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CASE REPORT

Early Onset Multiple Myeloma with an Unusual Presentation of Inflammatory Arthritis: A Case Report

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ABSTRACT

Introduction: Multiple myeloma (MM) is plasma cell neoplasm affecting persons over the age 60. Less than 2% of the cases occur below the age 40. MM accounts for about 1 % of all cancers and slightly more than 10 % of hematologic malignancies in the United States (US). It typically has one or more of the symptoms in the acronym CRAB (hypercalcemia, renal failure, anemia, bone pain). Rare symptoms, like joint involvement may cause significant delays in treatment and adverse outcomes.

Case Presentation: A young 38-year-old female presenting with an unusual presentation of inflammatory arthritis before the diagnosis of MM with 50% plasma cells on bone marrow biopsy.

Conclusion: Atypical presentation of MM challenged physicians and caused a delay in treating this life-threatening malignancy. Lack of response to treatment with rheumatoid arthritis (RA) should encourage us to re-evaluate the initial diagnosis and consider alternatives. Evaluating patients suspected of having MM in a timely manner is critical since a significant diagnostic delay has been associated with a negative impact on the progression of the disease.

Keywords: Multiple myeloma; rheumatoid arthritis; delayed diagnosis.

INTRODUCTION

MM is a plasma cell neoplasm that develops monoclonal antibodies. It typically has one or more of the symptoms in the acronym CRAB (hypercalcemia, renal failure, anemia, bone pain) [1]. Myeloma is usually diagnosed in patients over 40 years of age.MM accounts for about 1 % of all cancers and slightly more than 10 % of hematologic malignancies in the United States (US) [2]. The annual incidence in the US is about 4 to 5 per 100,000. A similar incidence has been reported in the South Thames area of the United Kingdom and in Europe in general [3-5].

Evaluating patients suspected of having MM in a timely manner is critical since a significant diagnostic delay has been associated with a negative impact on the progression of the disease [1].I will present a rare case of a young female presenting with an atypical presentation of MM in the form of inflammatory polyarthritis. A timeline of the patient's medical history and course of care is described in Table 1.

PATIENT INFORMATION

A 38-year-old female was referred to the rheumatology clinic for evaluation of arthralgia of the hands, wrists, and elbows. The patient's symptoms started 12 months prior and gradually worsened. The patient had swelling of the hands and wrists, difficulty making fists, as well as morning stiffness lasting more than sixty minutes. She denied any constitutional symptoms such as fever, weight loss, decreased appetite, or night sweats. The patient also denied any recent travel or sick contacts. Review of systems was negative for alopecia, dry eyes, dry mouth, mouth ulcers, and skin rash. She never smoked or consumed alcohol. Clinical exam revealed normal vitals, with normal head, neck, cardiopulmonary, and abdominal exams. No lymphadenopathy or skin bruises were observed. No abnormalities in musculoskeletal exam. Laboratory data at that time showed white blood cells of 10,000/mm, hemoglobin of 9.7 g/dl, hematocrit of 30.9%, and erythrocyte sedimentation rate (ESR) of 60 mm per hour. Laboratory tests of liver function, renal function, thyroid function, serum uric acid, calcium, and urine analysis were normal. Other normal tests included antinuclear antibody (ANA), rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP) antibodies, hepatitis B panel, hepatitis C antibody, and angiotensin-converting enzyme. The patient was diagnosed as seronegative rheumatoid arthritis and treated initially with prednisone, methotrexate and sulfasalazine with mild

improvement. Six months later, a follow-up visit showed persistent symptoms with appearance of bilateral pitting lower limb edema. Further workup included 24-hour urinary protein estimation which showed one gram proteinuria. She was diagnosed as lupus nephritis and started azathioprine and hydroxychloroquine, in addition to corticosteroids with stoppage of methotrexate and sulfasalazine. 1 month later, she was admitted to our hospital with persistence of symptoms associated with appearance of low back pain.

She reevaluated again by history, there was generalized bone ache, she denied any constitutional symptoms. There was no hematuria, oliguria or skin rash.

CLINICAL FINDINGS

Clinical examination was unremarkable.

DIAGNOSTIC ASSESSMENT

Investigations showed white blood cells of 9,000/mm, hemoglobin of 6.7 g/dl, hematocrit of 23.2%, MCV of 65 fl, platelets of 440,000/mm, serum total protein of 9.73 gm/dl, serum albumin of 2.93 gm/dl, serum calcium of 8.2 mg/dl with corrected calcium of 9.2 mg/dl, microalbuminuria of 30.59 mg/gm, C-reactive protein of 5 mg per liter, and ESR of 90 mm per hour. Thyroid function test, serum uric acid, renal function test, and urine analysis were normal. Other normal tests included chest x ray, pelviabdominal ultrasound, ANA, RF, anti-CCP antibodies, hepatitis B panel, and hepatitis C antibody. Bone survey was negative for any lytic or blastic lesions. As a result, serum protein electrophoresis (SPEP) was sent. Interestingly, SPEP was positive for M-band and showed decreased albumin, increased in alpha 1, alpha 2, beta 2 and gammaglobulin with sharp peak in gamma region. The patient was then referred to the hematologist for further evaluation and underwent a bone marrow biopsy, which was positive and showed hypercellularity due to infiltration by abnormal plasma cells; they were patchy in distribution and constitute about 50 % of the marrow intertrabecular spaces, findings consistent with MM as shown in figure 1. Immunostaining of the biopsy was CD 138 positive as shown in figure 1. Serum immunotyping showed monoclonal gammopathy IgG Kappa.

THERAPEUTIC INTERVENTIONS AND FOLLOW-UP

The patient started treatment for MM (bortezomib, dexamethasone and cyclophosphamide). Two-month follow-up showed significant improvement in symptoms.

Table 1: Timeline of Patient's Medical History and Course of Care

Relevant Medical History				
A 38-year-old female with history of arthralgia of the hands, wrists, and elbows. The patient's symptoms started 12 months prior and gradually worsened. The patient had swelling of the hands and wrists, difficulty making fists, as well as morning stiffness lasting more than sixty minutes. She denied any constitutional symptoms such as fever, weight loss, decreased appetite, or night sweats. The patient had no past history of medical or surgical diseases.				
Patient Visits	**Chief Complaints**	**Laboratory Biomarker**	**Diagnostic Significance**	**Recommendations and Interventions**
Visit 1: 11/2018	Arthralgia and swelling of the hands, wrists, and elbows, morning stiffness	Normal apart from microcytic anemia	Seronegative rheumatoid arthritis	prednisone, methotrexate and sulfasalazine
Visit 2: 05/2019	Persistent symptoms with appearance of bilateral pitting lower limb edema	Normal apart from anemia and nephritic range proteinuria	lupus nephritis	prednisone, azathioprine and hydroxychloroquine
Visit 3: 06/2019	Persistent symptoms associated with low back pain.	Positive SPEP for M-band, positive bone marrow biopsy (50 % plasma cell), positive Immunostaining of the biopsy for CD 138	Multiple myeloma	Bortezomib, dexamethasone and cyclophosphamide
Visit 4: 08/2019	Improvement of symptoms		Multiple myeloma	Continue treatment (Bortezomib, dexamethasone and cyclophosphamide)

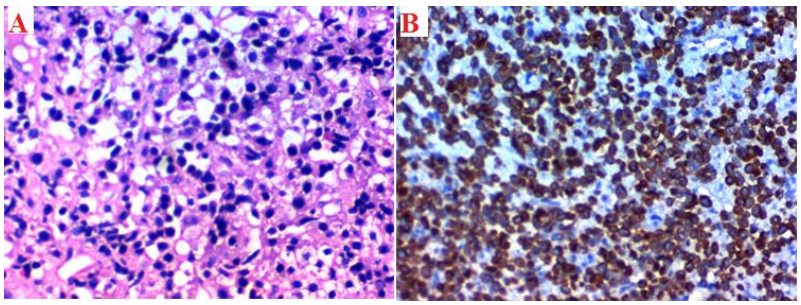

Fig 1: (A) Section of plasma cell myeloma showed malignant plasma cells (H&E x400) (B) Section of plasma cell myeloma stained with CD138 showed positive membranous stain (IHC x400)

DISCUSSION

MM is usually diagnosed after age 40. Under this age, only less than 1% of cases are diagnosed and the median age of diagnosis is about 70 years old[6].The incidences of MM symptoms are bone pain (58%), fatigue (32%), pathological fracture (26% to 34%), weight loss (24%), paresthesia (5%), and fever (0.7%) [7].Rare symptoms of MM, such as joint involvement that is usually an oligoarthritis or a rheumatoid-like polyarticular pattern, may cause significant delays in treatment and lead to adverse outcomes [8].The initial rare presentation of MM as inflammatory arthritis was published before in many reported cases similar to our case. Molloy et al. in 2007 highlighted a case of erosive seronegative inflammatory arthritis in association with bilateral carpal tunnel syndrome as rare symptoms of MM [9]In 2009, Alpay reported two patients with symmetric polyarthralgias of the small joints of hands, wrists, shoulders, and temporomandibular joints, both diagnosed with MM with amyloid deposition seen on synovial biopsy [10]. More recently, Schoninger et al. in 2018 reported a case of 58-year-old male with symmetrical inflammatory polyarthritis and was diagnosed seronegative RA. The diagnosis of MM was made after further workup due to failing many RA treatments [11].

CONCLUSIONS

Our case represents an atypical presentation of MM mimicking seronegative RA which challenged physicians and caused a delay in treating life-threatening malignancy. Lack of response to treatment with RA should encourage us to re-evaluate the initial diagnosis and consider alternatives. Increased awareness of atypical symptoms of serious diseases such as MM among health care providers is important and should be promoted in future practice.

CONSENT

Written informed consent was obtained from the patient for publication.

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