Case Report

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Internal Medicine Section

Multiple Myeloma Presenting as Digital Ischaemia Mimicking Rheumatoid Vasculitis: A Diagnostic Challenge

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ABSTRACT

Multiple myeloma commonly presents with anaemia, bone pain, renal dysfunction, hypercalcaemia, and lytic bone lesions. However, digital ischaemia and gangrenous ulceration as an initial manifestation are exceedingly rare and may mimic rheumatologic or vasculitic disorders, leading to diagnostic delay. A 45-year-old female with a history of type 2 diabetes mellitus and previously treated as seronegative rheumatoid arthritis presented with progressive blackish discolouration and ulceration of the right ring finger associated with whitish discharge for one month. She also complained of bilateral pedal oedema, difficulty in walking, low-grade fever, and melaena. Initial evaluation raised suspicion for rheumatoid vasculitis, Raynaud phenomenon, or peripheral vascular disease. Rheumatologic workup including rheumatoid factor, anti-Cyclic Citrullinated Peptide (anti-CCP) antibodies, Antinuclear Antibody (ANA) immunoblot, Antineutrophil Cytoplasmic Antibody (ANCA) profile, and nail fold capillaroscopy was negative. Arterial Doppler of the right upper limb demonstrated normal triphasic flow. Laboratory investigations revealed severe anaemia (haemoglobin 4.3 g/dL), thrombocytopenia, leucocytosis, markedly elevated inflammatory markers, and poorly controlled diabetes mellitus. Computed tomography of the thorax and abdomen demonstrated multiple extensive lytic lesions involving the axial and appendicular skeleton with associated soft tissue components, pathological destruction involving the humeral head, diffuse osteopenia, and hepatosplenomegaly. Bone marrow biopsy revealed hypercellular marrow largely replaced by sheets of plasmacytoid cells with suppression of normal haematopoietic elements. Immunohistochemistry showed diffuse CD138 positivity, confirming plasma cell neoplasm favouring multiple myeloma. The patient was initiated on bortezomib, lenalidomide, and dexamethasone-based chemotherapy. This case highlights an unusual presentation of multiple myeloma presenting as digital ischaemic ulceration mimicking rheumatologic vasculitis. In patients with atypical digital ischaemia associated with cytopenias, elevated inflammatory markers, and systemic manifestations, haematological malignancies including multiple myeloma should be considered in the differential diagnosis to avoid delay in diagnosis and management.

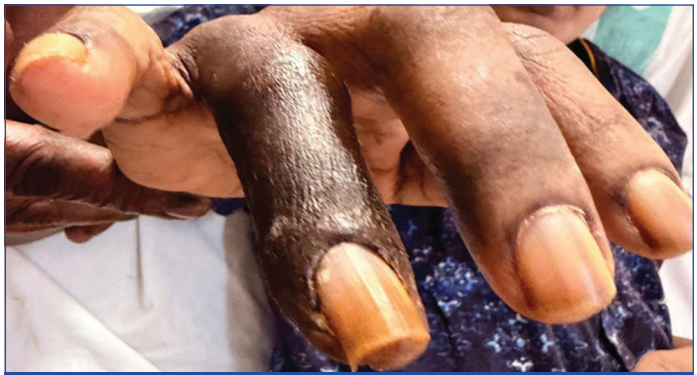
Keywords: Bone marrow examination, Immunohistochemistry, Osteolysis, Paraproteinemias, Plasma cell neoplasms

CASE REPORT

A 45-year-old female, known case of type 2 diabetes mellitus for five years on insulin and oral hypoglycaemic agents, presented with complaints of blackish discolouration and ulceration of the right ring finger for one month [Table/Fig-1]. The lesion initially involved the fingertip and progressively extended proximally, associated with whitish discharge. She had been receiving local dressings and antibiotics at an outside hospital without significant improvement. The patient also complained of bilateral pedal oedema for three days, more prominent on the left-side, difficulty in walking, increased frequency of micturition, low-grade fever for one day, and passage of black-coloured stools for four days. There was no history of cough, breathlessness, chest pain, abdominal pain, vomiting, or loose stools. She had previously been treated as seronegative rheumatoid arthritis for one year with steroids, methotrexate, folic acid, and hydroxychloroquine. Rheumatologic medications had been stopped one month prior to admission due to finger infection.

On examination, the patient was conscious and oriented. She was febrile with a temperature of 37.8°C, pulse rate of 100/min, blood pressure of 120/80 mmHg, respiratory rate of 20/min. Blackish discolouration with ischaemic changes involving the right ring finger was noted [Table/Fig-1]. Bilateral pedal oedema extending up to the knees was present. Cardiovascular, respiratory, and abdominal examinations were unremarkable. Neurological examination revealed power of 4/5 in both upper limbs and right lower limb, and 3/5 in the left lower limb.

Initial investigations revealed severe anaemia with haemoglobin of 4.3 g/dL, thrombocytopenia with platelet count of 62,000/mm^3,



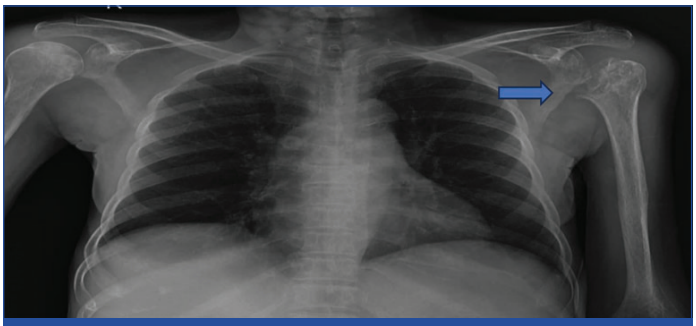
[Table/Fig-1]: Digital ischaemic changes and gangrenous discolouration involving right ring finger (4th digit).

leucocytosis, elevated Erythrocyte Sedimentation Rate (ESR) of 120 mm/h and C-Reactive Protein (CRP) 29 mg/L, macrocytosis, and poorly controlled diabetes mellitus with HbA1c of 9.9%. Renal function tests, liver function tests, serum electrolytes, complement levels were within normal limits. Rheumatoid factor, anti-CCP antibodies, ANA immunoblot, and ANCA profile were negative.

Given the digital ischaemic changes, rheumatologic and vascular aetiologies were initially considered. Rheumatoid vasculitis was suspected because of the presence of digital ischaemic ulceration involving the right ring finger in a patient previously diagnosed with rheumatoid arthritis and treated with methotrexate, steroids, and hydroxychloroquine. The acral ischaemic changes, elevated inflammatory markers, and absence of large-vessel arterial occlusion on Doppler examination further raised the possibility of

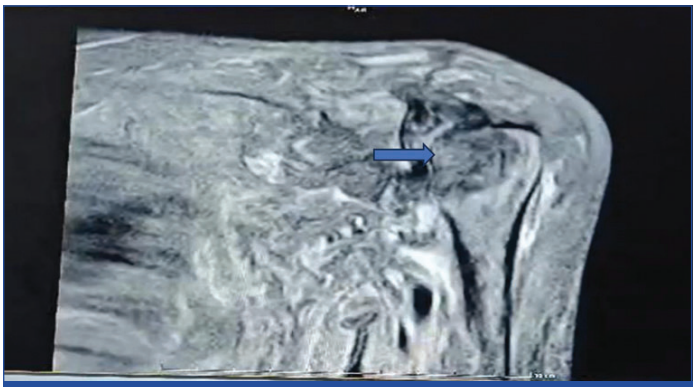
an underlying vasculitic process. Nail fold capillaroscopy did not demonstrate significant abnormalities. Right upper limb arterial Doppler showed normal triphasic waveforms without evidence of significant peripheral arterial disease.

Further evaluation with contrast-enhanced computed tomography of the thorax and abdomen revealed multiple lytic lesions involving the axial and appendicular skeleton, including bilateral humeral heads, vertebral bodies, sacrum, and femoral regions, associated with soft-tissue components and pathological destruction involving the left humeral head [Table/Fig-2]. Hepatosplenomegaly, diffuse osteopenia, mild ascites, and soft tissue deposits were also noted.



[Table/Fig-2]: Radiograph showing lytic lesion involving the proximal humerus (arrow), suggestive of plasma cell dyscrasia.

Magnetic resonance imaging of the left shoulder demonstrated multiple soft-tissue deposits involving the subacromial, subcoracoid, subscapular, and subdeltoid bursae with associated lytic lesions involving the proximal humerus [Table/Fig-3].

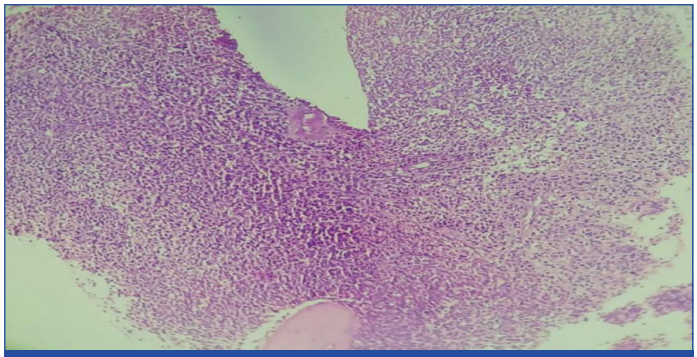


[Table/Fig-3]: Magnetic Resonance Imaging (MRI) of the left shoulder demonstrating multiple soft-tissue deposits involving the periarticular region with associated lytic destruction of the proximal humerus, consistent with plasma cell neoplastic involvement.

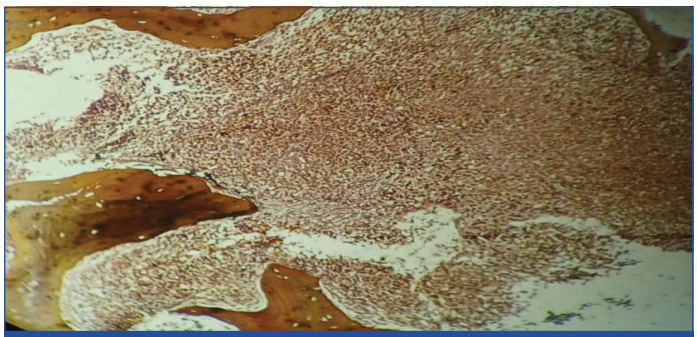
Serum protein electrophoresis demonstrated low serum albumin with a markedly decreased gamma-globulin fraction and a relatively increased alpha-2 globulin fraction. The electrophoretic pattern was abnormal.

Bone marrow biopsy demonstrated hypercellular marrow spaces largely replaced by sheets of plasmacytoid cells with suppression of normal haematopoietic elements [Table/Fig-4]. Immunohistochemistry showed diffuse strong membranous positivity for CD138, consistent with plasma cell neoplasm favouring multiple myeloma [Table/Fig-5]. High-power microscopic examination demonstrated sheets of atypical plasma cells with eccentric nuclei and abundant cytoplasm, consistent with plasma cell neoplasm [Table/Fig-6].

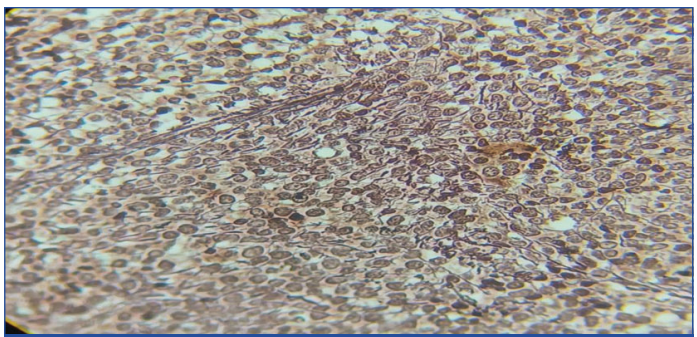
The patient received supportive treatment including three units of packed red blood cell transfusion for severe anaemia, resulting in improvement of haemoglobin from 4.3 g/dL to 8.2 g/dL. She was also treated with intravenous cefotaxime, metronidazole, pantoprazole, and ondansetron along with regular wound dressings. The digital lesion showed clinical improvement following local wound care and antibiotic therapy prior to initiation of chemotherapy. Following confirmation of multiple myeloma, the patient was started on chemotherapy with the bortezomib, lenalidomide, and dexamethasone



[Table/Fig-4]: Bone marrow biopsy showing diffuse infiltration by plasma cells replacing normal marrow elements (H&E stain, X100).



[Table/Fig-5]: Bone marrow biopsy immunohistochemistry showing diffuse strong membranous positivity for CD138 in sheets of infiltrating plasma cells, consistent with plasma cell neoplasm favouring multiple myeloma (IHC, X100).



[Table/Fig-6]: High-power microscopic image of bone marrow biopsy demonstrating sheets of atypical plasma cells with eccentric nuclei and abundant cytoplasm, consistent with plasma cell neoplasm (H&E stain, X400).

(VRd) regimen along with appropriate supportive medications including aspirin, aciclovir, trimethoprim-sulfamethoxazole prophylaxis, fluconazole, vitamin D, calcium supplementation, and glycaemic control with insulin therapy. On follow-up, the patient demonstrated improvement in the digital lesion with no further progression of ischaemic changes. She continues to receive chemotherapy under regular haematology follow-up.

DISCUSSION

Multiple myeloma is a malignant plasma cell disorder characterised by clonal proliferation of plasma cells within the bone marrow and associated end-organ damage. The disease commonly presents with anaemia, bone pain, renal dysfunction, hypercalcaemia, recurrent infections, and osteolytic skeletal lesions [1,2]. Although musculoskeletal manifestations are frequent, vascular manifestations are uncommon. Digital ischaemia and gangrenous ulceration are rare manifestations of multiple myeloma and may clinically resemble connective tissue disorders, vasculitis, Raynaud phenomenon, thromboembolic disease, or peripheral arterial disease, resulting in diagnostic delay [3-5].

Digital ischaemia in multiple myeloma has been attributed to several proposed mechanisms including hyperviscosity syndrome, paraprotein-mediated vascular occlusion, cryoglobulinaemia, vasospasm, thrombosis, and vascular compromise secondary to abnormal immunoglobulin deposition [3,4,6]. Multiple myeloma may

also present with other unusual vascular manifestations such as hyperviscosity syndrome, which can result in significant morbidity and mortality if not recognised early. Bhagawati J et al., reported a case of multiple myeloma presenting as fatal hyperviscosity syndrome [7], highlighting the diverse vascular complications associated with plasma cell dyscrasias. Such presentations may mimic rheumatologic disorders including rheumatoid vasculitis, systemic sclerosis, ANCA-associated vasculitis, and Raynaud phenomenon.

Several similar cases have been reported in the literature. Mejía-Zuluaga M et al., described a patient with multiple myeloma initially presenting as small-vessel vasculitis, resulting in diagnostic uncertainty before the underlying plasma cell dyscrasia was identified [5]. Khammar Z et al., reported digital ischaemia as the presenting manifestation of multiple myeloma, emphasising the importance of considering haematological malignancies in patients presenting with unexplained acral ischaemia [3]. Zrikem H et al., described digital necrosis as the initial manifestation of multiple myeloma, highlighting the potential for delayed diagnosis when vascular manifestations precede classical myeloma-related symptoms [8]. Similar atypical presentations have also been reported in patients initially evaluated for giant cell arteritis and other vasculitic disorders [9]. These reports, together with the present case, demonstrate that multiple myeloma may rarely manifest with peripheral vascular compromise before the development of classical clinical features.

Other uncommon initial manifestations of multiple myeloma have also been reported. Kumar S et al., described a patient presenting with multiple cystic swellings as the initial manifestation of multiple myeloma [10], further emphasising the heterogeneous clinical presentation of this disease and the potential for diagnostic delay when classical features are absent.

In the present case, rheumatoid vasculitis was initially considered because the patient had a prior diagnosis of rheumatoid arthritis and presented with digital ischaemic ulceration, a recognised manifestation of rheumatoid vasculitis. Furthermore, markedly elevated inflammatory markers and the absence of significant peripheral arterial disease on Doppler imaging supported this clinical suspicion. However, negative rheumatoid factor, anti-CCP antibodies, ANA profile, ANCA profile, and subsequent identification of extensive lytic skeletal lesions prompted evaluation for an alternative diagnosis, ultimately revealing multiple myeloma.

In the present case, the patient had initially been treated as seronegative rheumatoid arthritis. However, the absence of serological evidence of rheumatoid arthritis, negative autoimmune workup, normal arterial Doppler findings, severe cytopenias, markedly elevated inflammatory markers, and extensive skeletal lesions suggested an alternative systemic pathology.

The diagnosis became apparent following radiological identification of multiple lytic lesions with associated soft-tissue deposits and subsequent bone marrow examination demonstrating plasma cell infiltration with CD138 positivity [11].

An additional noteworthy feature in this case was the extensive extramedullary involvement, including soft-tissue deposits around the shoulder girdle and thoracic wall [12]. The previously presumed frozen shoulder may retrospectively represent early skeletal or soft-tissue manifestations of plasma cell disease.

This case highlights the importance of considering haematological malignancies in the differential diagnosis of atypical digital ischaemia, especially when associated with severe anaemia, thrombocytopenia, elevated inflammatory markers, and unexplained skeletal manifestations. Histopathological confirmation of digital vasculitis could not be obtained as biopsy from the affected finger lesion was not performed.

CONCLUSION(S)

Multiple myeloma may rarely present with digital ischaemic ulceration mimicking rheumatologic vasculitis, resulting in diagnostic delay. In patients presenting with atypical digital ischaemia associated with cytopenias, elevated inflammatory markers, and musculoskeletal symptoms, haematological malignancies including multiple myeloma should be considered even in the absence of classical renal dysfunction or hypercalcaemia.

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