with monoclonal immunoglobulins (M protein) in serum or urine. MM can manifest with an extramedullary disease, where the neoplastic plasma cells infiltrate organs outside of the bone marrow. Approximately 4% of patients with MM present with the extramedullary disease and less than 1% have cutaneous involvement.¹ Cutaneous MM usually develops during the late stage of the disease as a reflection of increased tumour cell burden. Secondary cutaneous manifestations can be classified into specific and nonspecific types.²

The specific type is rare and known as secondary cutaneous plasmacytoma that results from infiltration of malignant plasma cells in

the skin. Typically, it manifests in the form of erythematous plaques or nodules in the cephalic segment, upper limbs, or trunk region. It may directly relate to an underlying bone lesion or rarely metastasise via haematogenous dissemination.

The nonspecific cutaneous MM is associated with abnormal protein production without evidence of malignant cell infiltration in the skin. The common clinical manifestations include amyloidosis or cryoglobulinaemia. The other non-specific cutaneous manifestations of MM include Sweet syndrome, xanthomas, scleroderma, pyoderma gangrenosum and leukocytoclastic vasculitis.³ To date, there is limited medical literature on the cutaneous involvement of MM. We report a case of secondary specific cutaneous involvement of MM that developed five months after completion of chemotherapy and autologous stem cell transplant (ASCT).

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CASE REPORT

A 58 years old gentleman presented with right-sided chest wall pain and lower back pain. His chest X-ray showed a lytic lesion over the right third rib. A right upper lobe mass measuring 5.0 x 4.0 x 3.4 cm with infiltration to the right intercostal muscle and the eroded adjacent posterior right third rib was detected on computed tomography (CT) thorax. There were also multiple lytic lesions at the right posterior aspect of L2 and T6. Lytic lesions were also seen at the left sacral ala with adjacent soft tissue components.

Biochemical investigations showed haemoglobin of 10.5 g/dL, total white count of 5.5 K/uL, platelet 150 K/uL, serum calcium 2.29 mmol/L and serum albumin/ globulin ratio of 1.82. Serum protein electrophoresis showed a total of lambda and free lambda light chain paraprotein 3.1g/l in the same band near the cathodic end with no immune paresis. The urine protein electrophoresis showed a total of lambda and free lambda light chain paraproteinuria 2.30g/l. There was reduced trilineage haematopoiesis with the presence of plasma cells in bone marrow aspiration and trephine biopsy. Biopsy of the lung tumour showed atypical plasma cells with eccentric and binucleated nuclei. Immunohistochemistry study showed CD138 immunopositive and lambda light chain restriction. His diagnosis was multiple myeloma with lambda light chain restriction, International Staging System (ISS) stage III and plasmacytoma of the lung.

He achieved complete remission with eight cycles of VTD (Velcade® / Bortezomib-Thalidomide-Dexamethasone) and IV Zoledronic

acid followed by ASCT. Pre ASCT and his serum protein electrophoresis showed partial response; while post ASCT, his results showed complete remission, but the light chain ratio was not normalised.

Within 5 months post-ASCT, he developed multiple nodules on his scalp, face, neck, chest, back and inguinal region. They were firm, erythematous, non-tender nodules and some were ulcerated with a crusted centre (Fig. 1). He also experienced similar back pain again during this time. His full blood picture and bone marrow aspiration did not show abnormal amounts of plasma cells, but trephine biopsy revealed the presence of a single large cluster of atypical plasma cells expressing CD138 with lambda light chain restriction. Flow cytometry of the marrow showed 0.3% aberrant plasma cells.

Skin biopsy of the nodule over his chest showed an intradermal neoplastic cell infiltrate arranged in a diffuse pattern in between fibrous bundle (Fig. 2). There was the involvement of the reticular dermis with sparing of the upper papillary dermis and epidermis (i.e. Grenz zone). The neoplastic cells were monotonous and homogenous with different degrees of cytological atypia. Occasional cells showed distinctive plasma cell features (Fig. 3). Mitoses were brisk. No Russell or Dutcher bodies were identified. There was an increase in neutrophils, eosinophils and lymphocytic infiltrate. The overlying epidermis was unremarkable.

An immunohistochemistry study was conducted to assist in the final diagnosis. Plasma cell lineage was confirmed with CD138. They were immunoreactive to Kappa. Lambda stain was inconclusive (Fig. 4). Ki-67 showed more



FIG. 1: Metastatic cutaneous plasmacytoma over the face. The erythematous skin nodule has ulcerated surface.

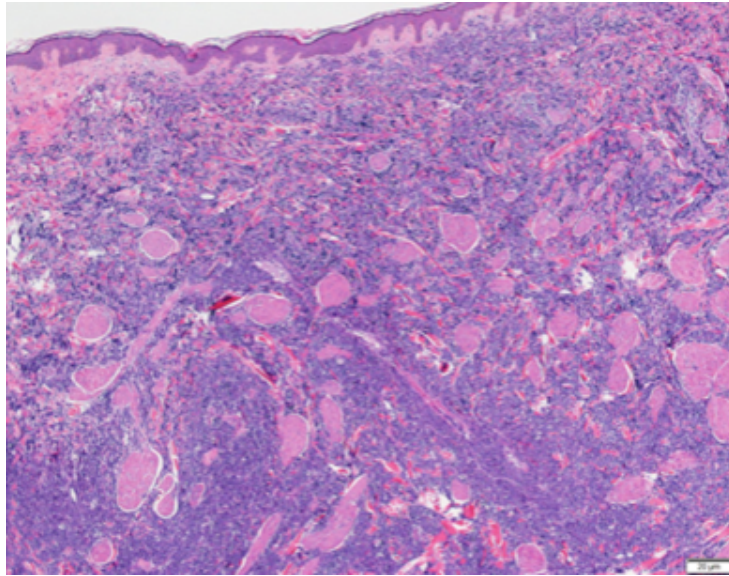


FIG. 2: Diffuse dermal neoplastic plasma cells infiltrate and the overlying Grenz zone. (Haematoxylin and eosin stain, Original magnification x40)

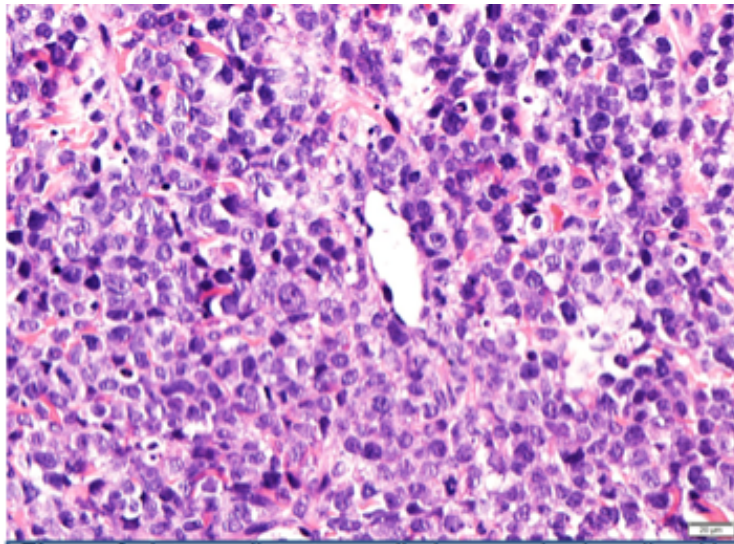


FIG. 3: Small to intermediate size neoplastic plasma cells infiltrate diffuse dermal neoplastic plasma cells infiltrate. Mitoses are brisk. (Haematoxylin and eosin stain, Original magnification x400)

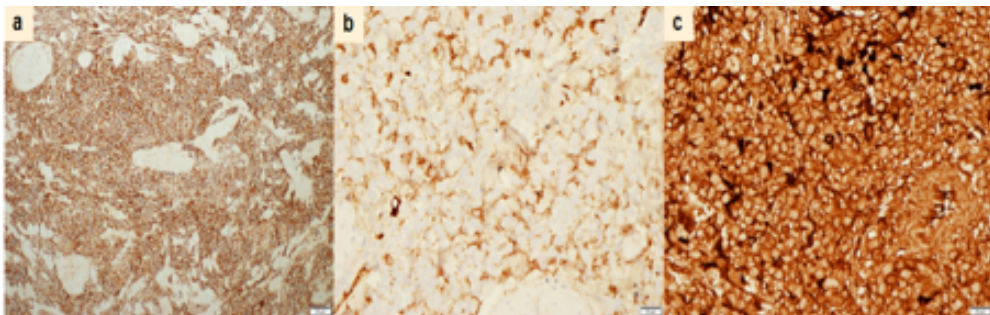


FIG. 4: The neoplastic plasma cells show diffuse immunoreactive for CD138 (a) with lambda light chain restriction; (b) kappa, (c) lambda.

than 90% proliferation index. They were non-immunoreactive to CD45 (leukocyte common antigen), CD3, CD20, CD79 alpha and CKAE1/AE3. The microscopic and immunohistochemical findings of the skin biopsy were most in keeping with a cutaneous involvement of MM.

DISCUSSION

Multiple myeloma is a haematological malignancy of plasma cells. It represents 1% of all malignancies with an annual incidence of 5 per 100,000 per annum. It is a disease of the elderly. 90% of cases occur in patients older than 50 with the average age of patients at diagnosis is 66 years.⁴

MM is mainly confined in the bone marrow (medullary) and manifested as lytic bone lesions. It also manifests as extramedullary disease, where the neoplastic plasma cells infiltrate organs outside of the bone marrow. The extramedullary MM occurs in approximately 4% of cases with less than 1% shows cutaneous involvement. Due to its rarity, little is known about cutaneous involvement by MM including its pathophysiology, as the medical literature describes only case reports or case series with a limited number of patients.⁵⁻⁶

Cutaneous MM can be classified into specific or nonspecific types.⁷ The specific type is very uncommon and usually occurs in the late stages of MM as a reflection of increased tumour burden. It is associated with a poor prognosis and requires aggressive management. Therefore it should be differentiated from solitary extramedullary plasmacytoma (SEP) and other cutaneous plasma cell infiltrates. SEP is diagnosed based on the presence of a discrete mass of monoclonal plasma cells proliferation with no evidence of multifocal disease on bone marrow and radiological examination.⁸ Other cutaneous plasma cell disorders usually show polyclonality, chronicity and benign processes.

Our case illustrates MM presenting with dermatological manifestations. The cutaneous lesion has nonspecific features and presents clinically as a common dermatosis; with differential diagnoses include leukocytoclastic vasculitis, pyoderma gangrenosum and vesiculobullous disorders. Its nonspecific features posed a challenge for dermatologists to suspect MM from the skin lesion. Thorough medical and treatment history with histopathological and immunohistochemical studies are mandatory for a prompt and accurate diagnosis.

The secondary specific cutaneous MM or secondary plasmacytoma occurs either through a direct extension to the skin, from the underlying bone lesions, or via haematogenous spread. The first mode of spread is more common, often soft at palpation and normochromic. The latter is usually represented by subcutaneous or intradermal violaceous nodules, with a hardened consistency, which occurs late during the disease. Our case might be represented by the latter mode of spread. They have a poor prognosis with an average life expectancy of 12 months after diagnosis.³

Microscopically, cutaneous involvement by MM must be distinguished from other malignancy and reactive plasma cell-rich infiltrates of the skin. The differentials include primary extramedullary plasmacytoma (PEMP), primary cutaneous marginal zone lymphoma with plasmacytic differentiation, plasmablastic lymphoma, and cutaneous involvement by Castleman disease, cutaneous and systemic plasmacytosis, and pretibial lymphoplasmacytic plaque.⁹ In addition, other inflammatory diseases which exhibit dense plasma cells infiltrate include syphilis, *Borrelia*, atypical mycobacteria, and fungal infections must be excluded from the diagnosis.

MM may be staged using the Durie-Salmon system. Recently, a new staging system called the International scoring system (ISS) for MM has been used. It relies mainly on albumin and beta-2-microglobulin levels in the blood. Our patient had beta-2-microglobulin levels of more than 4 ng/ μ L hence ISS Stage III. Other factors that affect survival include kidney function, age, labelling index and chromosomal abnormalities. About 35% of patients with a solitary plasmacytoma who receive treatment, including radiation, chemotherapy and surgical incision will ultimately develop MM. This evolution occurs up to 12 years following the initial diagnosis.¹⁰

In summary, an approach to the diagnosis of plasma cell proliferation includes reviewing all clinical, laboratory, and radiological/imaging workups, including bone-marrow biopsy in order to determine the presence of systemic disease. Immunohistochemical stains are required to confirm the diagnosis especially in the case of poorly differentiated tumours. CD138 positivity confirms the presence of plasma cells. These cells are negative for leukocyte common antigen (CD45) and maybe weakly positive for cytokeratin. They are frequently negative

for CD20, in contrast to other B-cell lineage neoplasms.

It is important to perform kappa and lambda light chain stains in order to differentiate between reactive and neoplastic plasma cells. The presence of kappa or lambda light chain predominance (light chain restriction) indicates the clonal plasma cell process. It is not seen in reactive plasma cell-rich infiltrates. Once a clonal plasma cell lesion is confirmed, it can be further divided into three categories namely primary cutaneous plasma cell neoplasm without systemic evidence of plasma cell neoplasm (i.e., PEMP); cutaneous plasma cell lesions in patients with an established diagnosis of MM (i.e., skin metastases) and cutaneous involvement from direct extension of underlying osteolytic lesions in MM.

MM has a wide spectrum of presentation. Our case illustrates that MM may present with nonspecific dermatological manifestations especially in the late stages of MM as a reflection of increased tumour cell burden. As specific cutaneous involvement in MM is very uncommon, a high degree of clinical suspicion, detailed medical history, histopathologic and immunohistochemical studies are valuable adjuncts to arrive at an early diagnosis.

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Conflict of interest: The authors declare no conflict of interest.

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