A Case of AL Amyloid that initially presented as new onset Heart failure with preserved ejection fraction

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Introduction

Amyloid light chain amyloidosis involves the slow proliferation of a bone marrow residing plasma cell clone and secretion of unstable immunoglobulin free light chains that infiltrate peripheral tissue and result in end-organ damage.[1]

Disease presentation is vague and once diagnosed, treatment decision is transplant driven. Roughly 20% of patients are eligible for autologous stem cell transplantation with or without bortezomib treatment.[1]

We present a case of AL Amyloidosis at an academic Military hospital that initially presented as new heart failure with preserved ejection fraction.

References

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Case Description

A 61-year-old male with a past medical history of hypothyroidism, anemia, and hypertension that initially presented with shortness of breath for one day. Patient had a subsequent coronary catheterization that showed mild non-obstructive coronary atherosclerosis. The patient had an Echocardiogram that showed a LV ejection fraction >70% with moderate diastolic dysfunction. There was features consistent with a pseudo-normal filling pattern with concomitant abnormal relaxation and increased filling pressure. Severe left ventricular hypertrophy was seen which led to the patient having serum kappa/lambda light chains drawn before his hospital discharge.

Several days later, the patient's labs showed that he had elevated lambda free light chains (91.5 mg/L) along with a kappa free/lambda free light chain ratio of 0.15. The patient was found to have microalbuminuria of 4790 mg/L.

These lab results led Hematology-Oncology to perform a bone marrow biopsy in September 2022. Along with the patient being scheduled for a Cardiac MRI.

Bone Marrow biopsy showed normocellular marrow with maturing trilineage hematopoiesis. Plasma cell neoplasm was seen. FISH showed CCND1/IGH- t(11:14). Flow: abnormal monotypic plasma cell population (2.0%) consistent with plasma cell neoplastic process (Smouldering MM)

Cardiac MRI showed severe concentric LVH along with the myocardium having delayed enhanced imaging. Pattern consistent with cardiac amyloidosis. Fat pad biopsy on December was positive for AL (lambda) type amyloid.

These findings led to referring patient to transplant center for autologous hematopoietic cell transplantation consideration. The patient has had multiple exacerbations of heart failure since. It was deemed that he be started on induction chemotherapy per ANDROMEDA with Dara-CyborD. He had doxycycline 100mg bid added given possible benefit. He had Valtrex 500mg bid given for ppx.

The patient's light chains have normalized. He is currently planned to undergo 4 more cycles followed by re-staging with BM/MRD testing. Pending his response and improvement in cardiac status options include consolidating autoSCT vs proceeding with maintenance therapy per ANDROMEDA. His diastolic heart failure stage B has been managed by Keesler Cardiology with a current regimen of torsemide 100 mg bid and Jardiance. He has reserve Metolazone 5 mg for days following chemotherapy/steroids to mitigate against fluid retention.

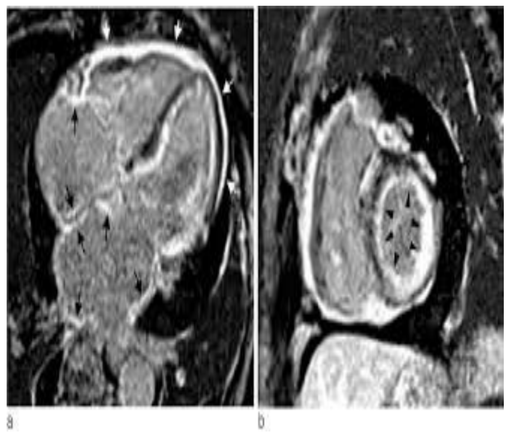

Figure 1. Cardiac MRI showing diffuse and irregular enhancement. Classically will have late gadolinium enhancement.

Discussion/Conclusions

- Light chain amyloidosis is the most common type of amyloidosis.[2]
- Diagnostic criteria for AL Amyloidosis includes: presence of amyloid related systemic syndrome, positive amyloid staining by Congo red in any tissue, evidence that amyloid is light chain related established by direct examination of the amyloid using mass spectrometry-based proteomic analysis or immuno-electron microscopy, and evidence of monoclonal plasma cell proliferative disorder
- Bortezomib belongs to reversible proteasome inhibitors that target specific cell receptors. Plasma cells of AL Amyloidosis patients are sensitive to reversible proteasome inhibitors.[2]
- ANDROMEDA trial looked at bortezomib, cyclophosphamide, and dexamethasone alone versus addition of daratumumab (human CD38 targeting antibody). The percentage of patients who had a hematologic complete response was significantly higher in the daratumumab group than control group (53.3% vs 18.1% with a CI, 2.1 to 4.1; P<0.001.[3]
- Our case highlights importance of keeping a broad differential diagnosis with heart failure with preserved ejection fraction. Heart failure is a common diagnosis and important to investigate the etiology.

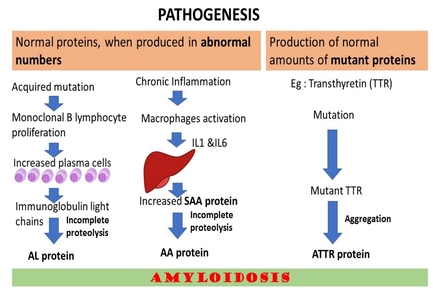

Figure 2. Basic pathogenesis of AL Amyloid vs Cardiac Amyloid