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Amyloid deposition in the glenohumeral joint: a case report

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Systemic amyloidosis is a disease caused by abnormally folded proteins that deposit in extracellular tissues. When aggregated in large enough quantities, the deposition causes organ dysfunction. There are 2 categories of systemic amyloidosis (primary and secondary) with multiple types of amyloid proteins characterized. The most common type is primary systemic amyloidosis caused by amyloid light-chain (AL), which also causes the most severe form of disease.[15,23,24] Symptomatic manifestations of amyloidosis include renal failure, congestive heart failure (CHF), carpal tunnel syndrome (CTS), and neuropathies.[21] Additionally, recent literature has identified the presence of amyloid proteins in the joints of patients presenting with joint pain and degenerative arthropathy.[9,15,22] Diagnosis is made by tissue biopsy with Congo red stain. Amyloidosis incidence ranges from 9.7 to 14 cases per million persons per year, with a predominance in people aged 55 and above. It is expected that with the rise in life expectancy, there will be an increased prevalence of amyloidosis.[15]

Arthropathy presents early, relative to cardiac or renal manifestations.[9,14,22] As a result, orthopedic surgeons are in a unique position to initiate the establishment of an early diagnosis, which may alter the course of this systemic disease. Orthopedic literature has discussed osteoarthritis of the hip and knee, spinal stenosis, atraumatic biceps tendon rupture, trigger finger, and rotator cuff tears, due to systemic amyloidosis.[9,14,21,22,26] However, no available case reports discuss amyloid deposition in association with glenohumeral arthritis. We present a unique case of glenohumeral arthritis associated with amyloid deposition in the joint.

Case discussion

A 65-year-old man with a past medical history of Addison's disease, treated with hydrocortisone, presented to the orthopedic sports clinic with a chief complaint of wrist pain. The patient was diagnosed with bilateral carpal tunnel syndrome and underwent 2 separate surgeries for treatment. After his second carpal tunnel surgery, a sample of carpal tenosynovium was sent to pathology, and a Congo red stain was positive for amyloidosis. The sample was then sent to Mayo Clinic and was confirmed to be positive. As a result, the patient was referred to cardiology and neurology for further workup. He was started on patisiran (Onpattro) infusions indefinitely.

Eight months later, the patient returned to the orthopedic sports clinic with a prolonged history of right shoulder pain that interfered with range of motion and sleep. He was diagnosed with severe glenohumeral degenerative joint disease (Fig. 1*A* and *B*). He failed nonsurgical treatment options, including steroid injections, oral pain medication, and activity modification. After a thorough discussion of available treatment options, the patient elected for total shoulder replacement. During the procedure, the operative surgeon encountered significant synovial fibrosis. Therefore, a biopsy from the tenosynovium was sent to pathology and Congo red stain was positive for amyloid deposition in the joint (Fig. 2). His surgery was completed without incident and the patient was discharged home and returned for 2-week, 3-month, and 6-month follow-ups (Fig. 3*A* and *B*).

At his 6-month follow-up appointment, the patient noted that his strength was still improving and that he had resumed downhill skiing without difficulty. Upon examination, the patient's shoulder range of motion and strength was similar to the nonoperative side (Fig. 4 *A* through *C*). The patient-reported outcome scores and functional status were high. His responses revealed an RC-QoL (Rotator Cuff Quality of Life) Index score of 95, an ASES (American

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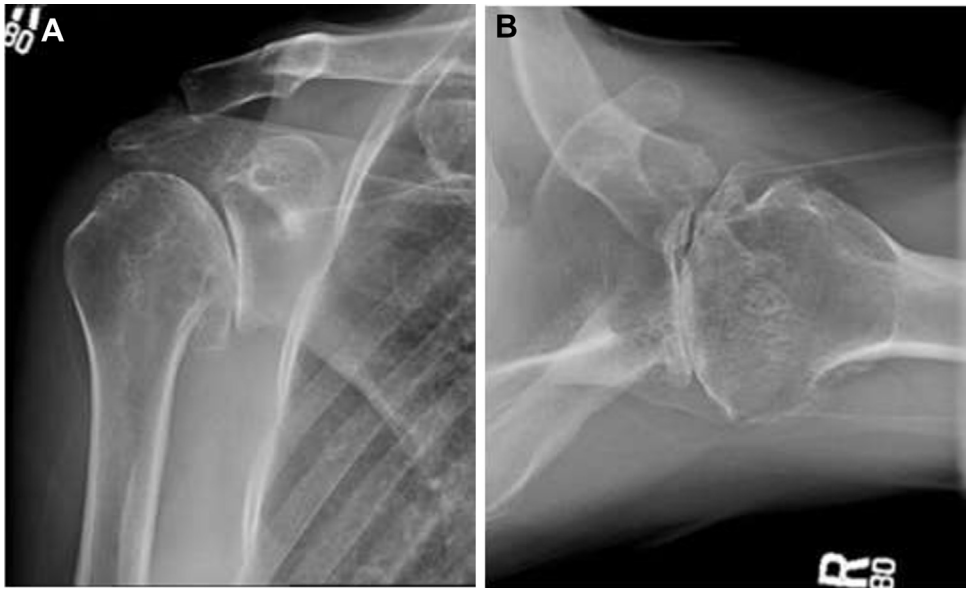

Figure 1 (**A**) Preoperative true AP X-ray of the *right* glenohumeral joint showing degenerative joint disease. (**B**) Preoperative axillary X-ray of the *right* glenohumeral joint showing degenerative joint disease.

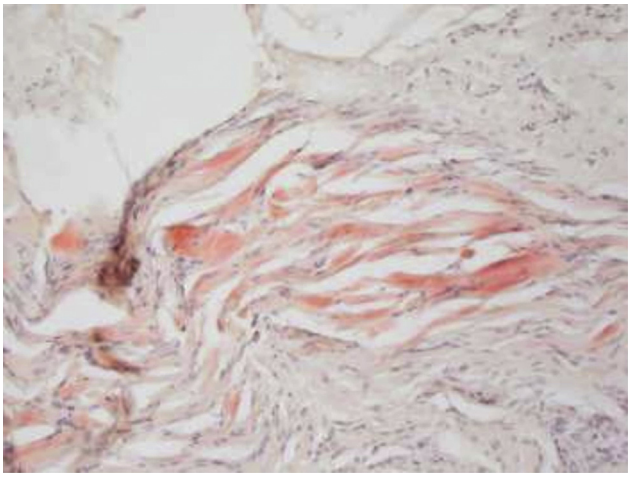

Figure 2 A microscopic slide showing Congo red stain applied to the synovium, which gives the amyloid protein a salmon-pink color. If placed under polarized light, the stain shows apple-green birefringence when place under polarized light.

Shoulder and Elbow Surgeons) score of 82, an SF-12 physical score (PCS-12) of 54.83, and mental score (MCS-12) of 59.78, and a Simple Shoulder Test score of 83.3%. The patient has an annual follow-up with his cardiologist for labs, including troponins and NT-BNP. He will also have Technetium pyrophosphate imaging performed every 2-3 years to evaluate for any changes in his amyloid plaques.

The patient provided written informed consent for this case report.

Discussion

Once diagnosed with amyloidosis, a patient's life expectancy is between 6 months and 4 years. Specifically, untreated cardiac amyloidosis carries a median survival of 6 months.[4] Historically, patients are diagnosed late in the disease process. The simplest explanation is that systemic amyloidosis causes symptoms of common medical problems and is an uncommon cause. Symptomatic heart failure is the worst prognostic indicator and determines available treatment options. Because of this, newly diagnosed patients undergo further testing to identify the extent of the disease.[19,20] This normally includes echocardiogram, MRI of the affected organ, and nuclear imaging of the heart.[10] There is currently no cure for amyloidosis. Treatment is targeted at silencing the responsible gene, stabilizing the abnormal proteins, and symptomatic relief (Example- reducing cardiac symptoms such as peripheral edema and arrhythmia). Treatment modalities include chemotherapy drugs, targeted gene therapy, and organ system-specific medications. Our patient received patisiran (Onpattro), an FDA-approved drug, to treat polyneuropathy due to familial transthyretin amyloidosis, which he will continue indefinitely. His ECHO and cardiology screening were negative.

Amyloid-induced synovial hypertrophy causing carpal tunnel syndrome has been studied and research has shown an association between carpal tunnel syndrome and cardiac amyloidosis in males aged 50 or older and women aged 60 or older.[2,6,11,13,17,24] Carpal tunnel syndrome precedes the diagnosis of cardiac amyloidosis, often by several years. Carpal tunnel is also often bilateral in this population of patients. Patients with carpal tunnel syndrome and biopsy-proven amyloidosis went on to receive earlier treatment that greatly improved their prognosis.[2,6,11,13,17] Amyloid induced hip and knee osteoarthritis has also been studied with amyloid deposition reported in the synovium in both total hip arthroplasty and total knee arthroplasty. One study also demonstrated that patients with a certain amyloid subtype in their synovium were greater than 5 times more likely to have had a hip replacement when compared to the general population.[3,5,7,16,22,25]

In this case, tissue biopsy was utilized to diagnose amyloidosis. An alternative to tissue biopsy is arthrocentesis with Congo red stain of synovial fluid.[1,8,12,18] Arthrocentesis may be considered in patients presenting to the outpatient clinic with bilateral carpal tunnel syndrome or arthritis in multiple joints. This method of diagnosis provides orthopedic surgeons the ability to diagnose amyloidosis prior to surgical intervention. Comparative studies between arthrocentesis and tissue biopsy as a diagnostic modality represent an avenue of future investigation.

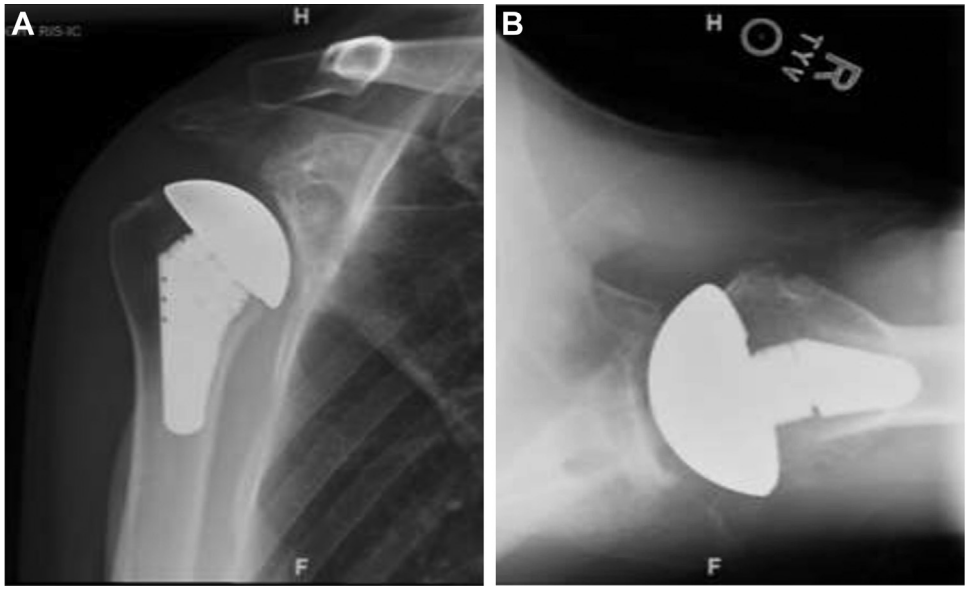

Figure 3 (**A**) Postoperative true AP X-ray of the *right* shoulder showing total shoulder arthroplasty. (**B**) Postoperative axillary X-ray of the *right* shoulder showing total shoulder arthroplasty.

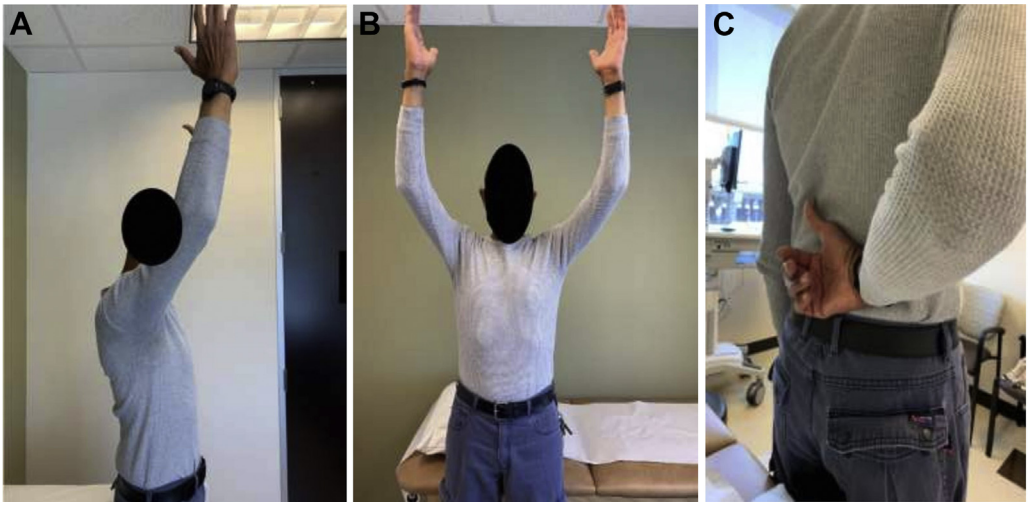

Figure 4 (**A**) Clinical photographs at 6 months postoperative follow-up demonstrating symmetric overhead motion with forward flexion (side view). (**B**) Clinical photographs at 6 months postoperative follow-up demonstrating symmetric motion with external rotation (front view). (**C**) Clinical photographs at 6 months postoperative follow-up demonstrating internal rotation of the *Right* shoulder (side view).

Glenohumeral joint arthritis is an important area of consideration for future amyloid research. The current standard of care does not include sending synovium to pathology for Congo red staining. The operating surgeon should have a high index of suspicion for glenohumeral amyloidosis if they encounter hypertrophied synovium that is out of the ordinary for generalized osteoarthritis. There may be a notable amount of accompanied fibrosis. If encountered, the synovium should be sent to pathology for amyloid staining. This is especially true in a patient with a history of any of the following: bilateral carpal tunnel, lumbar stenosis, CHF, or a prior diagnosis of amyloidosis. This is because orthopedic arthropathy is an accepted manifestation of systemic amyloidosis and often presents earlier than other organ system manifestations associated with poor prognosis.

Conclusion

This case report documents amyloid deposition in the glenohumeral joint in the setting of degenerative joint disease. Recognition of musculoskeletal presentations of systemic amyloidosis can lead to earlier diagnosis and treatment, which may prevent life-threatening manifestations. Considering that amyloid deposition in other joints is an accepted cause of arthropathy, further research needs to be conducted evaluating the prevalence of the amyloid-induced glenohumeral degenerative joint disease. The discovery of a causative association could lead to increased awareness, an earlier method of diagnosis, and decreased mortality in systemic amyloidosis patients.

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