Cardiac AL Amyloidosis in a HIV positive patient

AUTHORS

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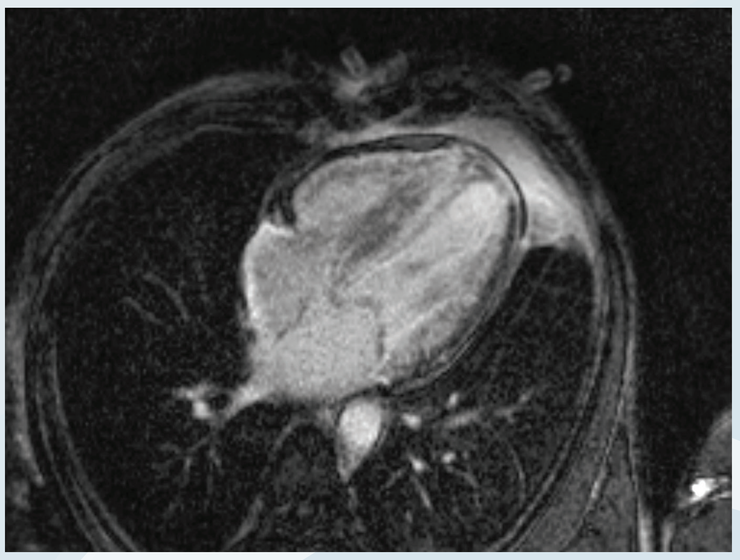
Introduction

- Systemic amyloidosis is a relatively rare multisystem disease caused by the deposition of misfolded protein in various tissues and organs. Approximately 23 different proteins have been found to form amyloid in humans, but only a few are associated with clinically significant disease[1].
- Amyloidosis is classified according to the protein that forms the amyloid fibrils. The two most common proteins are Amyloid Light chain (AL) and Serum Amyloid A protein (AA). These result in AL Amyloidosis which is two to three times more common than AA Amyloidosis in the UK[1]
- Nearly half of patients with AL amyloidosis develop cardiac involvement. Cardiac Amyloidosis is the leading cause of morbidity and mortality in patients with the disease[2].
- We describe a case of cardiac AL Amyloidosis in a newly diagnosed HIV positive patient and discuss investigations and management of AL Amyloidosis.

Case Report

- A 55 year old male Zimbabwean with schizoaffective disorder was admitted with extra pyramidal side effects, hypotension and tachycardia. On admission he was found to be pancytopenic and subsequently diagnosed HIV positive.
- Baseline investigations revealed a CD4 count of 33 cells/mm^3(4%) with a viral load of 6835 copies/ml. He was started on truvada, boosted darunavir and co-trimoxazole as pneumocystis jiroveci (PCP) prophylaxis.
- Extrapyramidal side effects improved after initiation of anticholinergics and withholding antipsychotic medication and he was discharged.
- During admission a pansystolic murmur was identified, therefore an outpatient echocardiogram was arranged.
- One week later he was re-admitted with a 4 day history of vomiting and constipation. The vomiting settled after 72 hours, but he was again noted to be hypotensive and tachycardic. Electrocardiogram showed T wave inversion in chest leads.
- **An echocardiogram** was performed which showed moderate concentric left ventricular hypertrophy, mildly impaired left ventricular systolic and diastolic function and reduced tissue doppler velocities. These are features consistent with amyloidosis.
- **Cardiac magnetic resonance imaging** was suggested and this demonstrated widespread late gadolinium enhancement involving the ventricles, atrial septum and right atrial wall, which is also in keeping with amyloidosis as [Figure 1].
- A **bone marrow biopsy** showed HIV inflammatory myelopathy, approximately 10% plasma cell neoplasia and vascular amyloid tissue deposition in accompanying connective tissue.
- To aid definitive diagnosis, a **rectal biopsy** was performed, which showed amyloid deposition on congo red staining.
- He was referred to the National Amyloidosis Centre in London where genetic testing was performed to exclude hereditary amyloidosis. **Serum amyloid protein scintagraphy (SAP)** was also performed, which showed increased cardiac uptake of radio labelled Serum Amyloid Protein [Figure 2].
- Staging of amyloidosis requires measurement of **Troponin I** and **NT Pro Brain Natriuretic Peptide**. As both were elevated he was diagnosed with Stage 3 Cardiac Amyloidosis and median survival is in the order of eight months[2][Figure 3].

Figure 1. MRI showing gadolinium enhancement



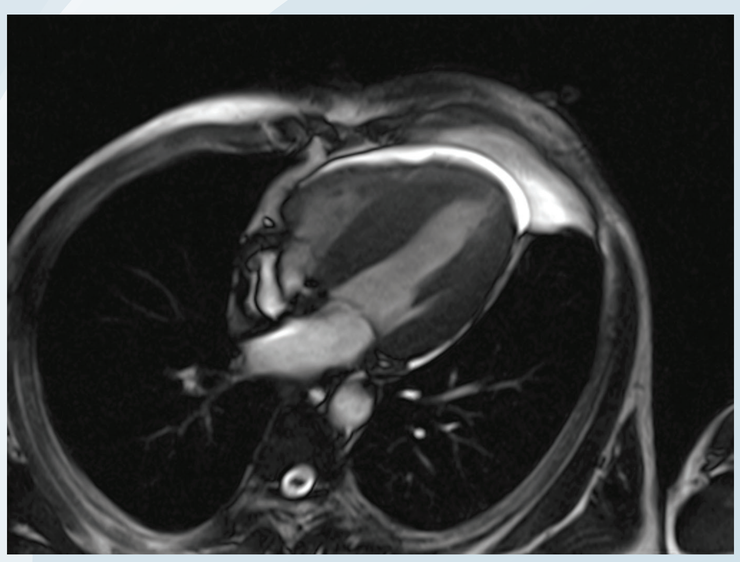


Figure 2. shows increased radiolabelled Serum Amyloid P uptake in the heart

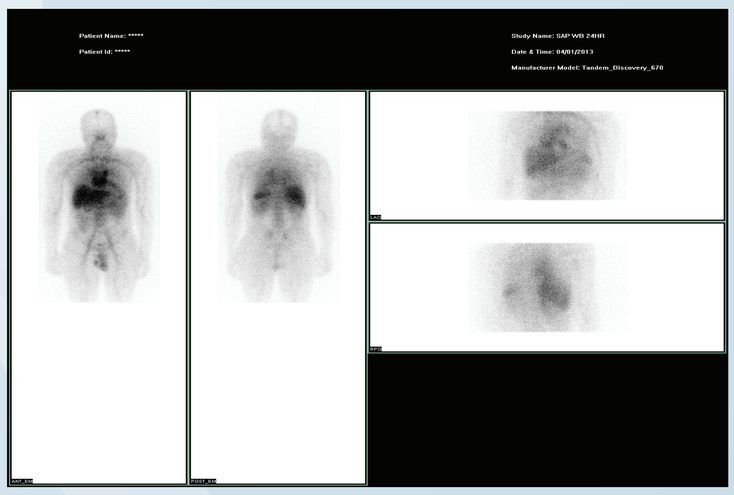
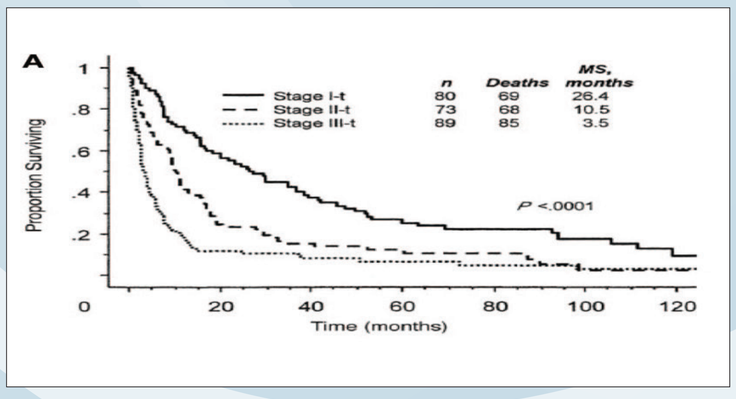


Figure 3. Mayo Staging of Amyloidosis



Treatment

- First line treatment for Cardiac AL Amyloidosis is bortezomib which is a proteasome inhibitor, followed by cardiac and stem cell transplant.
- The main side effects reported with bortezomib use are peripheral neuropathy, myelosuppresion and high rates of shingles. Ritonavir has a significant drug interaction with bortezomib and can increase its concentration by thirty five percent resulting in increased toxicity[3].
- In addition there are few ethnic minorities on the organ donor register, which coupled with this patient's poor prognosis, means first line treatment was not felt to be appropriate. The Queen Elizabeth Hospital is the only centre in the United Kingdom that still offers heart transplant as part of its first line treatment. Of approximately thirty patients that have been eligible for this, only one has completed first line treatment.
- Cardiac transplantation for amyloid cardiomyopathy is controversial owing to donor shortage and recurrence of amyloid in the cardiac allograft[4]. Survival is lower than in patients undergoing transplant for other cardiac conditions[4].
- For the above reasons second line treatment was considered in this case. This consists of treatment with dexamethasone and thalidomide followed by the addition of cyclophosphamide, if the clinical condition remains stable. It is important to note that ritonavir increases the effects of dexamethasone hence a risk of Cushing's syndrome. Ritonavir also increases cyclophosphamide therefore it is important to monitor for toxicity[3].

Conclusion

- AL Amyloidosis is usually secondary to plasma cell dyscrasia. As far as we are aware; there are no previous case reports on cardiac AL Amyloidosis in HIV positive patients. There are, however, cases of AA Amyloidosis and HIV.
- It has been speculated that chronic HIV-infection, as well as the associated immunosuppression, might promote development of renal AA-amyloidosis by increasing frequency and duration of infections acquired by intravenous drug user[5]. There are no links reported between AL Amyloidosis and HIV.
- AL Amyloidosis is often diagnosed late due to its wide range of non-specific symptoms. This case highlights how this multisystem disorder can present in any speciality. The investigations as performed in this case are important both for diagnosis and staging, so that appropriate treatment can be planned.

References

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