Cutaneous involvement by multiple myeloma presenting as erythematous indurated plaques at the site of cardiac pacemaker insertion

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INTRODUCTION
Cutaneous involvement by multiple myeloma (MM) is a rare extramedullary manifestation consisting of a proliferation of malignant plasma cells in the skin. This has sometimes been termed “secondary cutaneous plasmacytoma.” It most commonly affects the trunk and extremities; however, there have been rare cases involving surgical sites and sites of trauma. We describe an interesting case of cutaneous involvement by MM at the site of pacemaker insertion. To our knowledge, only 3 cases of cutaneous plasmacytoma arising at a pacemaker site have been published. Recognition of this rare manifestation is important as it has implications for treatment planning and portends a poor patient prognosis.

CASE REPORT
A woman in her 70s presented with a 1-month history of erythematous plaques over central portion of her chest and at a recent surgical site. The patient reported associated fevers and night sweats despite a recent course of intravenous and oral antibiotics. The patient had a known background of kappa IgG MM, which had been diagnosed 2 years earlier, and cardiogenic syncope requiring a permanent pacemaker (PPM), which had been inserted 5 months ago. Physical examination revealed 2 indurated, ill-defined, erythematous-to-violaceous plaques (Fig 1). The lesions were nontender with no overlying erosion or ulceration. No other lesions were noted on the skin or mucous membranes, and no palpable lymphadenopathy was noted. An incisional biopsy was performed for histopathology and tissue culture (Fig 2).

Histopathologic examination revealed medium-to-large malignant plasmacytoid cells with enlarged nuclei, prominent nucleoli, and moderate amounts of eosinophilic-to-basophilic eccentric cytoplasm. The dominant population exhibited a plasmablastic morphology with smaller numbers of admixed mature plasma cells. The cells were CD138+, CD56+, CD20−, CD79a−, and kappa light chain-restricted on immunophenotyping. Tissue cultures for bacterial, fungal, and atypical organisms were negative. A diagnosis of cutaneous involvement by the patient’s known MM was made.

Further history taking revealed that the recent surgical site was the result of a pacemaker removal procedure. The initial treating team interpreted the systemic symptoms, raised inflammatory markers, and erythematous plaques overlying the previous PPM as medical device infection, and the patient had undergone device removal and new pacemaker insertion as well as a prolonged course of oral antibiotics.

Abbreviations used:
MM: multiple myeloma
PPM: permanent pacemaker

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Following the diagnosis of cutaneous involvement, a bone marrow biopsy was performed that demonstrated the progression of the patient’s MM. Treatment was escalated to the CyBorD regimen (cyclophosphamide, bortezomib, and dexamethasone). Unfortunately, after 2 treatment cycles, serial positron emission tomography imaging demonstrated rapid progression of the disease with extensive metastases. The patient clinically deteriorated over the next 2 months, with the persistence of the cutaneous lesions, and ultimately succumbed to her illness. The patient passed away 4 months after the emergence of the cutaneous lesions.

**DISCUSSION**

Cutaneous involvement by MM is a rare extramedullary manifestation occurring in approximately 1% of the patients. It presents as nodules or plaques, which can be erythematous, violaceous, or skin-colored. In most cases, the condition occurs in patients with known MM and is associated with relapse or progression of the disease. Less commonly, it can be the presenting feature of MM. Cutaneous involvement by MM, as with other extramedullary involvement, portends a poor prognosis with significantly reduced overall survival and progression-free survival. The median survival from the time of cutaneous plasmacytoma occurrence is 8-9 months.

Common sites involved are the trunk and extremities; however, rare cases involving surgical sites such as pacemaker insertion or fracture sites have been described in the literature. The mechanism for these occurrences at sites of trauma is not well understood, though it may potentially involve local inflammatory mediators released following surgery, which contribute to the clonal expansion of a plasma cell population.

In 1976, Hamaker et al reported the first case of cutaneous plasmacytoma in a pacemaker pocket, which occurred 16 months after insertion (Table I). Plasmacytoma was the presenting feature of MM in
**Table I: A summary of case reports of cutaneous plasmacytoma involving pacemaker insertion sites**

| Author                  | Demographics | Presenting feature | Known MM at time of diagnosis | Prognosis |
|-------------------------|--------------|--------------------|-------------------------------|-----------|
| Hamaker et al (1976)    | 48-year-old man | Violaceous lesion over pacemaker site | No, diagnosed in 2013 | Deaths due to progressive disease within 10 months |
| Sasaki et al (1992)     | 74-year-old woman | Mass overlying pacemaker site | Yes, diagnosed 18 months earlier | Deaths due to MM and heart failure |
| Li et al (2013)         | 89-year-old man | Nontender erythematous plaque | No, diagnosed 4 months after plasmacytoma presentation | Deaths due to MM and progressive disease within 4 months |
| Choong et al (present study) | 76-year-old woman | Erythematous indurated plaque at pacemaker site | Yes, diagnosed 2 years earlier | Deaths due to MM and progressive disease within 4 months |

**Note:** MM, Multiple myeloma.

**Legend:**
- **Rapidly growing lesions:** treated with radiotherapy and systemic chemotherapy.
- **Initial response to chemotherapy:** observed when systemic therapy had been administered for several weeks after surgery and radiotherapy.
- **Repeated chemotherapies:** given over a period of 10 months due to progressive disease and heart failure.
- **Second chemotherapies:** administered after surgery and radiotherapy.
- **Recurrence:** at the site of new pacemaker insertion.
- **Prognosis:** deaths due to progressive disease.
overlying the PPM site in a patient with known MM (Table I). Their patient passed away 10 months after the emergence of the plasmacytoma.

Other cutaneous plasma cell and B-cell neoplasms can also present as erythematous plaques or nodules and are differential diagnoses for cutaneous involvement by MM. Extranodal marginal zone B-cell lymphoma is a rare non-Hodgkin lymphoma that primarily affects the skin. It can present with solitary or multifocal red to brown plaques or nodules distributed over the trunk and arms. Biopsy demonstrates a lymphocytic infiltrate in dermal or superficial subcutaneous tissue with marginal zone cells and a characteristic immunophenotype with BCL-2 positivity and BCL-6 negativity. Cutaneous plasma cell granuloma is a rare benign inflammatory tumor that often presents with an asymptomatic erythematous-to-hyperpigmented solitary dermal nodule. Biopsy demonstrates a well-circumscribed, nonencapsulated dermal infiltrate of polyclonal plasma cells, which may extend to the subcutaneous tissue. It is often associated with a prominent sclerosing collagenous stroma.

Other differential diagnoses for cutaneous involvement by MM include primary cutaneous plasmacytoma, plasmablastic lymphoma, and lymphoplasmacytic lymphoma. The correlation of clinical and histopathologic features helps distinguish these; however, diagnosis can be challenging, as cutaneous MM involvement has varied morphologic appearances, including plasmacytic, plasmablastic, and lymphoplasmacytic variants.2,7 Plasmablastic features were seen in 40% of cases in a series by Panse et al,7 in 2021, as was seen in our patient. Interestingly, a case of plasmablastic lymphoma occurring in a pacemaker pocket has been described.9

This case highlights the importance of considering the rare manifestation of cutaneous involvement by MM and the possible predilection it has for surgical sites or sites of trauma. In our patient, earlier recognition may have avoided unnecessary pacemaker replacement operation and multiple courses of antibiotics. This disease manifestation carries a poor prognosis and may prompt discussions regarding end-of-life care planning with these patients.

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Conflicts of interest
None disclosed.

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