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Case Report Open Access

# Cutaneous vasculitis in Multiple myeloma and other rare manifestations: case report

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Multiple myeloma can have different clinical manifestations, and not all patients present with a classic CRAB component. The acronym CRAB stands for the following traits of multiple myeloma: C = Calcium (elevated), R = Renal failure, A = Anemia, B = Bone lesions (bone pain). We describe a 53-year-old man who referred to our hospital with a complaint of a rapidly progressive purpura/petechiae on the lower limb and abdomen, and multiple lytic lesions in the skull and spine, and multiple fractures. We documented an increased presence of plasmacytes in bone marrow aspiration and multiple lytic bone lesions, which led to a diagnosis of multiple myeloma. Although multiple myeloma presenting with purpura/petechiae is uncommon, it must always be considered as a differential diagnosis with this clinical finding.

**Keywords:** Multiple myeloma, Petechiae, Purpura, Skin lesion

## Introduction

Multiple myeloma (MM) is a malignant disease caused by uncontrolled proliferation of clonal plasma cells and giving rise to widespread complications that lead to organ dysfunction and, eventually, death [1]. MM makes up 10% of blood malignancies. The disease develops from a precancerous condition called monoclonal gammopathy of undetermined significance (MGUS) [2] and has a variety of symptoms, including bone pain (60%), fatigue (30%), weight loss (25%), paresthesia (5%), fever (0.7%), hepatomegaly (4%), splenomegaly (1%), and lymphadenopathy (1%) [3-4]. Skin rash is a very rare manifestation of multiple myeloma [5]. This case report describes a 53-year-old man who came to the hospital with skin presentations and various organ involvements.

## Case presentation

The patient is a 53-year-old man with a history of hypertension, thrombocytopenia, and splenomegaly who has been under follow-up for the past five years. The patient underwent BMA (bone marrow aspiration) in 2018, and its report was normocellular marrow with mild megakaryocytic lineage hyperplasia without evidence of malignancy. At that time, the patient was only followed, and no special treatment was performed for him. He suddenly suffered from skin lesions with a purpura/petechiae form (starting on the lower limbs from the legs then extending up to the abdomen), recurrent fevers, abdominal and back pain, and weight loss of approximately 8 kg from one month before the visit (Figure 1). The symptoms were progressive. The patient referred to another hospital one month after the onset of symptoms. He was examined at that center, and paraclinical findings showed high blood creatinine level (4.1 mg/dl), high blood calcium level (18 mg/dl), and cytopenia (PLT: 81*103 /µl and RBC: 3 * 106/µl). In previous follow-ups, the patient's creatinine was never high. He underwent dialysis four times. BMA was performed for him, and its report was normocellular marrow with mild myeloid preponderance. Electrophoresis was also performed for him, and the “M component” finding was seen. Due to his normal BMA, vasculitis-like skin lesions, and multi-organ involvement, vasculitis was suggested for the patient, and he was referred to this center to rule out this condition. In the center’s paraclinical examinations, multiple lytic lesions in the skull and spine and several fractures in lumbar vertebrae were seen on X-ray and CT SCAN (Figure 2). In various tests for vasculitis assessment, ANA and ANCA were negative, and ESR was high (78), CRP was high (57), bicytopenia (thrombocyte-openia and anemia), high calcium level (despite four rounds of dialysis, calcium was 12), and high creatinine level (1.8) were observed. The rest of the patient's tests



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including bacterial, parasitic, and endocrinological tests (including PTH) were normal.

Abdominal and pelvic ultrasonography showed splenomegaly and increased renal echo, and the rest was normal. A skin biopsy was performed for the patient, and the report showed normal DIF with leukocytoclastic small vessel vasculitis with focal subcorneal pustulosis (orthokeratosis with focal subcorneal neutrophilic aggregation, slight spongiosis, infiltration of mixed inflammatory cells with neutrophil preponderance in superficial dermis).

According to all the findings for this patient, a high probability of multiple myeloma was considered. A second BMA was performed for him, which again showed a normocellular marrow with mild myeloid preponderance. A PET scan was then performed, and multiple myeloma were suggested (diffused heterodense bone marrow showing mild FDG uptake along with innumerable small faintly FDG avid lytic lesions throughout the axial and proximal appendicular skeleton). Because of the high suspicion of multiple myeloma, a third BMA was performed, and the results finally confirmed multiple myeloma.

As a first step, glucocorticoids were started, but the patient showed no response. Then chemotherapy was performed for the patient. After treatment, skin lesions and other complications such as bone pain, AKI, and high calcium level were dramatically resolved, and his clinical manifestations recovered after chemotherapy.

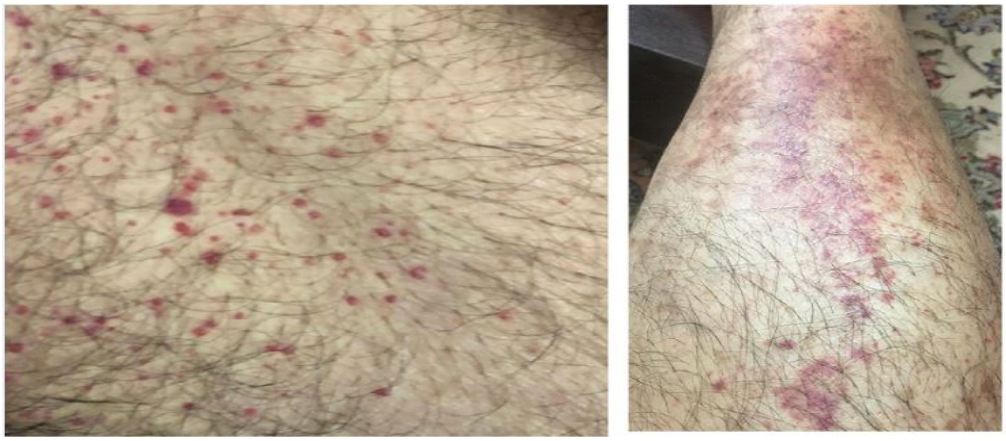

**Figure 1.** Cutaneous rash in first vist.

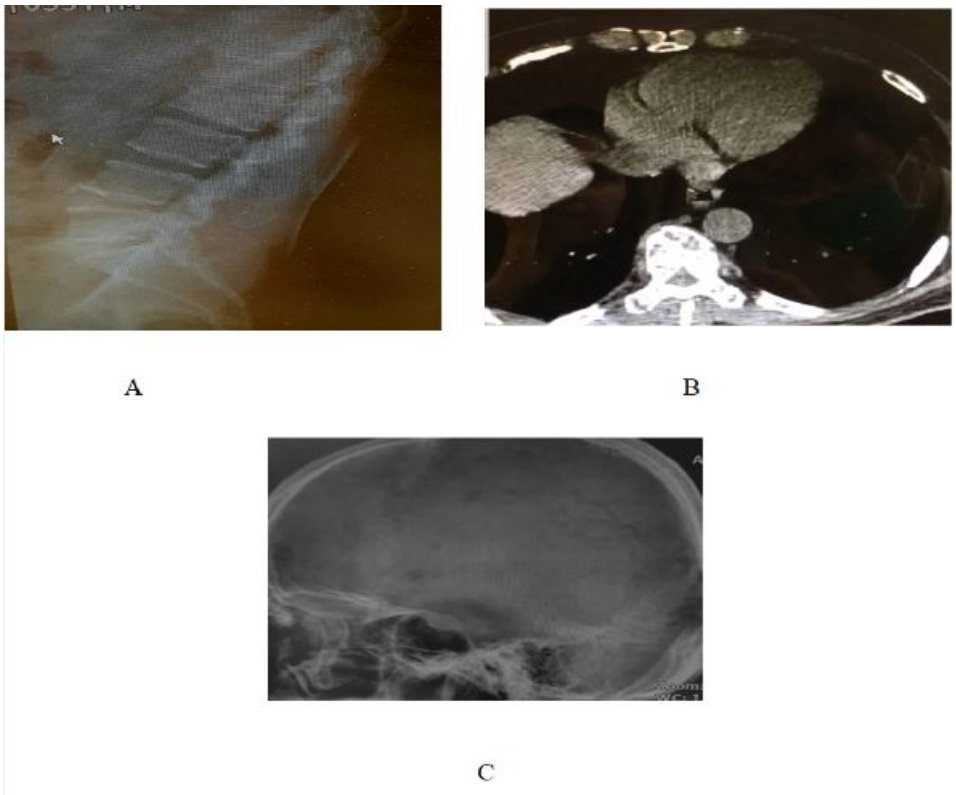


**Figure 2.** A) Multiple fractures in vertebra; B) Lytic lesions in vertebra; C) Lytic lesions in skull

**Table 1.** Cutaneous manifestation of multiple myeloma

| Specific manifestations | | Nonspecific manifestations | |
|---|---|---|---|
| **Primary** | **Secondary** | **vasculitic** | **Non Vasculitic** |
| ➢ Cutaneous plasmacytoma | ➢ Direct extension to the skin from adjacent bony lesions<br>➢ Cutaneous metastases | ➢ LCV:<br>● Drugs<br>● Infections<br>● Paraneoplastia<br>➢ crayoglubulinemia | ➢ Pyoderma gangrenosum<br>➢ Autoimmune bullous disease<br>➢ Hyperviscosity syndrome<br>➢ Amyloidosis<br>➢ urticaria |

## Discussion

The patient discussed herein presented with rare manifestations of multiple myeloma, including skin lesions in the form of a petechial rash, purpura, and three normal BMA reports. He had renal involvement in the form of AKI as well as multiple fractures in the spine.

Vasculitis, in association with malignancy, is uncommon and has a reported prevalence of only 8% in patients with malignancy [6]. The association seems to be significantly higher with lymphoproliferative and myelo-proliferative disorders than with tumors, and vasculitis commonly predates malignancy identification. Up to 5% of patients with cutaneous vasculitis have an underlying neoplasm [7]. Rona et al. found that the skin manifestations related to multiple myeloma are late manifestations, while in this case report, skin manifestations were the first manifestations and differed from the study of Rona et al. in terms of presentation time [5]. Nguyen's study also showed that the most common skin manifestation in patients with multiple myeloma is multiple papules with cutaneous and subcutaneous nodules measuring 1-5 cm in diameter. In the present patient, however, the manifestations occurred in the petechial form, so purpura and nodules did not exist [8]. The patient had recurrent fevers, which is also a very rare symptom of multiple myeloma. Müller et al. conducted a study over 25 years and reported that only 9 cases of fever were seen in 5,523 patients with multiple myeloma [9]. In the patient discussed herein, an abdominal ultrasound indicated increased renal echo, and mild splenomegaly was also seen. The patient had also had mild splenomegaly on the ultrasonography performed two years prior to his visit at our center; however, it did not appear to be related to multiple myeloma and was an old finding. AKI also caused ultrasound changes in the patient's kidneys. The patient's creatinine had a sudden increase to the level of 4.1 mg/dl, which was still 1.8 mg/dl creatinine after four times dialysis. High calcium levels with normal PTH levels, normal phosphorus levels, high CRP, and ESR with thrombocytopenia and anemia were also present in this patient. ANCA and ANA levels were negative. M-COMPONENT was observed on the patient's electrophoresis. Accordingly, all the above findings confirmed multiple myeloma. Anemia is observed in 75% of patients, increased creatinine levels in 50%, and hypercalcemia in 25%. ESR is high due to increased immunoglobulins [4].

The M-component is found in electrophoresis in 97% of patients [10]. A PET scan was also performed on the current patient and showed evidence of multiple myeloma. A BMA performed two years prior was negative, and in the last hospitalization, two BMAs were negative. Ultimately, a third BMA was performed, and evidence of multiple myeloma was seen. In most cases, BMA indicates multiple myeloma, but in 4% of cases, BMA may be negative due to bone marrow patch involvement. This finding was confirmed in a study by Kyle et al. [4]. PET scan can also be used when BMA is not diagnostic, but there is a strong suspicion, which shows radiological manifestations of multiple myeloma [11].

One important differential diagnosis for multiple myeloma is Waldenström macroglobulinemia. They are IgM monoclonal gammopathy, but there are some differences in clinical manifestations. Monoclonal immunoglobulin in the blood or urine and CRAB are seen in multiple myeloma, but in Waldenström macroglobulinemia, hepatomegaly and splenomegaly, anemia, lymphadenopathy, IgM component–related symptoms such as peripheral neuropathy, and constitutional manifestations are common. Clinical manifestation is a way to differentiate between these diseases [12-15].

## Conclusion

In the clinic, patients with multiple myeloma presenting with skin involvement, especially petechial and purpuric vasculitis-like rash, as well as fever are very rare. In patients with vasculitis-like skin manifestations with nonspecific symptoms, malignancies such as multiple myeloma should be considered. Cutaneous manifestations are a very rare finding of multiple myeloma. Therefore, manifestations are divided into specific and nonspecific categories. Specific manifestations include cutaneous plasmacytoma, cutaneous metastasis, and bone-to-skin invasion. Non-specific demonstrations fall into two categories: vasculitic manifestations that include LCV (following medications, infection, and paraneoplastic syndromes) and cryoglobulinemia that includes pyoderma gangrenosome, vesicular autoimmune disease, hyperviscosity syndrome, urticaria, and amyloidosis. The patient in this study had vasculitis-like manifestations (Table 1). Treatment often requires the use of

glucocorticoids in addition to therapy directed against the underlying malignancy.

It is noteworthy that multiple myeloma can involve bone marrow with patchy involvement and does not specify BMA once or twice. In such cases, if other evidence and findings are in favor of multiple myeloma, biopsies should be taken from different parts of the bone marrow. PET scans can also diagnostic when performed on patients.

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## Conflict of interest

None.

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