Photoclinic

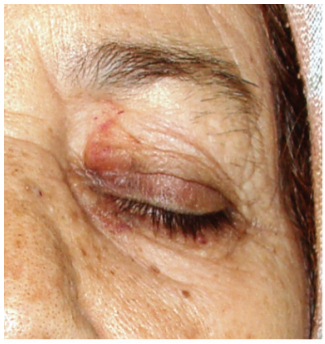

Figure 1. Raccoon eye in a 65-year-old lady.

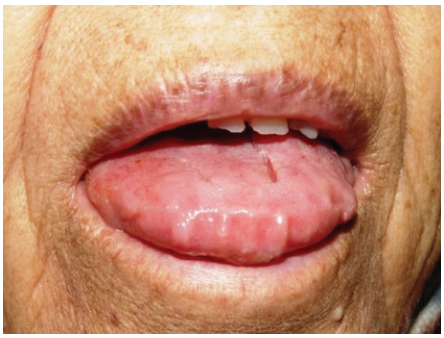

Figure 2. Macroglossia in the patient.

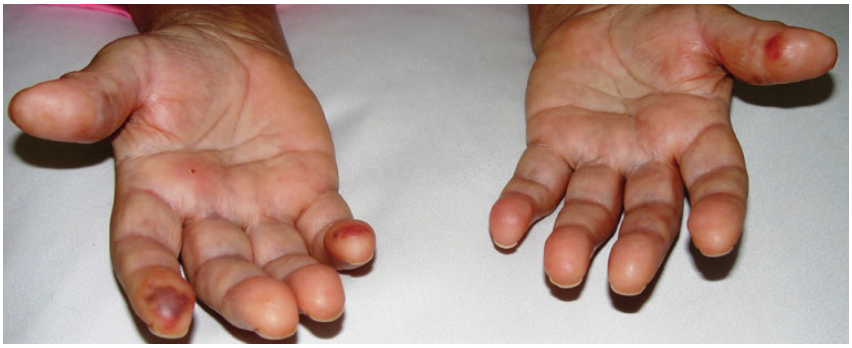

Figure 3. Diffuse bilateral hand arthritis (diffuse erythema and swelling) as well as vasculitic lesions on distal pulp of fingers.

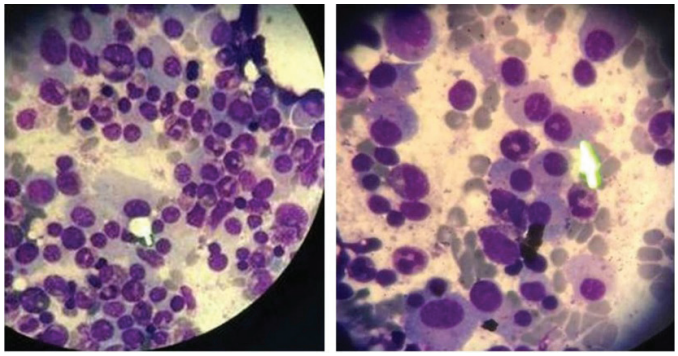

Figure 4. Wright-Giemsa staining of bone marrow aspirate smear of the patient showing plasma cell infiltration (Hematoxylin and Eosin; X100).

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A 64-year-old lady presented to the rheumatology clinic with sudden onset of painful diffuse bilateral hand arthropathy since a week ago. She complained of impaired function and burning sensation of the hands which caused her trouble in sleep. She also reported a gradually increasing fatigue and mild intermittent pain of hand joints in the past year, but with no definitive diagnosis.

On physical examination, she was pale and had ecchymosis around her left eye with no history of trauma (Figure 1). Vital signs were in normal range. In the head and neck region, tenderness and marked enlargement of her shoulder girdles were evident. In addition, three ulcers in the oral cavity and macroglossia were found (Figure 2). The most significant clinical finding of the patient was diffuse bilateral erythema, swelling and tenderness in hands with limitation in movements as well as vasculitic-like lesions on distal pulp of the fingers (Figure 3). Tinel's and Phalen's tests were positive bilaterally consistent with carpal tunnel syndrome. The rest of musculoskeletal and other system organ examinations were unremarkable.

What is your diagnosis?
See the next page for diagnosis.

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Photoclinic Diagnosis: Puffy Hands as the Initial Manifestation of Multiple Myeloma

The clinical picture of the patient was suggestive of systemic amyloidosis. Nonetheless, musculoskeletal manifestations and vasculitic-like lesions especially in the patient's hand brought up other differential diagnoses, including small vessel vasculitis, neoplasm associated vasculitis, cryoglobulinemia, atypical chronic Raynaud's disease, hand-foot syndrome (palmar-plantar erythrodysesthesia), infectious palmar arthritis, systemic sclerosis, rheumatoid arthritis, seronegative arthritis, crystal-induced arthropathy, scleredema (Buschke disease) and polymyalgia rheumatica.

On complete blood count, severe hypochromic normocytic anemia was found (erythrocyte count = 2.6×10^6, hemoglobin = 7.7 mg/dL, MCV = 95.6 fl). In addition, the patient had an increased creatinine (1.7 g/dL), high erythrocyte sedimentation rate (51 mm/h) and 2+ proteinuria. Twenty-four hour urine collection documented a high urine protein (1.6 g). Serum protein electrophoresis showed 1 g/dL alpha 2 protein (15.5%) and 0.2 g/dL gamma protein (3.7%). Urine protein electrophoresis revealed a faint albumin band and also sharp band of low molecular weight proteins (Bence-Jones proteins). Other laboratory investigations on the basis of our differential diagnoses including serum cryoglobulin, anti-nuclear antibody profile, anti-nuclear cytoplasmic antibody and anti-phospholipid antibodies were normal. On plain radiography of hands, osteopenia, mild erosion and joint space narrowing were found. Bone mineral density test showed osteoporosis. Electromyography and nerve conduction studies confirmed entrapment neuropathy.

With respect to these findings, abdominal fat pad biopsy was performed and Congo red staining of amyloid on the sample showed apple-green birefringence in polarized light. Hence, AL amyloidosis was suggested for the patient. Subsequently, bone marrow aspiration and biopsy were performed and revealed uniformly appearing monotonous infiltrate of plasma cells with a percentage of 20%–25% (Figure 4), consistent with the diagnosis of multiple myeloma (MM).

Our active symptomatic MM patient was a good candidate for induction for hematopoietic stem cell transplantation; so, a combination regimen of bortezomib, cyclophosphamide, and dexamethasone was started. The patient responded favorably to the treatments and periorbital ecchymosis disappeared in 3 to 4 days. Hand arthritis and vasculitic lesions resolved gradually in 10 days. The patient was discharged from hospital after 2 weeks in good condition and was then referred to a transplant specialist.

Diffuse bilateral hand arthropathy, so-called puffy hands, is not a common clinical presentation. Identifying its underlying etiology might be a diagnostic challenge. There are a number of causes leading to diffuse puffy hands that clinicians should be aware of. Although uncommon, one of them is amyloidosis secondary to plasma cell dyscrasia. Only a few reports of arthropathy as the first or main clinical presentation and complaint of MM patients are available in medical literature.[1-3] MM usually manifests with bone pain, pathologic fractures, weakness, anemia, recurrent infections and hypercalcemia at first stages.[4] MM and other plasma cell dyscrasia can cause AL amyloidosis.[5] In this process, extracellular deposition of insoluble fibrils (amyloid) derived from light chain components of immunoglobulins occurs majorly within the connective tissue, musculoskeletal system, nervous system, kidney, liver and heart.[4,5] When these hydrophobic proteins accumulate and aggregate with other insoluble particles, balls of fragments stabilized by glycosaminoglycans and serum amyloid P will be produced, and hence, they will be protected againt proteolytic cleavage.

Amyloid arthropathy is not commonly seen in our daily practice. Any joint may be involved, but most frequently shoulders, hips, wrists and knees are affected.[3] The edematous appearance of limbs and other peri-articular structures can be the result of either direct accumulation of amyloid balls and consequently soft tissue thickening or inflammatory response to these insoluble fragments.[2,4,5] Moreover, in case of MM, plasmacytic infiltrations of synovium can cause tumoral arthritis.[2,3]

In addition to articular presentations, many MM patients including this case manifest with easy bruising, vasculitic lesions and ecchymosis (especially around the eyes giving the "raccoon-eye" sign) which are due to either amyloid depositions upon vascular walls and making them vulnerable to disruption, or deficiency of clotting factor X after binding to amyloid proteins.[4–6]

Reviewing this case history attracts our vigilance over plasma cell dyscrasia when evaluating patients with acute presentation of diffuse bilateral seronegative hand arthropathy.

Competing Interests

The authors have declared that no competing interests exist.

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