Case report

A case report on multiple myeloma: A masquerading neoplasm in a 36-year-old female.

ABSTRACT –

Aim: Weaim to highlight this rare presentationto alert clinicians to atypical multiple myeloma(MM) cases, enabling earlier diagnosis and better patient outcomes.This report may contribute to the medical literature by illustratinghow MM can masquerade as other conditionsin the absence of characteristic clinical features, leading to potential diagnostic dilemmas and pitfalls, hence, encouraging clinicians to maintain a high index of suspicion, particularly in unusual demographics. It can help identify patterns or variations and stimulate further investigations into MM's different presentation and progression.

Presentation of case: This article features a 36-year-old female with an initial presentation of fever, multiple symmetrical joint pains, oral ulcer, and alopecia with normal serum calcium levels and no lytic bone lesions, and provisional diagnoses of connective tissue disorders, lymphoma, leukemia, and infectious etiologies but confirmatory tests conclusive of MM.

Discussion: MM is a clonal plasma cell proliferative disorder, which characteristically presents with osteolytic bone lesions accompanied byhypercalcemia, anemia, bone pain, or renal dysfunction. It predominantly occurs in elderly males, with 70 being the median age of diagnosis. MM is rare in younger people under 40, hence creating less suspicion and late diagnosis. However, age is a pivotal prognostic feature because of its associated comorbidities and performance index; thus, young patients have a better prognosis, making early diagnosis even more important.

Conclusion: The consequences of undiagnosed MM are severe and show an increased risk

of death underlining the cruciality of quick diagnosis with a Sherlockian mindset and interdisciplinary approach for lowering morbidity. Hence, this case underscores the importance of considering MM in differential diagnoses, even when it seems unlikely.

INTRODUCTION –

Multiple myeloma (MM), a plasma cell dyscrasia, accounts for 10% of all hematological malignancies, characterized by an abnormal increase of monoclonal paraprotein leading to specific end-organ damage.[1] It is more common in males[2] and has a lower incidence in Asians than Caucasians.[3] In India, the incidence is about 0.95 per 100,000.[3] The incidence increases with age, especially after 40, with two-thirds diagnosed over 65.[4,5] It is rare in young adults (19-40 years), comprising 2% of cases.[6,7] Clinical manifestations include hypercalcemia, bone pain with lytic lesions, renal dysfunction, or anemia, with 80% having osteolytic bone disease at diagnosis.[8] It is diagnosed per the International Myeloma Working Group (IMWG) diagnostic criteria, significantly refined in 2014.[9]

This discussion features a case of a 36-year-old female, with initial presentation of fever, multiple symmetrical joint pains, oral ulcer, and alopecia with normal serum calcium levels and no lytic bone lesions, but confirmatory tests conclusive of multiple myeloma.

CASE DISCUSSION–

A 36-year-old lady presented with complaints of fever for the last four months and multiple symmetrical joint pains for the past two months. Her fever was remittent, low-grade, and associated with weight loss, anorexia, and dry cough. Joints involved were knee, ankle, wrist, and elbow with associated swelling and morning stiffness. She also had a history of easy fatiguability, painless oral ulcers, and hair fall. There was no history of rash, frothy urine, abdominal pain, dry eyes, or any dyspnea, or tuberculosis.The patient underwent a

hysterectomy procedure for menorrhagia four months before her current presentation, even after which she required blood transfusions over the last three months for anemia.

On examination, the patient had a low BMI(17.5 kg/m^2) and pallor, non-scarring alopecia, with normal vitals.

A respiratory examination revealed bilateral decreased breath sounds suggestive of pleural effusion. On musculoskeletal examination, joints were tender and swollen with decreased range of motion. Lymphoreticular and gastrointestinal findings were non-contributory.

Based on history and examination findings, connective tissue disorders, hematological malignancies like lymphoma or acute leukemia, or infections like tuberculosis were the differentials.

Laboratory investigations revealed pancytopenia (Hb – 5.9g/dl, Platelets $0.8x10^5$/cc, Total leukocyte count – 3400/cc), a low corrected reticulocyte count (1.05) with a normal (Neutrophil/Lymphocyte) ratio. Renal function tests (RFT) showed an increase in serum urea (24 mg/dL), creatinine (1.9 mg/dL), and uric acid (10.8 mg/dL) levels. LDH (537 U/L), INR (1.64), PT (19.4s), and aPTT (45.3s) were elevated. Serum total protein (4.5 mg/dL) and serum albumin (2.23 g/dL) levels were low. Urine routine examination showed a strong presence of protein (+++), while blood was weakly present too. Normal urine albumin: creatinine ratio (138 mg/gm), however, the 24-hour urinary protein level (2748 mg/day) was grossly elevated. A direct Coombs test performed to rule out a delayed blood transfusion reaction was negative. The rheumatological panel for antinuclear antibodies, rheumatoid factor, anti-CCP, and other autoantibodies were all negative.

A high-resolution computed tomography (HRCT) of the chest gave an impression of pneumonia in the right middle lobe with bilateral pleural effusion (right > left). Serological tests and microscopic examinations for tuberculosis, HIV, hepatitis, and other relevant infectious diseases were negative.

Bone marrow aspiration done in the view of pancytopenia revealed reactive marrow. A renal biopsy could not be done due to a deranged coagulation profile.

Following preliminary investigations, neither of the differential diagnoses was favorable as major investigations for them were not in tandem. Hence, further investigations had to be conducted to reach a diagnosis.

Owing to deranged RFT values and overflow proteinuria, a serum protein electrophoresis was performed, which revealed hypoalbuminemia with an M band peak, a characteristic of multiple myeloma (MM) that came as a surprise as the history and clinical features did not raise suspicion towards its diagnosis.

Consequently, specific investigations for MM were performed, where ESR (15 mm/1st hour), serum calcium (9.2mg/dL), and albumin: globulin ratio (1.34) were normal, and radiological investigations did not reveal any lytic lesion of bone, which was again atypical because usually these parameters are deranged in MM.

However, further blood investigations like serum free light chain assay revealed the presence of a kappa: lambda ratio > 936.6 (kappa-free light chain= >12260 mg/L; lambda-free light chain=13.1mg/L) and monoclonal gammopathy. Immunohistochemistry was positive for CD38, CD138, and CD56. A bone marrow biopsy performed to confirm the diagnosis showed 30% cells with a moderate amount of amphophilic cytoplasm and eccentric nuclei with perinuclear-hoff suggestive of plasma cell dyscrasias with no evidence of parasites.

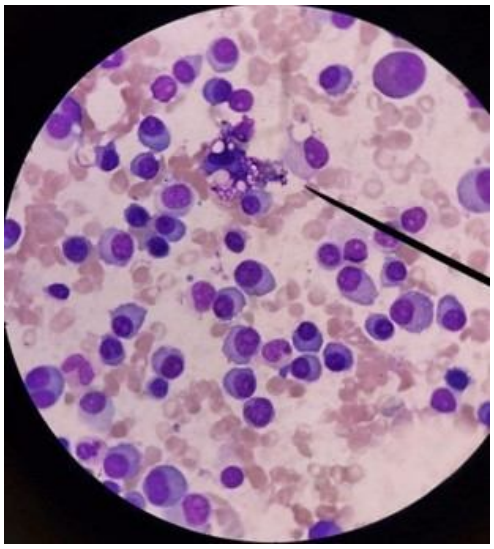

Figure 1: Bone marrow biopsy showing cells with moderate amphophilic cytoplasm and eccentric nuclei with perinuclear-hoff

Thus, the patient was diagnosed with multiple myeloma per the International Myeloma Working Group Diagnostic Criteria for multiple myeloma and related plasma cell disorders.[9]She was started promptly on a CyBorD (Cyclophosphamide 300 mg/m^2 weekly per oral + Bortezomib 1-3 mg/m^2 weekly + Dexamethasone 20 mg per oral twice weekly) treatment regimen. There has been a decrease in plasma cell levels. The patient is now on regular follow-up.

DISCUSSION –

Multiple myeloma occurs predominantly in the geriatric population, with the median age of diagnosis being 70 years[1], with more than 66% of newly diagnosed cases in people older than

65.[3] Only 2% of people diagnosed with MM are less than 40 years old,[7]unlike our case where the patient was a 36-year-old female. Classically, complications that multiple myeloma clinically manifests include hypercalcemia, renal insufficiency, osteolytic lesions, infection, and anemia.[1] However, our case followed a young female primarily presenting with the chief complaints of fever associated with dry cough, symmetrical joint pains, oral ulcer, alopecia, and examination findings suggestive of pleural effusion, which invariably led the physicians to consider connective tissue disorders, acute leukemia, lymphoma or infectious aetiologies. Approximately 75% of patients at diagnosis have pancytopenia, though only about 10% have a haemoglobin level lower than 8 gm/dl.[10]Calcium levels were normal without any evidence of lytic lesions of the bone - studies on myeloma bone disease place osteolytic bone diseases as one of the most prominent features, with almost 80% of patients presenting with it.[10] Thus, the absence of classical features raises low clinical suspicion of such neoplasms and misguides further away into a dilemma. Epidemiological studies have shown that mild renal impairment, maybe acute or chronic, is observed in about 25% of cases where raised serum creatinine levels fulfill the increased calcium, renal insufficiency, anemia, or bone lesions (CRAB) diagnostic criteria.[9] Hence, the evidence of deranged renal function test and overflow proteinuria of the patient raised curiosity furthering investigations like serum electrophoresis, which revealed an M band, a characteristic finding. Hence, this case highlights how thorough routine tests, prompt evaluation, and effective teamwork are pivotal in diagnosing patients with seemingly atypical presentations, especially in diseases like MM with heterogeneity across age, sex, and geography, which masquerades undiagnosed.[3]

MM is probably the cancer with most prognostic parameters described, where age remains a crucial factor because of its associated comorbidities and performance index, besides other factors.[11]According to an analysis of 10,549 patients from the International Myeloma Working Group, MM was uncommon in young persons and more frequent in

males.[12]However, young patients present with a significantly lower International Staging System(ISS) stage and consequently have a less frequent elevation of β2-microglobulin and better normalization of low serum albumin levels.[12] Hence, patients younger than 50 seem to have a better prognosis.[12] Survival was better but shorter in the younger age group as they showed an increased risk of death[13], thus, suspecting varied differential diagnoses of multi-symptom diseases like MM in the absence of conventional featuresand quick diagnosis is prime toallow a better recovery and prevent fatal outcomes.

CONCLUSION –

Multiple myeloma, a clonal plasma cell dyscrasia can be referred to as a 'masquerading neoplasm' due to its varied clinical features and diagnostic tests, which can mimic other common malignancies and allow it to remain undetected in circulation. Although rare, it can present in young and female patients without typical signs such as hypercalcemia and osteolytic bone lesions. Therefore, it is crucial to maintain a high index of suspicion and conduct thorough testing to rule out MM. Early and accurate diagnosis is vital, as it is a treatable neoplasm with a favorable prognosis in younger patients, ultimately saving lives through timely intervention.

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