

Amyloidosis in a patient with confusing RA and PsA manifestation: a case report

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Amyloidosis is a rare condition that develops when an irregular protein called amyloid accumulates in the organs and interferes with their normal function. In conjunction with other disorders such as rheumatoid arthritis (RA) and psoriasis, amyloidosis may occur due to a chronic inflammatory process. With treatment of the underlying disease, amyloidosis can be addressed. Certain forms of amyloidosis can lead to life-threatening organ failure. In fact, it can involve the heart, kidneys, and nervous system. As the signs and symptoms can imitate those of more common illnesses, amyloidosis is sometimes ignored. Early diagnosis may help minimize additional injury to organs. Precise diagnosis is important, because based on the individual case, care differs greatly. Herein, we present a patient who referred to our hospital with some manifestations of RA and psoriatic arthritis (PsA) that were compatible with amyloidosis and discuss the treatment of this patient.

Keywords: Adalimumab, Amyloidosis, Psoriatic arthritis, Rheumatoid arthritis

Introduction

Amyloidosis is a heterogeneous condition caused by the deposition of harmful insoluble beta-sheet fibrillar protein aggregates in various tissues [1]. AA amyloidosis has an inflammatory mechanism that is reactive caused by chronic inflammation [2]. The worldwide prevalence of amyloidosis is estimated to be between five and nine cases per million patients per year [3]. Diagnosis is by clinical suspicion and confirmed by biopsy from the involved organ [4-5]. One diagnostic and defining characteristic of amyloidosis is the apple-green birefringence of amyloid on Congo red staining. Apart from that, the amyloid has an amorphous eosinophilic appearance as seen with hematoxylin and eosin staining [6]. In this case report, we present a patient with a confusing manifestation and a final diagnosis of amyloidosis.

Case presentation

A 45-year-old man was admitted to the rheumatology ward for swelling of the legs and ankles from a few months prior to admittance. He had a history of poly-arthritis from 5 years before that had started from the small joints of both hands and was symmetric; then his ankles and knees became involved. The patient was prescribed methotrexate, prednisolone, hydroxychloroquine, and sulfasalazine due to his rheumatoid arthritis diagnosis by another rheumatologist, but he wasn't using the medication regularly due to a lack of compliance. He was taking NSAIDs

arbitrarily for pain control. The disease course was frequently relapsing and remitting. The patient developed an increased number of scaling erythematous skin lesions (dry, raised, red lesions covered with silvery scales that were not tender or itchy) on his legs, knees, buttocks, and back from one year before this hospitalization. At the time of admission to Loghman Hospital, he had arthralgia with inflammatory pattern (morning stiffness, swollen and tender joints) in both knees and ankles, especially on the right side, and his skin lesions had progressed. He had exertional dyspnea (FCII) and edema, especially in both legs and the dorsum of both feet. There were no other symptoms. The patient had a past medical history of hypertension and took losartan 50 mg/d and prednisolone 10 mg/d, and he smoked 20 packs of cigarettes per year. In his familial history, a sister had psoriasis.

In the physical exam, we observed that the patient was obese, had scaling erythematous plaques on his legs, knees, sacrum, and back, but showed no nail change. Generalized edema especially in the lower extremities (3+ pitting edema), arthritis in the knees and ankles (prominent effusion in right knee), and edema in the dorsal side of the hands were also found. Other physical examinations were normal.

Vital signs were blood pressure: 140/90 mmHg; pulse rate: 90 beat/minute; respiratory rate: 17/minute; oral temperature: 37 °C

The patient’s laboratory data is presented in [Table 1](#). At the last check-up performed for the patient in another center about 3 months prior to this hospitalization, the

patient’s creatinine level was 0.7; at admission time, it had risen.

Table 1. patient’s laboratory data

| laboratory data | | | | | |
|-----------------|--------|---------------|----------|-------------------|----------------|
| Blood | | Blood | | Urine 24h | |
| WBC | 12.7 | calcium | 8.7 | 24 h U volume | 2800 ml |
| RBC | 4.75 | phosphor | 3/9 | 24 h U creatinine | 1366 |
| Hb | 12.7 | Total Protein | 5.7 | 24 h U protein | 7504 |
| HCT | 39.4% | Albumin | 2.1 | U/C | 100.000 E.coli |
| MCV | 82.95 | | | | |
| PLT | 413 | | | | |
| Neutrophil | 68.5 % | U/A | | | |
| Lymphocytes | 23.8 % | PH | 5 | | |
| Urea | 61 | Protein | 3+ | | |
| Cr | 1.4 | Glucose | negative | | |
| Na | 141 | Blood | 2+ | | |
| K | 4.7 | Ketone | negative | | |
| Uric acid | 9.1 | Nitrite | positive | | |
| TG | 161 | WBC | 2-4 | | |
| Cholesterol | 290 | RBC | 15-18 | | |
| HDL | 63 | Ep-cell | 3-5 | | |
| LDL | 187 | Bacteria | many | | |
| CRP | 74.1 | dysmorphic | not seen | | |
| ESR | 99 | RBC | not seen | | |
| | | Cast | not seen | | |

LFT was normal
viral markers
and PPD were
negative

Arthrocentesis was performed from the patient’s right knee that had significant effusion. The results of this procedure were: WBC: 50 cell/mm³ (PMN: 70 %); crystal: not seen; Smear and culture: negative.

Rheumatologic tests: C-ANCA (Anti-PR3), P-ANCA (Anti MPO), anti-GBM antibody, ANA, anti-ds DNA, anti-Ro, anti-La, C3, and C4, and CH-50 levels were normal. Anti-CCP-antibody was measured twice for the patient; the first result was 171.7 U/ml (up to 12), and the second was 207 U/ml (up to 5). RF level was 90.9 IU/ml (up to 20). In serum and urine protein electrophoresis, a poly-clonal pattern was observed.

X-rays from the axial and extremity bones were performed to assess joint changes. There were no changes in vertebrae. In the hand X-ray, only narrowing in joint spaces and no erosion were observed ([Figure 1](#)). Mild sclerosis was seen in the left sacroiliac joint ([Figure 2](#)). Abdominal sonography (due to the patient having proteinuria and elevated creatinine) showed only grade 2 fatty-liver and no other finding. Color-doppler sonography (due to edema) was performed on both lower extremities, and the results were normal. Echocardiography and lung CT scan (due to exertional dyspnea) were normal. The cutaneous lesion on the patient’s back was biopsied, and a psoriasiform reaction compatible with psoriasis was seen (section showed skin tissue with mounds of parakeratosis, psoriasiform acanthosis, aggregation of neutrophils in summit of parakeratosis and hypogranulosis, tortuous vessels, and moderate lymphocytic and few neutrophilic infiltration in superficial dermis).



Figure 1. Hand X-ray



Figure 2. Pelvic X-ray

The patient was started on methotrexate 10 mg weekly (low dose due to patient's obesity, fatty liver, kidney injury, and other complications), prednisolone 10 mg daily (because of previous consumption; we tapered it slowly), allopurinol 100 mg daily (for hyperuricemia), atorvastatin 20 mg daily (for cardiovascular risk management), furosemide 40 mg daily (for edema), and losartan 50 mg daily (for hypertension and proteinuria), and we discontinued NSAID (because NSAIDs can exacerbate kidney injury).

After UTI treatment with ciprofloxacin 500 mg twice daily for 5 days, a kidney biopsy was performed, and its results were "apple green birefringence" under polarized light in Congo red stain and strongly positive for amyloid A in IHC. At that time, a diagnosis of AA amyloidosis was made. We started adalimumab for the patient after a negative PPD, and in the patient's next visits the proteinuria was resolved (last U/A showed no protein at all), creatinine was decreased (last creatinine: 1 mg/dl), edema was decreased, arthritis in the knees and ankles was resolved, and the skin lesions had significantly improved.

Discussion

The patient discussed herein had a 5-year history of poly-arthritis, especially in the small joints of his hands, and was now referring to us with oligo-arthritis in the large joints of his lower extremities, psoriasiform skin lesions, high-titer RF and anti-CCP, obesity, hyperlipidemia, hyperuricemia, fatty liver, and also >7 grams proteinuria. The main question was what disease did the patient have: RA in association with psoriasis, or psoriatic arthritis in addition to proteinuria? The ACR criteria (2010) were met in the patient, but some manifestations made us suspect psoriatic arthritis. Psoriasiform skin lesion, Hyperlipidemia, hyperuricemia, and some other comorbidities led us to the diagnosis of psoriatic arthritis. A definite diagnosis was very challenging to make for the patient, because he had some manifestations that were compatible with RA and others that were compatible with PsA as well as some common to both diseases. In terms of clinical manifestations, psoriatic cutaneous manifestation in addition to arthritis and oligo-arthritis (asymmetrical involvement in lower extremities) were more compatible with psoriatic arthritis in this patient.

Laboratory findings show that ESR and CRP levels are higher in RA. RF and anti-CCP become positive in approximately 80% of RA patients with RA, but both of them can be positive in psoriatic arthritis [7]. Cruyssen et al. reported that 7.8% of patients with psoriatic arthritis had positive anti-CCP with levels even higher than 1600 U/ml. Moreover, it has been said 8.3% of psoriatic arthritis patients have positive RF, with levels even higher than 1000 IU/ml. RF and anti-CCP are not specific for RA and can be positive in psoriatic arthritis [8]. Alenius et al. found that the poly-arthritis presentation is related to positive anti-CCP in psoriatic arthritis, but there is no relation between radiological changes and/or deformity and functional impairment and positive anti-CCP [9].

Because the current patient had proteinuria and an underlying rheumatologic disease, we strongly suspected amyloidosis in this patient. Rheumatic diseases such as RA and psoriatic arthritis are the most common causes (70%) of AA amyloidosis [10].

Therefore, we had to use a treatment with coverage of RA, PsA, and also amyloidosis. Adalimumab was started for the amyloidosis, and to treat the RA and PsA, because this drug has a good effect on all three conditions [7]. Esatoglu et al. reported that treatment with anti-TNFs may be associated with a higher survival rate compared with historic cohorts of AA amyloidosis, especially when started early with a lower serum creatinine level at baseline [11]. In choosing anti-TNF drugs, certolizumab and tocilizumab could not be used as they are not available in Iran. Because infliximab increases the risk of tuberculosis, it could not be used, as TB is endemic in Iran [12]. Etanercept demonstrated markedly lower activity levels in comparison with adalimumab [13]. Therefore, adalimumab was used.

Conclusion

Secondary amyloidosis affects multiple organs, including the heart, skin, kidney, gastrointestinal tract, bones, and joints. It is important to diagnosis this disease rapidly and choose the best treatment. When a patient has proteinuria and some rheumatologic manifestations simultaneously, performing a renal biopsy can be helpful. If a patient does not comply in using oral drugs and/or also has amyloidosis, anti-TNF drugs are helpful as a first step in treatment.

Acknowledgments

None.

Conflict of interest

None.

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