Multiple Myeloma and Atopic Eczema in an Adult

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Key Words

Multiple myeloma · Atopic eczema · Early symptoms · Diagnostic criteria

Abstract

Multiple myeloma is the fourteenth cause of cancer-related death. The symptoms of myeloma are mostly nonspecific, and there is significant delay between the first symptoms and diagnosis of myeloma. Atopic eczema is a common chronic inflammatory skin disease associated with dysregulation of the immune system. It generally develops in early childhood but can also occur in adults. Eczema is associated with a variety of hematological and solid malignancies, and possibly multiple myeloma. We report a patient with eczema that developed 5 years before the diagnosis of multiple myeloma but was mistaken for psoriasis.

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Introduction

Multiple myeloma (MM) is one of the most common hematological malignancies, the majority of which remain incurable. The common presenting symptoms of MM, such as bone pain, asthenia, fatigue, weight loss, and dyspnea, are nonspecific, which may contribute to the significant delay in the diagnosis in almost half of MM cases after the onset of the first symptom [1]; furthermore, 20% of patients have no or mild symptoms at the time of diagnosis. There might be other possible less well-known clinical features associated with MM; for example, eczema may slightly increase the risk of the IgG myeloma subtype [2]. However, this needs further investigation and confirmation. We report a case where eczema preceded the diagnosis of MM by at least 5 years in the hope of adding confirmatory evidence for the association between eczema and myeloma. With the advancements in the therapeutic ap-

proaches to myeloma, the recognition of early myeloma symptoms would lead to prompt diagnosis and treatment before the development of serious organ damage, and prolong life.

Case Description

A 68-year-old male presented for progressive loss of appetite and lethargy for 3 weeks. He also developed persistent low back pain in the last 2 months. The past medical history included hypertension, hyperlipidemia, coronary artery disease with multiple percutaneous coronary interventions (the most recent one was 3 weeks prior to the admission), congestive heart failure with automated implantable cardioverter-defibrillator placement, and psoriasis diagnosed 5 years ago. The patient had a history of smoking one pack of cigarettes per day for 40 years. The vital signs were within normal range; he was lethargic and dehydrated. There were multiple large erythematous plaques of skin in the bilateral inguinal and axillary and right hip areas weeping serous discharge (fig. 1).

The laboratory tests showed normal hemoglobin initially, which dropped to 8.5 within 1 month after admission, hypercalcemia, M spike, and elevated β_2 -microalbumin and IgG levels (table 1).

The CT scan of the head demonstrated multiple ‘punched out’ lucencies within the skull (fig. 2a). Bone survey revealed innumerable lytic lesions throughout the visualized bones: cranial vault (fig. 2b), proximal shaft of femur bilaterally, hips, and pelvic bones (fig. 2c, d). Bone marrow core biopsy showed increased plasma cells up to 10%, confirmed on CD138, with predominance of monoclonal lambda. Skin biopsy revealed epidermal spongiotic dermatitis with acanthosis and parakeratosis, the upper dermis with perivascular lymphocytic exocytosis and rare eosinophils. In addition, the patient had eosinophilia and elevated IgE (table 1); atopic eczema was the most likely diagnosis.

Discussion

MM, one of the most common hematological malignancies, represents 1.4% of all new cancer cases in the United States and accounts for 2% of cancer-related mortality. Although the 5-year survival has been improving, most of the MM cases remain incurable. In addition, there has been a rise in the incidence of new MM cases of 0.7% each year over the last decade [3].

Diagnosis of MM

The revised criteria for the diagnosis of MM issued by the International Myeloma Working Group (IMWG) [4] utilize biopsy and clinical clues (table 2). The evidence supporting the diagnosis of MM in this case includes: (1) 10% clonal plasma cells on bone marrow biopsy (see Case Description); (2) corrected calcium above 11 mg/dl; (3) although the renal function was normal at admission, the creatinine level reached 3.1 during the hospital course transiently; (4) the hemoglobin fell to 8.5 g/dl after admission (table 1), and (5) extensive lytic bone lesions on CT and bone survey (fig. 1). Although not required by the revised IMWG diagnostic criteria, the presence of an M spike provides further support of the diagnosis of MM (table 1).

The levels of β_2 -microalbumin (3.7 mg/l) and albumin (2.7 g/dl) help classify the MM as stage II IgG lambda MM, according to the International Staging System for Multiple Myeloma (table 3) [5].

Eczema as a Marker of MM

The common presenting symptoms of MM are nonspecific, i.e. bone pain, asthenia, fatigue, weight loss, and dyspnea. However, early-stage MM does not cause obvious symptoms. About 20% of patients have no symptoms or mild ones at the time of diagnosis. This might contribute to the delay in the diagnosis. More than 40% of MM patients were diagnosed more than 6 months after the onset of the first symptom. The prolonged delay commonly occurs in patients who first present to their general practitioner and is associated with more complications, advanced stage of malignancy, and reduced disease-free survival [1]. Therefore, it is critical to increase the awareness of myeloma and associated symptoms among medical communities, especially general practitioners.

We report a case of MM where eczema occurred 5 years prior to the diagnosis of MM. Unexplained eczema of adult onset has been reported to be a marker of a variety of hematologic malignancies and solid tumors [6–8]. The risk of MM is positively related to the number and duration of inflammatory conditions [9]; a prior history of eczema has been reported to slightly increase the risk of myeloma [10]. Therefore, in the absence of an identifiable etiology, recalcitrant eczema in an adult should raise the suspicion of an internal malignancy, including MM. The possibility of MM should be evaluated systematically with meticulous physical examination, complete blood count, blood film, serum protein electrophoresis, chest X-ray, and CT scan of the trunk [6]. Additionally, the association between MM and eczema needs further investigation.

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Table 1. Laboratory test results

Items	Value	Normal ranges
Hemoglobin ^a , g/dl	11.9→8.5	11.6–16.8
Hematocrit, %	35	35.1–50
White blood cell, /μl	8.0	3,600–11,000
Platelet, /μl	349	150,000–372,000
M spike, g/dl	2.1	0
β ₂ -Microalbumin, mg/l	3.7	0.6–2.4
IgG, mg/dl	3,688	700–1,600
IgA, mg/dl	121	91–414
IgM, mg/dl	22	40–230
IgE, IU/ml	136	0–100
Uric acid, mg/dl	3.3	3.4–7
BUN, mg/dl	16	6–20
Creatinine, mg/dl	0.9	0.7–1.2
Calcium, mg/dl	10.6	8.6–10.2
Corrected calcium, mg/dl	11.6	
Albumin, g/dl	2.7	3.5–5.3

^a The hemoglobin dropped to 8.5 within 1 month after admission.

Table 2. Revised criteria for the diagnosis of MM by the IMWG

Biopsy	≥10% clonal bone marrow plasma cells, or biopsy-proven plasmacytoma
Clinical	≥1 of myeloma-defining events: a. End-organ damage attributable to myeloma (CRAB): C: Hypercalcemia: serum calcium >1 mg/dl higher than the upper limit of normal or >11 mg/dl R: Renal insufficiency: creatinine clearance <40 ml/min, or serum creatinine >2 mg/dl A: Anemia: hemoglobin value >2 g/dl below the lower limit of normal, or hemoglobin value <10 g/dl B: Bone lesions: ≥1 osteolytic lesions on skeletal radiography, CT, or PET-CT b. ≥1 of the following malignancy biomarkers of Clonal bone marrow plasma cell ≥60% Involved:uninvolved serum free light chain ratio ≥100 >1 focal lesion on MRI studies (≥5 mm).

Table 3. International Staging System for Multiple Myeloma [5]

Stage	Criteria
I	Serum β ₂ -microglobulin level <3.5 mg/l Serum albumin ≥3.5 g/dl
II	Not stage I or III
III	Serum β ₂ -microglobulin level ≥5.5 mg/l

Fig. 1. Chronic and itchy skin lesions in the groin areas and the right hip. This skin condition had been treated for psoriasis for 5 years with topical steroid.

Fig. 2. Extensive bone lysis. **a** Head CT shows multiple 'punch out' bone lesions in the skull. **b–d** Bone survey demonstrated innumerable lytic bone lesions throughout the visualized bones: cranial vault, proximal shaft of femur bilaterally, hips, and pelvic bones.