Case Report

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A case of multiple myeloma misdiagnosed as seronegative rheumatoid arthritis: a rare case report

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Introduction: Multiple myeloma (MM) is a malignant plasma cell proliferation producing large numbers of monoclonal immunoglobulins. Typical MM symptoms include anemia, bone pain, hypercalcemia, and renal failure. Atypical presentations like joint involvement were rarely reported in the literature and may cause significant delays in treatment and adverse outcomes.

Case presentation: The authors report a case of a 54-year-old female who presented with symmetrical polyarthritis and was misdiagnosed with rheumatoid arthritis. The diagnosis of MM was made after failing many treatments of rheumatoid arthritis and with further laboratory tests and procedures.

Conclusion: This rare manifestation of MM carries a diagnostic challenge and causes a significant delay in treating such patients. Here, the authors report this unusual initial presentation with a review of several cases in the literature describing similar presentations.

Keywords: MM, monoclonal immunoglobulin, RF, seronegative

Introduction

Multiple myeloma (MM) is a plasma cell tumor that accounts for 1% of cancer and 10% of hematologic malignancies[1], with a 10-year survival rate of about 30%[2]. First described in 1848, MM is part of a spectrum of diseases ranging from monoclonal gammopathy of unknown significance to plasma cell leukemia and can range from asymptomatic to severely symptomatic with complications requiring emergent treatment[3]. The frequent presenting symptoms of MM are fatigue, anemia, renal insufficiency, and hypercalcemia[1]. An atypical manifestation could be a challenge for diagnosis causing a delay in treatment[2]. We describe a 54-year-old female who presented with symmetrical synovitis as a first sign of MM.

Case presentation

A 54-year-old female, nonsmoker, nonalcoholic, presented to the out-hospital rheumatology clinic for evaluation of generalized arthralgia, mainly in the hands, wrists, elbows, knees, and ankles as well as morning stiffness lasting 1 h for 3 months prior and gradually worsened.

She denied any recent travel, sick contacts, or tick bites. The patient had no past medical, surgical, or family history. A clinical exam revealed synovitis of the second through fifth metacarpophalangeal and proximal interphalangeal joints of hands, wrists, and elbows (shown in Fig. 1). In addition, to pain on a touch of the knees and ankles. The rest of the clinical exam was unremarkable.

Radiographs of the hands and wrists and chest radiograph were normal. The patient was diagnosed because it does not with the results of cell count, biochemical tests, RF, or anti-CCP[3], as he had symmetrical polyarthritis in small and large joints, morning stiffness, in addition to a high level of acute phase reactant.

The patient was treated initially with prednisone 20 mg/day and 10 mg/week methotrexate, which was quickly escalated to a dose of 15 mg/weekly, with no response after 3 months of treatment. She was subsequently started on antitumor necrosis factor inhibitors, but the follow-up visit after 6 months showed persistent symptoms. Alternative anti-TNF inhibitors were tried with no improvement. Serum calcium, uric acid, and creatinine remained normal during the time of rheumatoid arthritis (RA) treatment. As a result, serum protein electrophoresis and urine protein electrophoresis were performed. Interestingly, the

HIGHLIGHTS

- Multiple myeloma is a malignant plasma cell proliferation producing large numbers of monoclonal immunoglobulins.
- We report a case of a 54-year-old female who presented with symmetrical polyarthritis and was misdiagnosed with rheumatoid arthritis.
- We report this unusual initial presentation with a review of several cases in the literature describing similar presentations.

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Figure 1. Show synovitis of the second through fifth metacarpophalangeal and proximal interphalangeal joints of hands, wrists, and elbows.

electrophoresis identified a small paraprotein band (2 g/l), and a large amount of free kappa light chains in both the serum and the urine (8.8 mg/l), and serum protein electrophoresis was positive for M-band.

The patient was then referred to the hematology department for further evaluation and underwent a bone marrow biopsy, which was positive for more than 24% plasma cells, as well as being Congo red stain negative, findings consistent with MM.

FISH analysis was positive for monosomy 13 in 88% of the cells. The patient then started treatment for MM with bortezomib and dexamethasone. Six-month follow-up showed complete resolution of arthritis of the hands, wrists, elbows, knees, and ankles. Her MM remained quiescent with chemotherapy, and the patient did not require a bone marrow transplant.

Our study is compatible with the surgical case report (SCARE) guideline checklist[4].

This case is submitted on the research registry dashboard[5].

Discussion

MM is a cytogenetically heterogeneous, plasma cell proliferative disorder, which can produce a monoclonal immunoglobulin[1]. Typical MM symptoms include anemia, bone pain, hypercalcemia, and renal failure[1,2]. The incidences of presenting symptoms of MM are bone pain (58%), fatigue (32%), pathologic fracture (26 to 34%), weight loss (24%), paresthesias (5%), and fever (0.7%)[6,7], as in our case. Rare presenting symptoms of MM can cause a delay in treatment and lead to unfavorable outcomes[6]. Our case is unusual initial presentation of MM was as inflammatory arthritis. The diagnosis is made depending on clinical and laboratory findings (Tables 1, 2). Our diagnosis was compatible with the mentioned criteria.

Table 2

The diagnosis criteria, evaluation, and staging of MM

Diagnostic criteria
Diagnosis of myeloma
At least 10% clonal bone marrow plasma cells
Serum or urinary monoclonal protein
Myeloma-related organ dysfunction (CRAB criteria)
Hypercalcemia (serum calcium >11.5 mg/dl [2.88 mmol/liter])
Renal insufficiency (serum creatinine >2 mg/dl [177 μmol/liter])
Anemia (hemoglobin <10 g/dl or >2 g/dl below the lower limit of the normal range)
Bone disease (lytic lesions, severe osteopenia, or pathologic fracture)
Diagnostic evaluation
Diagnosis
Medical history and physical examination
Routine testing: complete blood count, chemical analysis with calcium and creatinine, serum and urine protein electrophoresis with immunofixation, quantification of serum and urine monoclonal protein, measurement of free light chains
Bone marrow testing: trephine biopsy and aspirate of bone-marrow cells for morphologic features; cytogenetic analysis and fluorescence in situ hybridization for chromosomal abnormalities
Imaging: skeletal survey, magnetic resonance imaging if skeletal survey is negative
Prognosis
Routine testing: serum albumin, β_2-microglobulin, lactate dehydrogenase
Staging
International Staging System
Stage I: serum β_2-microglobulin <3.5 mg/liter, serum albumin ≥3.5 g/dl
Stage II: serum β_2-microglobulin, <3.5mg/liter plus serum albumin <3.5 g/dl; or serum β_2-microglobulin 3.5 to <5.5 mg/liter regardless of serum albumin level
Stage III: serum β_2-microglobulin ≥5.5 mg/liter
Chromosomal abnormalities
High-risk: presence of t(4;14) or deletion 17p13 detected by fluorescence in situ hybridization
Standard-risk: t(11;14) detected by fluorescence in situ hybridization

Table 1

Laboratory data

White blood cells	10 000/mm	ast	16 mg\dl
Hemoglobin	9.3 g/dl	ur	24 mg\dl
C-reactive protein	38 mg per liter (reference value <6)	cr	0.8 mg\dl
Erythrocyte sedimentation rate	50 mm per hour (reference range 0–20).	Tsh	0.7 μ (reference range 00.3–5.5)
Alt	12 mg\dl	ca	11.3 md\dl
Uric acid	4	urinalysis	Normal without proteinuria
Rheumatoid factor (RF)	Negative	ana	Negative
(anti-CCP)	Negative	KLM	Negative
Anca	Negative	hepatitis B panel	Negative
Hepatitis C antibody	Negative	QuantiFERON-TB Gold test and angiotensin-converting enzyme were negative	Negative

We searched the PubMed literature from 1990 to 2023 and found only 12 cases that were similar to or closely related to our case. All patients were seronegative. First, the shoulder, hand, and knee joints are most affected[10]. Two patients who suffered from symmetrical polyarthritis simulating RA. The acute phase response was almost within normal limits, and autoantibodies including rheumatoid factor were negative. Both of them were diagnosed as having amyloid arthropathy (AmyA) secondary to kappa MM based on the deposition of κ-light chain-immunoreactive amyloid in biopsied tissue and Bence Jones protein in the urine[8] and one patient had sacroiliitis[9]. Four patients had amyloidogenic MM[11]. Wang *et al*.[13] reported a 74-year-old man with a history of hypertension presented to the rheumatology department with polyarticular swelling and tenderness and through tests, it was found that he had MM. Ardalan and Shoja[12] reported a patient who initially presented with polyarthritis and rapidly progressive renal failure. Through our in-depth review we noted that the hand and wrist joints were most affected in patients with MG-like RA and all patients were RF-negative. It is worth noting that anti-CCP antibodies had not yet been discovered at the time and were therefore not mentioned in the old regulations.

Conclusion

This case was misdiagnosed due to delayed treatment of this malignant tumor due to the atypical manifestations of MM seronegative RA. Lack of response to RA treatment should prompt physicians to reconsider the initial diagnosis and consider alternative diagnoses like malignancy. Better differential diagnostic observations in serious diseases such as MM are important and should be performed more frequently in future practice.

Ethical approval

This case report was approved by The Ethical approval was given by the Ethical Committee of the Faculty of Medicine, Damascus University (N: kd 336,2023).

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

M.K.: literature review, manuscript writing and editing, final manuscript review and approval, and clinical follow-up; T.D., G.H., Y.H.R.T.: obtaining informed written consent, clinical follow-up, manuscript writing, and approval of the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: Maysoun Kudsi.
2. Unique identifying number or registration ID: 10108.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-theregistry#home/.

Guarantor

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Data availability statement

Datasets generated during and/or analyzed during the current study are publicly available, available upon reasonable request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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