Establishing the Type of Cardiac Amyloidosis: A Clinical Challenge

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Background: There has been substantial advancements in the diagnosis and treatment of cardiac amyloidosis (CA) but the diagnosis continues to be challenging and is often delayed or missed. In order to plan an effective treatment strategy, the type of amyloidosis (either AL, TTR, or other) is of paramount importance. Our primary objective was to better understand the diagnostic challenges and present an algorithm to streamline diagnosis.

Methods and Patients: A retrospective analysis of 40 patients from October 2010 to February 2016 diagnosed with TTR CA treated by the Vanderbilt Amyloidosis Multidisciplinary Program (VAMP) was conducted. Diagnostic testing included cardiac biomarkers (n=30), EKG (n=34), TTE (n=38), cMRI (n=21), right heart cath (RHC) with endomycardial biopsy (EB) (n=33) with fibrillary typing (n=30), fibrillary typing on other tissue (n=3), TTR genetic testing (n=30), and testing for plasma cell dyscrasia (PCD) (n=30).

Results: Summarized in Table 1. 3 of 19 (16%) patients with wildtype TTR by fibrillary typing were actually found to have a genetic mutation. 4 of 30 (13%) patients with confirmed TTR CA were found to have evidence of a PCD.

Conclusion: The diagnosis of CA and exact subtyping remains challenging. Although other noninvasive studies are now available, definitive diagnosis by RHC and EB should be considered. We propose a comprehensive algorithm for initial diagnostic work up for suspected CA (Figure 1). The validity of this algorithm should be confirmed in an independent cohort of patients.

Table 1. Demographics and Results of Patients with Confirmed TTR CA (N=40)

Age, median (range), years	72 (54-89)
Male gender, n (%)	30 (75)
Abnormal Cardiac Biomarker	30 (75)
Electrocardiogram suggestive of amyloidosis	34 (85)
TTE with LVPW thickness > 1.2 cm, n (%)	34 (89)
cMRI suspicious for amyloidosis, n (%)	17 (81)
Fibrillary typing: TTR wildtype:mutated Genotyping: TTR wildtype:mutated	19:14 15:14
Median time from symptoms to TTR-CM diagnosis, years (range)	1.14 (1-4)

Figure 1: Proposed diagnostic algorithm for suspected cardiac amyloidosis