

Ultrasound findings in AL musculoskeletal amyloidosis

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Abstract

Systemic AL amyloidosis is one of the differential diagnosis of chronic musculoskeletal disease, especially when swollen and painful joints is associated with claw hands. Ultrasound evaluation is a good diagnosis tool, showing a characteristic joint and tendon involvement and assisting in guided biopsy procedure. We report a 55 year old caucasian woman, diagnosed for two years with RA without improvement under different DMARDs, admitted for fixed flexion contractures of both hands („claw hands”), worsening pain and swelling of small joints of hands and feet, elbows and shoulders. Pad shoulder sign and bilateral anterior wrist and elbow pads, macroglossia, thickened skin of fingers and ecchymotic rashes on forearm and around eyes were observed. Ultrasound examinations showed subdeltoid and bicipitoradial bursitis, presence of inhomogeneous hypoechoic material around bicipital tendons and tenosinovitis of the extensor tendons of the hand, and synovial thickening of elbow and shoulder joints. Complete analysis of the bone marrow biopsy and biopsy specimens from subacromial bursa were positive for AL amyloidosis.

Keywords: amyloidosis, ultrasound, bursitis, claw hands

Rezumat

Amiloidoza sistemică AL constituie un diagnostic diferențial important al bolilor inflamatorii articulare, mai ales atunci când durerea și tumefierile se însoțesc de contractura fixă a mâinii (aspectul de ghieră). Ecografia musculoscheletală aduce o contribuție importantă evidențiind modificări tendinoase și articulare caracteristice și ghidând obținerea biopsiei sinoviale. Prezentăm cazul unei femei de 55 ani, diagnosticată cu poliartrită reumatoidă în urmă cu doi ani, pentru care a urmat diferite tratamente, fără ameliorare și la a cărei simptomatologie (artrite ale articulațiilor mici și mari) s-a adăugat aspectul de mână „în ghieră”. La examenul obiectiv s-au evidențiat: macroglosie, echimoze perioculare, tegumente îngroșate la degete, tumefiere ca o periniță la nivelul coatelor, umerilor și regiunii anterioare a radiocarpului. Ecografia musculoscheletală a evidențiat bursită subacromio-subdeltoidiană și bicipito-radială, formațiuni inhomogene, hipocogene în jurul tendonului bicepsului, tenosinovită a extensorilor mâinilor, îngroșarea sinoviei cotului și umărului. Investigațiile clinice și paraclinice, incluzând examenul histopatologic al țesutului obținut biptic din bursa subacromială au stabilit diagnosticul de amiloidoză AL.

Cuvinte cheie: amiloidoză, bursită, ecografie, mâna în ghieră

Introduction

Immunoglobulin-related amyloidosis is a rare disorder in which secreted monoclonal immunoglobulin

forms fibrillar deposits (in most cases monoclonal light chain fragments) in organs and tissues. Kidney, skin, heart, liver involvement is common, but musculoskeletal deposition is not so frequent [1,2,3]. In this case report, we describe a patient with AL systemic amyloidosis with the main complaints in the musculoskeletal system, without other systemic signs at the onset of disease.

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Case Report

A 55 year old lady diagnosed two years ago with rheumatoid arthritis (symmetrical polyarthralgias, morning stiff-

ness and decreased motion in both shoulders) was referred to our department for the lack of therapeutic response to classic DMARDs and new onset of fixed flexion contractures of both hands. The patient reported pain and swelling in her wrists, elbows and shoulders, bilateral numbness of the thumb, index, radial half of the ring finger (consistent with carpal tunnel syndrome) and violaceous spots on her forearms and eyelids. Apart from these complaints, no other symptoms were noted. At the time of presentation, she was on methotrexate, hidroxicloroquine and nimesulide therapy.

Physical examination revealed fixed contractures of fingers („claw hands”), with thickening of the fingers’ skin, swelling of shoulders and anterior region of wrists and elbows with limited motion, positive Phallen’s sign, decreased grip strength on both sides, enlarged tongue with dental imprints, multiple small waxy nodules in a periorbital and perioral distribution, mixed with an ecchymotic rash around eyes and forearms (fig 1). Her cardiac, pulmonary and abdominal examination results were normal, with no enlargement of liver, spleen and peripheral lymph nodes.



Fig 1. Skin amyloidosis – multiple periorbital small waxy nodules mixed with ecchymotic rash – and claw hands

Routine laboratory tests showed no anemia (haemoglobin 12g/dl, haematocrit 35%), normal number of white cells (6,850/ mm³) and platelets (315,000/mm³), a normal erythrocyte sedimentation rate (13 mm/h) and normal C reactive protein level (0,5 mg/dl). Calcium, hepatobiliary parameters and renal indices in serum were within normal limits. Urinary tests showed proteinuria (0.630 g/24h) and a slightly positive test for Bence–Jones proteins. Autoantibodies including rheumatoid factor, anti-cyclic citrullinated peptide antibody, anti-nuclear antibody, anti-neutrophil cytoplasmic antibody were all negative. Serum immunoglobulins showed decreased values of all three lines: IgA (31 UI/ml, normal 60-240 UI/ml), IgG(90UI/ml, normal 90-220UI/ml), IgM (70 Ui/ml normal 70-250 UI/ml) and urinary protein electrophoresis with immunofixation detecting lambda chains. A bone marrow smear revealed plasma cell content of 10 % with no abnormal cells. Chest radiograph, abdomi-

nal ultrasonography, EKG and echocardiography did not find any abnormalities. Anteroposterior radiograph of both shoulders showed small irregular- shaped geodes of the humerus, with small calcifications proximal to great tuberosity on the left.

Assay of the synovial fluid from subacromial-subdeltoidian (SASD) bursa, evidenced a low number of mixed cells (polymorphonuclear and mononuclear leucocytes), with predominance of plasma cells, no crystals and positive Congo red stain of the centrifuged sediment.

Shoulder ultrasound depicted important distension of SASD bursa in all sections (anterior, posterior and lateral), with irregular and thickened walls. Hypochoic, inhomogeneous material appeared to surround the proximal brachial biceps tendon (fig 2). Despite the thickened biceps tendon sheath, there was not a clear involvement of the bicep tendon as well as rotator cuff tendons, both size and ultrasound structure being normal. A synovial enlargement with proliferated inhomogeneous hypochoic mass was found, but the power Doppler signal was absent.

Elbow ultrasonography found thickening of bicipitoradial bursa, with an important effusion and a heterogeneous mass within the bursa and joint space (fig 3).

Wrist ultrasound revealed well defined flexor tendons surrounded by a hypochoic, inhomogeneous mass which bulged the flexor retinaculum. The median nerve cross-sectional area in the carpal tunnel was enlarged bilaterally (fig 4).

Ultrasound guided needle biopsy of the right SASD bursa was performed. The examination of the biopsy

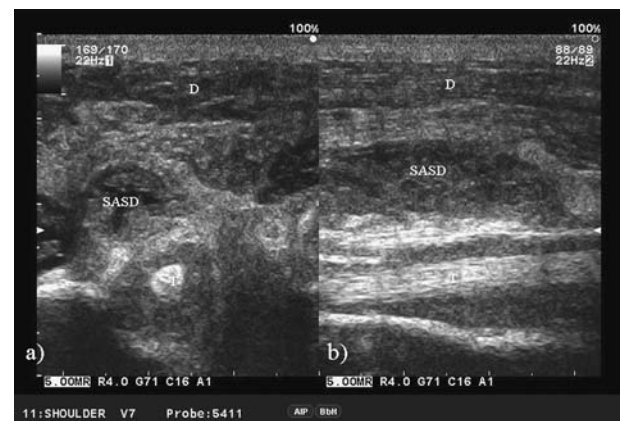


Fig 2. Transverse (a) and longitudinal (b) scan of the long head of biceps tendon: normal tendon (T) and synovial sheath filled with an hypochoic and homogeneous material, thickness of subacromial-subdeltoidian bursa (SASD) with inhomogeneous hypochoic mass within. D – deltoid muscle

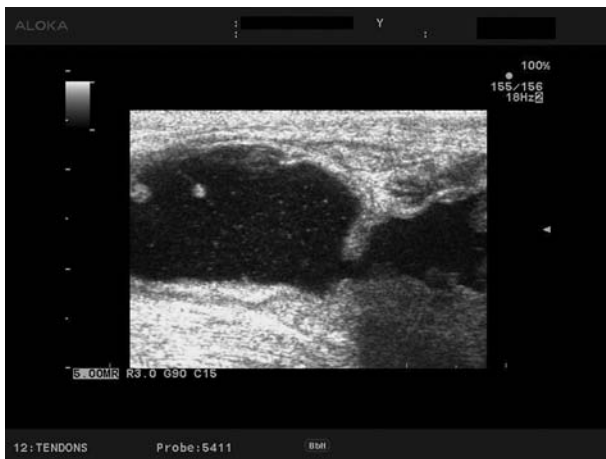


Fig 3. Longitudinal scan in the anterior part of elbow – bicipitoradial bursa with thick walls, filled with hypoechoic and inhomogeneous material.



Fig 4. Transverse scan of the carpal tunnel: swelling of the median nerve (sectional area 14mm²) (arrow), hypoechoic mass around flexor tendons, normal flexor tendons

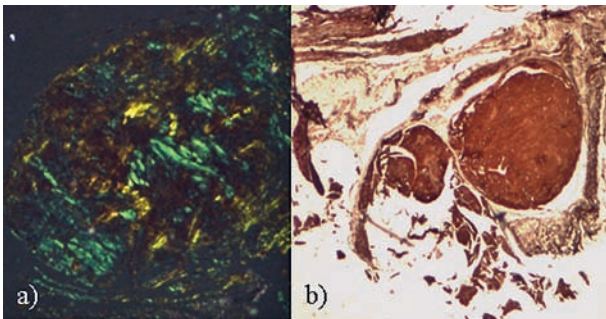


Fig 5. Immunohistochemistry images: a) specific staining with antibodies against lambda L chains proves the diagnosis of L chain – type amyloidosis; b) amyloid material stained with Congo red and viewed under polarized light appears bright green.

specimen disclosed very few plasma cells around the vessels, irregular broad bands and nodules of Congo red stain- positive fibrous material, which exhibited apple green birefringence under polarized light. By immunohistochemistry, the tissue material was stained by lambda- chain antibodies, confirming the diagnosis of AL amyloidosis (fig 5).

Investigations including urinary immunoelectrophoresis, bone marrow aspiration established the diagnosis of lambda- light chain amyloidosis with musculoskeletal, nervous, skin and renal involvement. Treatment consisted of melphalan and prednisolone for six months, followed by Bortezomib, without an improvement of symptoms, clinical findings and ultrasonographic aspect of joints after another six months.

Discussion

AL amyloidosis belongs to monoclonal gammopathies disorders, characterized by the proliferation of clonal plasma cells that secrete a monoclonal immunoglobulin. Organ and tissue involvement occurs due to tissue depositions of insoluble fragments of monoclonal light chains. The deposits contain immunoglobulin light (L) chains lambda or kappa or L – chains fragments. The diagnosis is dependent on histological studies of biopsy specimens, first of all Congo red staining and apple green birefringence under polarized light being characteristic for all types of amyloidosis: immunohistochemistry should be used to determine the type of amyloid [4].

From a clinical point of view, musculoskeletal involvement is rare, but when it happens, there are a few important clues that help the diagnosis. Symmetrical swelling of shoulders, the so – called “shoulder- pad - sign”, as well as the presence of atypical swollen joints- in our case the anterior surface of wrists and elbow (resembling with a wrist, respectively a elbow pads) and “claw hands “are characteristic [1]. The clinical picture of the presented patient resembled rheumatoid arthritis with symmetrical joint pain and swelling, morning stiffness, but with negative serology and without elevation of acute phase reactants. The musculoskeletal symptoms and signs are caused by amyloid deposits within the joints, bones, peritendinous structures and soft tissues.

A rigorous screening is required when AL amyloid diagnose is established in order to detect other potential organ involvement. In this case, renal and skin damage were found, but heart damage was not identified by EKG and echocardiogram. This is important because cardiac involvement is usually a determinant for prognosis in patients with AL amyloidosis [5].

Standard radiographs, computed tomography (CT) and magnetic resonance (MRI) are good tools for the evaluation of musculoskeletal involvement in both primary and secondary amyloidosis. Classic X-ray usually demonstrates irregular-shaped geodes rimmed with sclerosis in the affected bone (where amyloid deposition is present). In some cases CT finds diffuse infiltration of the muscle and bone [1] and MRI evidences low-intensity signals on both T1 and T2-weighted images in places where normal tissue is substituted by amyloid [2]. Scintigraphy with radiolabeled serum amyloid P component is a specific investigation which can provide a map of amyloid deposition in tissues [5].

Ultrasonography is a simple and reliable imaging modality for diagnosing the presence of amyloid in symptomatic patients, where clinical suspicion is formulated. The majority of the data has come from cases with musculoskeletal β_2 amyloidosis due to long-term dialysis. In our knowledge, this is the first case of an AL amyloid joint ultrasonography description. The findings include thickening of supraspinatus and biceps tendons (changes absent in the presented case), synovial thickening and the presence of hypoechoic masses around tendons and within bursas [6,7,8].

The bicipital tendon sheath was thickened, surrounded by a hypoechoic area with a "halo" aspect. The appearance is nonspecific because in the early stages the aspect could be confused with tendinosis [9]. Other ultrasound aspects of amyloid arthropathy such as synovial enlargement and effusion within the bursa, are found also in rheumatoid arthritis, chondrocalcinosis or polymyalgia rheumatica. These conditions should be ruled out. The absence of power Doppler signal in amyloid arthropathy could also help in the differential diagnosis.

Regarding the treatment of AL amyloidosis, chemotherapy regimens are similar to those used in multiple myeloma and the first therapy course is melphalan and

prednisone [5]. Bortezomib is a new drug indicated for AL amyloidosis. Unfortunately, despite this treatment in the presented case, the symptoms did not improve after 12 months and the general status worsened.

In conclusion, systemic AL amyloidosis rarely causes musculoskeletal symptoms which can be distinguished from other inflammatory conditions and ultrasonography could be a helpful tool in the diagnosis.

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