Case Report: Type V CardioRenal Syndrome complicating a progressive wild-type transthyretin amyloidosis (ATTRwt)

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Clinical History

A 73 year old gentleman of African descent has frequently presented to our cardiology facility with episodes of exacerbation of congestive cardiac failure (CCF). In 2014, there was progressive deterioration noted in his left ventricular systolic function along with worsening diastolic dysfunction (E'E of 18). This finding lead to a right ventricular (RV) biopsy in August 2014. **See Figures 1A and 1B.** The biopsy results subsequently revealed the diagnosis of cardiac amyloid disease. **See Figures 2 and 3.** He additionally was followed up in haematology clinic and diagnosed with a wild type transthyretin (TTR) amyloidosis. He was commenced on doxycycline and tauroursodeocycholic acid to slow the rate of amyloid deposition in the heart.

Over the last 4 years he has had multiple admissions for biventricular CCF, two episodes of VT arrest requiring AICD insertion, atrial arrhythmias, cirrhosis and portal hypertension complicated by recurrent ascites eventually leading to chronic kidney disease (CKD). The aetiology of the CKD was deemed to be mixed cardio-renal syndrome and amyloid nephropathy. During his last two admission required inotropic support (dobutamine) to assist with failing systolic function, with moderate effect, however failing to improve his renal function. He became anuric with a creatinine of up to 643 umol/L/ complicated by refractory uraemic pleuritis. He was referred to Palliative Care for comfort therapy as he was previously deemed not suitable for Haemodialysis or peritoneal dialysis. He passed away comfortably in August 2016, exactly two years after his diagnosis of cardiac amyloid disease.

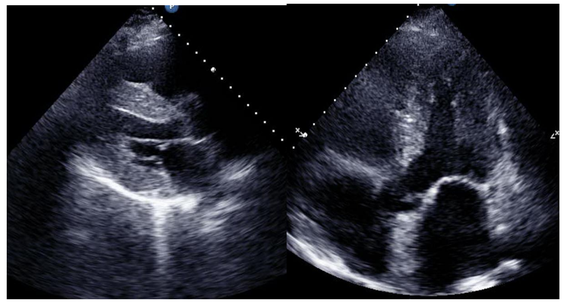

Figure 1A + 1B: Echocardiogram showing concentric LVH & preserved apical function. Sparkling texture also visible in both images.

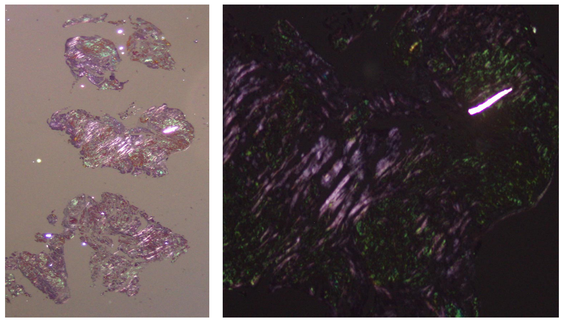

Figure 2A + 2B: RV Biopsy: Apple Green Birefringence under polarized light

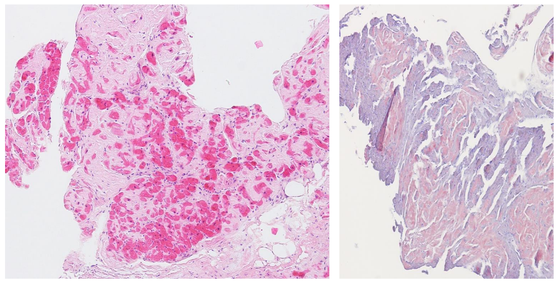

Figure 3A + 3B: RV Biopsy: Salmon-pink colour with Congo-red staining

Discussion

Systemic amyloidosis is a disease that causes extracellular deposition of misassembled proteins in various organs causing dysfunction.[1] Wild-type Transthyretin amyloidosis (ATTRwt) accounts for 18% of all cases of cardiac amyloidosis.[2] The most common presentation of cardiac amyloid disease is congestive cardiac failure specifically with a restrictive pattern; our patient had both moderate-severe impairment of both systolic and diastolic dysfunction. CCF predominantly presents with right sided heart failure over left sided. [3 - 5] If a diagnosis is suspected, echocardiography is frequently performed to assess for thickening of atrial and ventricular walls, abnormal myocardial sparking texture and apical sparing. [1] The definitive diagnosis however remains endomyocardial biopsy, which would typically show apple green birefringence under polarized light and salmon pink by light microscopy, specifically for ATTRwt. The median survival of patients with cardiac amyloidosis is 13 months, with the median survival after onset of CCF only 6 months. [1-4] Treatment protocols have largely expanded over the last few years with chemotherapy, autologous stem cell transplant and dual heart / liver transplantation in attempts to prolong survival.

Cardio-renal syndrome (CRS) is an entity, with a poorly understood pathophysiological basis and treatment approach, that entails decompensated cardiac failure and carries an overall worse prognosis. [6] Our patient's creatinine doubled in a space of 8 days being extremely resistant to both diuretic and dobutamine therapy. Whilst management is classically around diuresis and inotropes, there are certain studies underway investigating ultrafiltration as a palliative measure and AVP receptor antagonists & adenosine receptor antagonists as potential treatment options.

Gottieb et al has shown that administering A1 receptor antagonist with diuretics increases urinary output whilst protecting renal function. [6] The Efficacy of Vasopressin Antagonism In Heart Failure Outcome Study with Tolvaptan (EVEREST) did show patients receiving tolvaptan has significant reductions in mean body weight and dypnoea but there was no effect on long term mortality or morbidity. [6] Further studies are required in both ATTRwt and CRS to improve both long term heart failure morbidity and mortality.

Conclusion

Cardiac amyloidosis is a disease with a poor prognosis, when compared to systemic amyloidosis without cardiac involvement. Together with development of cardio-renal syndrome, has shown, particularly in this case, a high mortality with resistance to medical therapy. Further large-scale studies are required for understanding of the pathophysiology and treatment paradigms to advance in directed therapy.

References

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