

## Skin Involvement in Immunoglobulin E Multiple Myeloma

A 71-year-old male was diagnosed in 2001 with a solitary extramedullary plasmacytoma of the left vocal cord. After radiation therapy of the area, he reached complete remission and was monitored with observation. In 2004, he developed left hip pain, and work-up showed a plasmacytoma of the bone arising from the left acetabulum. At the time of recurrence, serum immunoglobulin (Ig) levels were normal with the exception of IgE, which was elevated at 824 kU/L (normal, < 114 kU/L), and serum immunofixation was positive for monoclonal IgE-kappa proteins. Serum albumin was 3.7 g/dL, beta-2 microglobulin was 2.3 mg/L, and bone marrow biopsy was negative for plasma-cell infiltration. Patient was again treated with radiation therapy, followed by oral dexamethasone and thalidomide and monthly zoledronic acid. After 1 year of remission, his disease progressed with multiple bone lesions, and the patient received high-dose chemotherapy followed by an autologous stem-cell transplantation (ASCT). IgE levels correlated with disease response, and they decreased to normal range after the ASCT. Remission lasted approximately 1 year, when additional lytic lesions were documented on the skeletal survey, and treatment with lenalidomide was initiated. On fourth relapse/progression of the disease, intravenous bortezomib was begun. The latter controlled the multiple myeloma (MM) for 11 months, after which the patient developed progressive disease with symptomatic hypercalcemia. Physical examination revealed two small tender skin nodules below the left knee (Fig 1), and fine-needle aspirate documented the presence of plasma cells infiltrating the skin. Morphology varied from mature to blastic, and several cells had

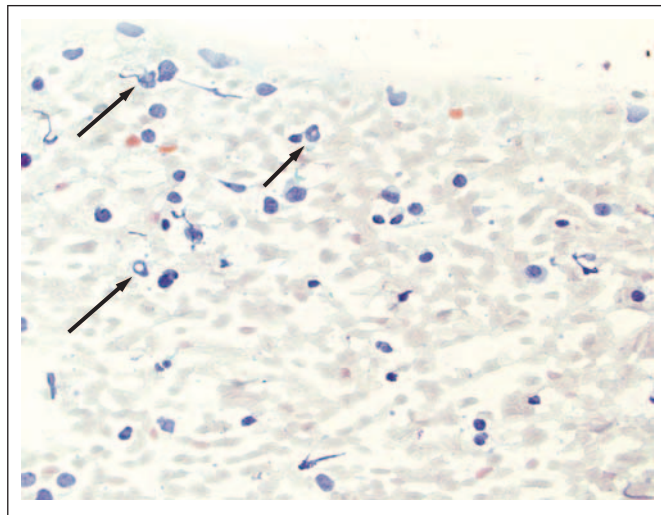


Fig 2.

intranuclear inclusions (Fig 2, arrows). Positron emission tomography/computed tomography scan showed multiple areas of intense [ $^{18}\text{F}$ ]fluorodeoxyglucose avidity throughout the bones (Fig 3), consistent with active MM.

IgE myeloma is a rare subtype of MM, and it is thought to represent less than 0.01% of all plasma cell dyscrasias.<sup>1</sup> Since the first case was described in 1967, approximately 44 cases of IgE MM have been reported in the literature.<sup>2,3</sup> For clinicians, it is important to remember that commonly available serum immunofixation testing screens only for monoclonal IgG, IgM, and IgA chains, and immunofixation specific for IgD and IgE needs to be requested when these rare subtypes are suspected (eg, when a monoclonal protein has been detected in the serum protein electrophoresis, but routine immunofixation is negative). Many consider IgE MM an aggressive disease, with a more rapid progression than other subtypes.<sup>4</sup> While there are no specific clinical manifestations for IgE MM, it has been associated with a significantly higher rate of plasma-cell leukemia.<sup>4,5</sup> Moreover, osteosclerotic and osteoblastic lesions are more likely to occur in this subtype of MM than in other forms of the disease, although osteolytic lesions remain the most common type.<sup>4,6,7</sup> A review of the first 19 reported cases of IgE MM showed no difference in the incidence of extramedullary plasma cell infiltration compared with other subtypes of the disease.<sup>7</sup> In our patient, IgE MM manifested primarily with extramedullary organ involvement, both at the time of diagnosis and at the terminal phase of the disease. Metastatic skin lesions are rare in MM, and they appear as erythematous nodules or plaques in a wide anatomic distribution. Although skin lesions may develop early in the course of the disease, cutaneous involvement in MM is commonly associated with extensive tumor burden, advanced disease, and poor prognosis, with death often occurring a few months after development of the skin lesions.<sup>8</sup> In a literature review of 100 cases of MM

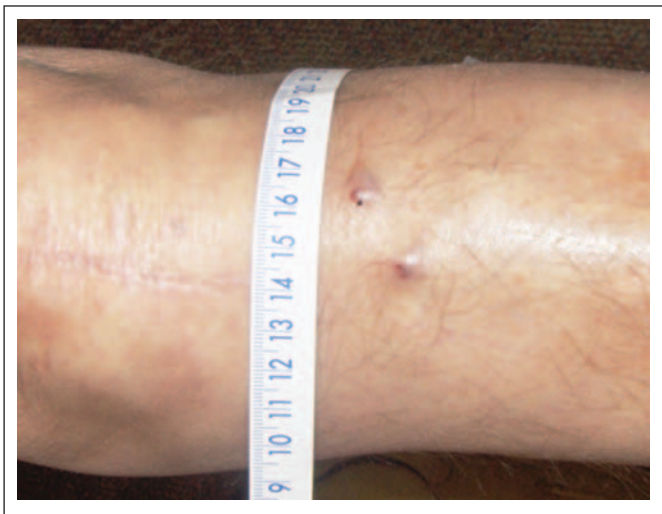


Fig 1.

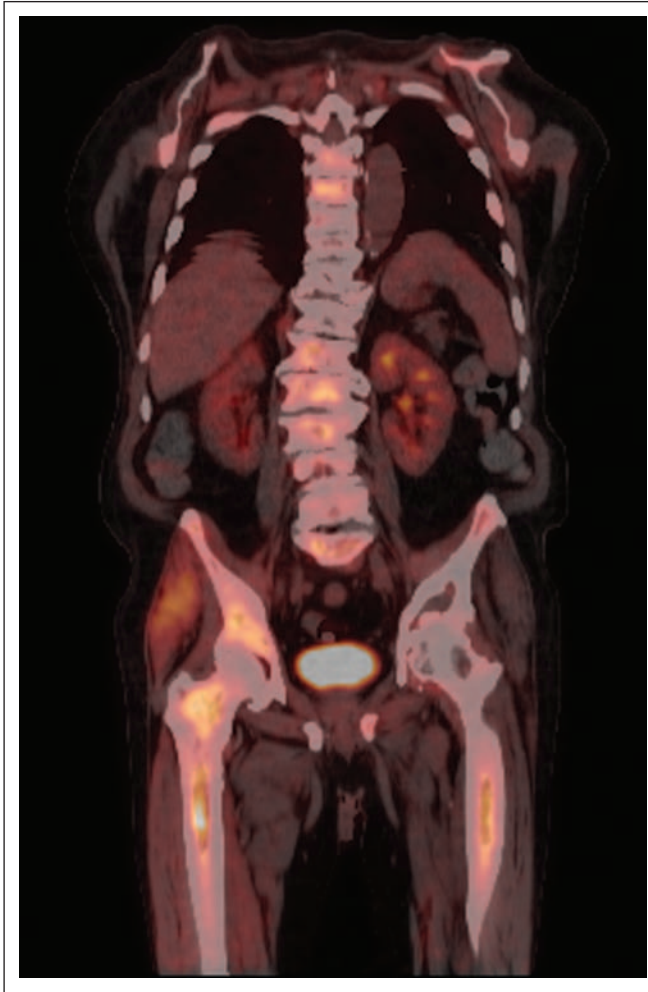


Fig 3.

with cutaneous involvement, plasma cells secreted various types of paraprotein, including IgG (54%), IgA (28%), IgD (12%), light chains only (4%), and IgM (1%).<sup>8</sup> To our knowledge, our case is the first reported instance of cutaneous plasmacytomas in a patient with IgE MM.

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#### AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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