Multiple Myeloma Unveiled by Multiple Hyperkeratotic Spicules

Adam Dalal MD¹, Michael David MD¹, Meora Feinmesser MD² and Akiva Trattner MD¹

¹Department of Dermatology and ²Institute of Pathology, Rabin Medical Center (Beilinson Campus), Petah Tikva, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

KEY WORDS: multiple myeloma, skin involvement, monoclonal gammopathy, multiple hyperkeratotic spicules IMAJ 2010; 12: 709–710

> **M** ultiple myeloma is a malignant hematologic disorder characterized by a proliferation of monoclonal plasma cells, leading to overproduction of monoclonal immunoglobulins. It accounts for approximately 1% of all cancers and 10% of all hematologic cancers [1]. The typical age at occurrence is 40–70 years. The

Multiple hyperkeratotic spicules on the nose and face



protean manifestations of MM are well known among clinicians and include bone pain, anemia, renal disease, weight loss, and susceptibility to infections, among others. Skin involvement is relatively rare, though the spectrum of lesions is wide, including extramedullary plasmacytoma, cutaneous amyloidosis, pyoderma gangrenosum, and vasculitis.

We describe a case of MM in which the diagnosis was unmasked by the occurrence of a unique skin eruption.

PATIENT DESCRIPTION

A 67 year old woman presented to the dermatology department with a 4 month history of psoriatic eruption. In the month prior to admission she had begun treatment with acitretin and topical steroids, but there was little improvement. Other medical problems included hypertension, osteoporosis, and mild depression, for which she was prescribed tritace, raloxifene, and paroxetine, respectively. She was also a heavy smoker. Her son had been diagnosed with psoriasis several years earlier. These data together with findings of a typical psoriatic rash on physical examination led to a diagnosis of psoriasis vulgaris. Blood workup was remarkable only for mild anemia (hemoglobin 11.3 g/dl). The rash responded well to phototherapy and coal tar, and the patient was discharged with a recommendation to continue follow-up for the anemia on an ambulatory basis.

Four months later, the patient was readmitted with a psoriatic flare-up.

MM = multiple myeloma

Physical examination revealed red welldemarcated plaques with a white scaly surface distributed symmetrically along wide areas of her body, compatible with the diagnosis of psoriasis. In addition, however, there was an unusual rash on her face, characterized by multiple follicular yellowish spicules [Figure]. The facial rash alerted us to the possible diagnosis of MM. The medical history was retaken, with a focus on the typical complaints of MM. This time, the patient reported a 10 kg weight loss in the last year and bone pain of recent onset. Complete laboratory workup revealed high levels of total protein (10.7 g/dl) with a low albumin/ globulin ratio and elevated erythrocyte sedimentation rate (> 100 mm/hr). The other biochemistry results were unremarkable. Electrophoretic serum analysis revealed M component of immunoglobulin G type (4.5 g/L) and monoclonal kappa light chains. Bone marrow biopsy was performed, establishing the diagnosis of MM with involvement of more than 25% malignant plasma cells. Skin biopsy taken from the nose showed multiple follicular plugs.

Dermatological treatment consisted of a regimen similar to that followed for the psoriasis and there was a moderate improvement in the rash. The spicular eruption was treated with a combination of various agents including keratolytic preparations, topical steroids, and a mild chemical peel that yielded only minimal effect. The patient was discharged after amelioration of the skin condition and referred for hematologic evaluation and systemic treatment in accordance with the diagnosis. Within less than 2 weeks she was admitted for the third time because of a poorly controlled psoriatic eruption. On examination the patient showed an exacerbation of the spicular eruption together with an extension to formerly uninvolved areas (mainly the back). Having determined that the patient's dermatological and general condition was an expression of the malignant disease, we tried to hasten the start of chemotherapy. However, shortly after discharge, her condition rapidly deteriorated and she died from severe pneumonia complicated by *Pneumocystis carinii* superinfection.

COMMENT

Blufarb [2], in an early study, classified the myriad cutaneous manifestations of MM into two categories, specific and non-specific. The specific skin lesions include extramedullary plasmacytoma and direct invasion of the skin from bony tumors; the non-specific cutaneous involvement is caused by other hematologic alterations such as paraproteinemia and cryoglobulinemia. A later classification, relating to all the monoclonal gammopathies, divided the skin involvement in MM into four groups: group I - infiltration of the skin by tumor cells or deposition of paraprotein; group II - skin disorders strongly associated with monoclonal gammopathy; group III - dermatoses with an anecdotal association with monoclonal gammopathy; and group IV - miscellaneous non-specific conditions, mainly complications of the disease [3].

Our patient presented with an unusual skin condition with clinical and laboratory features of multiple hyperkeratotic spicules. This phenomenon has also been termed filiform hyperkeratosis, parakeratotic horns, follicular hyperkeratosis, and multiple minute digitate hyperkeratosis.

There are only 16 reports (including 17 patients) of spiculosis associated with MM [4]. An additional case was described as a manifestation of monoclonal gammopathy of undetermined significance. Hyperkeratotic spicules are not pathognomonic for MM, and have also been reported in hypovitaminosis A, chronic renal failure, Crohn's disease, and other malignancies. However, this eruption is a highly characteristic sign of MM. The spicules can appear anywhere on the skin, although the face, particularly the nose, and scalp and neck are the most common sites. The exact mechanism underlying the formation of skin spiculosis remains unclear. Bork et al. [5] were the first to demonstrate that follicular plugs contain the M protein itself and postulated that the accumulation of the protein together with cryoglobulin precipitation is responsible for the predilection of the spicules to cold-exposed areas. Since then, however, other cases have called this theory into doubt. The skin biopsy in our case failed to show paraprotein deposition or other infiltration by cells that could directly explain the underlying mechanism of spiculosis. Histological examinations in other cases were also unrevealing. The absence of a direct link between the spicular eruption and the MM leads us to assume that the creation of spiculosis is complex and may encompass more than one mechanism. It is possible that an abnormal keratinization process is incited by the paraproteinemia. These mechanisms can be associated with the type of paraprotein, the stage of the disease and other factors noted in the patient.

As in our case, in about half of the reports the appearance of the spicular eruption preceded the diagnosis of MM. A growing number of reports suggest that spiculosis occurs in parallel with the progression of MM and can even indicate a disease relapse [4].

The spicular rash is also distinguished by its poor response to topical treatment. To date, most of the cases report systemic chemotherapy as the treatment of choice. This treatment usually results in hematological containment followed by cutaneous recovery. A novel report offers the idea that the improvement of skin symptoms does not necessarily overlap the regression of blood disease [4]. Whether spiculosis is a poor prognostic factor in MM is hard to determine on the basis of the available data. In many of the reported cases, the cutaneous response was described without referring to the patient's general outcome. Nevertheless, our case, along with previous reports, reinforces the view that multiple hyperkeratotic spicules herald a poor outcome.

In conclusion, cutaneous involvement is an important, albeit infrequent, part of MM. We describe an unusual eruption of multiple hyperkeratotic spicules that may be the presenting sign of monoclonal gammopathy. Therefore, its recognition by dermatologists, internists, family physicians and general practitioners is mandatory. The appearance of the rash should prompt a comprehensive laboratory workup to identify the underlying malignant blood clone. We believe, supported by several earlier reports, that it may be an adverse prognostic factor, necessitating early intervention and treatment by hematology specialists. Further studies are needed to ascertain the prevalence, pathogenesis, and clinical implications of hyperkeratotic spiculosis in MM.

Corresponding author: Dr. A. Trattner

Dept. of Dermatology, Rabin Medical Center (Beilinson Campus), Petah Tikva 49100, Israel Phone: (972-3) 937-7196 Fax: (972-3) 937-7162 email: atrattner@clalit.org.il

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