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# The case report of multiple myeloma and symmetric seronegative polyarthrititis

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Multiple Myeloma (MM) is a malignant proliferation of plasma cells producing monoclonal proteins. MM may manifest as skeletal pain, pathological fractures, fatigue, anemia, infection, hypocalcemia, spinal cord compression or renal failure. Proliferating plasma cells are responsible for these clinical symptoms. Seronegative erosive poly/oligoarthrititis may be observed in patients with MM and other monoclonal gammopathies concurrently at the time of diagnosis, after the diagnosis or occasionally before it.

The patient admitted to hospital in May 2012 with the complaint of fatigue, polyarthralgia, limitation of hand joints' movements. Her physical examination revealed flexion contractures in elbows, fingers, knee, feet joints bilaterally. Laboratory examination revealed a sedimentation rate of 106 mm/h; rheumatoid factor (RF), C-reactive protein (CRP) and anti-cyclic citrullinated peptide (anti-CCP) was negative and anti nuclear antibody (ANA) tested by immunofluorescence technique was positive. The patient is considered and followed up as an inflammatory arthritis developed in MM process. The joint involvements were symmetric, erosive pattern and seronegative tested. The diseases with monoclonal gammopathies may lead to erosive polyarthrititis or oligoarthrititis so we should investigate the immunopathogenesis of arthritis process.

**Keywords:** Multiple myeloma - seronegative polyarthrititis – plasma cell dyscrasia.

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## ТАРАЛҒАН МИЕЛОМА МЕН СИММЕТРИЯЛЫҚ СЕРОНЕГАТИВТІ БУЫН ҚАБЫНУЫНЫҢ КЛИНИКАЛЫҚ ЖАҒДАЙЫ

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Таралған миеломалар (ТМ) – моноклоналды ақуыздарды бөліп шығаратын қан сарысуы жасушаларының қатерлі көбеюі. ТМ клиникалық көріністері көп, ол буындардағы ауырсыну синдромымен, патологиялық сүйек сынуымен, шаршандықпен, қаназдықпен, әр түрлі жұқпалармен, гипокальциемиямен, жұлын компрессиясымен және бүйрек жетіспеушілігімен көрініс табады. Бұл клиникалық белгілердің пайда болуына қан сарысуының пролиферацияланған жасушалары жауап береді. Сонымен бірге ТМ бар науқастарда серонегативті эрозиялық поли/олигоартрит байқалуы мүмкін.

Біздің науқасымыз 2012 жылдың мамыр айында ауруханаға шаршандық, полиартральгия, саусақ буындарының қимыл қозғалысының шектелуі секілді шағымдармен түскен болатын. Физикалық тексеру кезінде науқаста шынтак, тізе, қол мен аяқтың саусақ буындарының екіжақты контрактурасының бар екені байқалды. Зертханалық тексерулер барысында ЭТЖ-ның 106 мм/сағ. дейін жоғарылағандығы және ревматоидты фактор, С-реактивті ақуыз, анти-КПК көрсеткіштерінің теріс, ал АНА көрсеткішінің оң екендігі анықталды. Бұл жағдай ТМ нәтижесінде болған артрит ретінде қарастырылды. Буындардағы эрозиялық зақымданулар симметриялық түрде болды. Моноклоналды гаммапатиялармен болатын аурулар серонегативті эрозиялық поли/олигоартриттерге әкелуі мүмкін. Сондықтан буын қабынуының иммуногенезін зерттеген жөн.

**Маңызды сөздер:** таралған миелома – серонегативті полиартрит – қан сарысуы жасушаларының дискразиясы.

## КЛИНИЧЕСКИЙ СЛУЧАЙ МНОЖЕСТВЕННОЙ МИЕЛОМЫ И СИММЕТРИЧНОГО СЕРОНЕГАТИВНОГО ПОЛИАРТРИТА

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Множественной миеломы (ММ) – это злокачественное размножение плазматических клеток, продуцирующих моноклональные белки. Клинически ММ может проявляться суставным болевым синдромом, патологическими переломами, усталостью, анемией, инфекциями, гипокальциемией, компрессией спинного мозга или почечной недостаточностью. За эти клинические симптомы отвечают пролиферирующие плазматические клетки. Также у пациентов с ММ может наблюдаться серонегативный эрозивный поли/олигоартрит.

Наш пациент госпитализирован в мае 2012 года с жалобами на усталость, полиартралгию, ограничение движений в суставах кистей рук. При физическом осмотре выявлены двухсторонние контрактуры локтевых, коленных суставов, кистей рук и ног. Лабораторные исследования показали следующие данные: СОЭ - 106 мм/ч; ревматоидный фактор, С-реактивный белок и анти-КПК были отрицательными, АНА были положительными. Данный случай рассматривался как воспалительный артрит вследствие ММ. Эрозивные поражения суставов были симметричными. Заболевания с моноклональными гаммапатиями могут привести к серонегативным эрозивным поли/олигоартритам. Поэтому необходимо исследовать иммунопатогенез артрита.

**Ключевые слова:** Множественная миелома – серонегативный полиартрит - дискразия плазматических клеток.

## Introduction

Multiple myelom (MM) is malign proliferation of the plasma cells that produce monoclonal protein. It forms 10% of all hematological malignities. It is the most common malign neoplasm of the bone marrow. Besides its clinical signs as bone pain, pathological fractures, asthenia, anemia, infection (mostly pneumococcal), hypocalcemia, spinal cord injury or renal impairment, it is generally diagnosed with blood examinations done for unrelated problems. The plasma cell proliferation that increases in bone marrow is responsible of the clinic signs. 1/3 of the patients are diagnosed after pathological fracture. 2/3 of the patients complain about bone pain. Nonspecific constitutional complaints caused by hyperviscosity and hypercalcemia may be seen. Lumbago, weakness and sense disorder in extremities should be warning for spinal cord injury. Spinal cord injury may be related to plasmocytoma or vertebrae pathologic fracture.

For diagnosis, 10% and above monoclonal plasma cell increase in bone marrow or/else end organ injury associated plasmocytoma and underlying plasma cell disorders are needed. Final diagnosis is done with biopsy of bone marrow and serum

protein electrophoresis.

Our case showed erosive arthritis clinic in symmetric seronegative pattern with MM. We examined the relation between these two clinic entities with literature review.

## Case

B Our case appealed on May 2012 with complaints of asthenia, artralgia, limitation of movement on hand joints. In 2003, She was diagnosed with MM at outer center, with complaints of asthenia and anorexia. In her history; we learned that in 2010, arthritis had developed on hand, wrist and elbow joints bilaterally; similar complaints had developed on feet, ankle and knee joints 3 months before she comes here. In 2010 the patient was started to zolendronic acid treatment for 6 months. Increase in thoracic kyphosis and costocondral sensitivity was existing in locomotor system examination. Flexion contracture was diagnosed in both elbows and hand joints.

There was limitation of movement in patient's both hands, wrists, elbows, knees and feet with soft tissue hypertrophy. She has no nail and skin symptoms. (Image 1,2,3,4).



**Image 1-** Both hands and wrist



**Image 2-** Flexion contracture in left elbow



**Image 3-** Hypertrophy of soft tissue in both knees



**Image 4-** Hypertrophy of soft tissue in both ankles

In conventional radiographies; we diagnosed cortical erosions in hand metacarpophalangeal (MCP) joints, proximal interphalangeal (PIP) joints and intercarpal joints and symmetric

narrowing in interarticular space. Loss of length in thoracic vertebrae in spinal graphy and locally osteolythic lesions showed in pelvic graphy is showed (Image 1,2,3,4).



**Image 1-** Anteroposterior view of hand and wrist: symmetric intraarticular narrowing and local cortical erosions are seen in intercarpal joints and MCP, PIP



**Image 2-** Anteroposterior view of shoulder: no lesion seen in clavicle and humerus bones



**Image 3-** Lateral view of thoracolumbar: loss of length in vertebrae and kyphosis is seen



**Image 4 -** Anteroposterior view of pelvis: lytic lesions are observed in iliac crest

There was normochrom normocytic anemia (Hb:9.7 gr/dl, MCV:89.9), increase of blood urea (BUN):64 mg/dl (10-50) and reverse in albumin/globulin ratio with laboratory examination (alb:3.6 g/dl, glob:4.8 g/dl).

While rheumatoid factor (RF) and C-reactive protein (CRP) value is negative in the serologic evaluation, sedimentation value is measured as: 106 mm/h. In urinalysis 30gr/dl protein is found. While anti-CCP value is negative, anti-nuclear antibody (ANA) value that is examined with immunofluorescent technique is two positive tested. Synovial membrane analysis couldn't be practiced because the patient hasn't active arthritis. All examined abdomen ultrasonography (USG) is normal. With the measurement of spinal DEXA (dual X-ray absorptiometer) total t score:-2.6, z score:-0.5 with osteopenia is determined.

Our patient is evaluated as inflammatory joint disease that developed in MM process. Joint involvement is erosive and seronegative. It is very similar to rheumatoid arthritis (RA) clinic. Negativity of anti-CCP and RF, absence of rheumatoid nodule despite erosive progress we excluded RA. Even tenosynovitis in hand finger flexor tendon and PIP, MKP joints limitation of movement seemed like sclerodactyly in clinic; there was no skin thickening in hand and face of the patient also there was no brown pigmented lesions, this is why we excluded scleroderma, oftenly with Raynaud phenomenon characterized, as our pre-diagnosis. Likewise there was no internal organ involvement.

We examined the patient in the aspects of other connective

tissue diseases that may cause inflammatory arthritis (Sjogren syndrome, polymyositis, systemic lupus erythematosus etc...). We also examined our patient in terms of other destructive joint pathologies. There were seen locally osteolytic lesions. We didn't determine lytic or sclerotic lesion in long bones (humerus and femur). No focal symptom associated to spinal cord injury was found in the neurologic examination. No destructive vertebral pathology was seen in the conventional radiographies. We gave our patient TENS (transcutaneous electrical nerve stimulation) and exercise program for joint movement limitations and pain treatment. We provided vertebral steel brace corset and double cane support to prevent pathologic fractures. Patient's pain decreased from 8 cm to 4 cm according to VAS (visual analogue scale). We thought that immunogenetic process of MM can activate inflammatory synovitis cascade.

## Discussion

Besides clinical signs in MM like pathological fractures, bone pain, fatigue, anemia, infection (especially pneumococcal), hypocalcemia, spinal cord compression or renal insufficiency may be revealed; it is usually determined randomly. Patients can refer to clinic with the complaints of nonspecific constitutional symptoms cause of hyperviscosity and hypercalcemia. Low back pain, weakness and numbness of the extremities should be warning in terms of spinal cord compression. Spinal cord compression may lead to pathological fractures of the vertebrae

or plasmocytoma. Such neurologic findings; carpal tunnel syndrome, meningitis, peripheral neuropathy may rarely seen in clinic process.

Pathological fractures and sensitivity of bones due to focal lytic lesions are oftenly seen. Typical radiological appearance is lytic lesions. The other types of bone lesions include changes in sclerotic, porotik and rarely (3%) lythic-sclerotic pattern. Extrameduller plasmocytoma (soft tissue masses consisting of plasma cells) can be seen all over the body. Also, hepatosplenomegaly and cardiomegaly can be seen. In some cases, amyloidosis may contribute to clinic. The physical signs due to amyloidosis are bilateral swelling of shoulders, makroglossus, skin lesions, peripalpebral purpura etc... [2]. MM rarely comes with signs of arthritis. In cases related to arthritis associated with monoclonal gammopathies, joint involvement develops simultaneously or a period of time after diagnosis. Arthritis pattern is, similar to RA, symmetric polyarthritis or oligoarthritis; unlike RF is negatively tested.

Three pathogenetic pathways can cause joints symptoms of MM. These are erosive arthritis caused by malignant plasmocytes; arthritis or trap neuropathies caused by precipitating paraproteins or amyloid proteins. It is observed that paraproteins that cause arthritis clinic are frequently in monoclonal pattern [3,4].

In patients with MGUS (unknown-featured monoclonal gammopathies) arthritis are seen in both sexes equally and RF tested negatively. Also, in cells lead to arthritis, there was no heavy chains detected, besides 89% light chain kappa have been identified [5,6]. In arthritis process it was thought that kryopresipitat paraproteins activate inflammatory cascade in synovial fluid by crystallization [7,8].

In addition, amyloid proteins in plasma cells dyscrasia are also, similar to paraprotein kryopresipitat in synovium, can cause carpal tunnel syndrome by accumulinating.

AL amyloidosis that seen in MM can cause joint involvement similar to RA. It is find out that symptoms in acute phase responses are similar to RA while RF is negatively tested. In chronic polyarthralgia systemic AL amyloidosis is an important differential diagnosis. Rarely, plasma cell dyscrasia may bring up with atypical joint involvement. Therefore, by immunohistochemically and cytogenetically plasma cell dyscrasia should be investigated in patients come with atypical

arthritis clinic elderly [9,10].

Result of studies, arthritis clinic has been regressed with the chemotherapeutic agents we give in MM treatment. Bisphosphonates that is given to prevent MM and skeletal complications in solid bone tumors are useful. Zolendronik acid is a bisphosphonate commonly used for this purpose. It is revealed that the zolendronic acid treatment is useful for pathologic fracture, cord compression and mortality. Especially when the treatment lasts for 18 months [11,12].

It should be kept in mind that MM disease can be seen as comorbid in patients with RA. B cell dyscrasia may occur at 3.8% frequency in long-term RA patients. But these cases are long-termed (at least 10 years) and RF positively tested. IL-6 cytokine plays an important role in terms of pathogenetic in both cases. This is why Tocilizumab treatment can be useful in these cases existing togetherly [13].

In literature examination some MM cases show symptoms similar to scleroderma in atypical pattern. It is thought that processes associated with MM may cause scleroderma-like lesions. Fibroblast activation that cause tissue fibrosis in related organs plays a role in scleroderma pathogenesis. Immune system activation associated with endothelial cell apoptosis, dysfunction and activation of fibroblasts result skin and internal organ fibrosis. Fibrotic process is sustained autonomous autocrine by activated fibroblasts. Raynould phenomenon is the earliest symptom in systemic sclerosis. Musculoskeletal symptoms are oftenly seen. Early symptoms include arthralgia, myalgia and in some patients inflammatory arthropathy may occur. The most commonly involved joints are the PIP, MCP, wrist and ankle joints. Progressive skin lesions can lead to flexion contractures of joints. Muscle weakness and fatigue symptoms are frequently seen symptoms. As well as myopathy caused by fibrosis in muscles may occur; polymyositis clinic may be added too. In addition, many organs, especially in genitourinary gastrointestinal tracts, can be involved in systemic sclerosis [14].

As a result; we should remind that plasma cell dyscrasia may induce erosive polyarthritis or oligoarthritis clinic, so immunogenetic process in arthritis clinic should be disclosed. Our case of MM with symmetric erosive and seronegative inflammatory polyarthritis has been a guide between these two entity for us. To sum up; in elderly atypical oligo/polyarthritis clinic should remind us for plasma cell dyscrasia.

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