



ORIGINAL RESEARCH PAPER

Pathology

STUDY OF SENILE CARDIAC AMYLOIDOSIS – A PROSPECTIVE AND POST MORTEM ANALYSIS

KEY WORDS: Senile cardiac amyloidosis (SCA), Congo Red, Tofamedis

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ABSTRACT Amyloidosis is defined as a disease with deposition of amyloid in extracellular space. Senile cardiac amyloidosis (SCA) consists of deposition of the insoluble amyloid protein within the heart leading to restrictive cardiomyopathy. A few post mortem studies reported the prevalence of amyloidosis as 22-25 % in patients older than 80 years of age. Indian and Asian data are scanty. With this background the aim and objective of the present study is to investigate the frequency and association of cardiac amyloidosis. Fifty four deceased cases were studied belonging to age group of 51 to 80 year and 46 (85%) were males and 8 (15%) were females. 11 cases (21%) were detected to be having SCA of which 9 (82%) were males and 2 (18%) were females in the age group of 61-70 years (73%) which is statistically significant (P<0.05). Majority (64%) showed amyloid deposition in left ventricular wall which is again statistically significant (P=0.023). Commonest causes of death was due to cardiac arrhythmia.

Introduction:

Amyloidosis is defined as a disease with deposition of amyloid. The term 'amyloid' refers to the precipitation of protein in tissue mainly as an extracellular deposition of protein fibrils and with a characteristic appearance in electron microscopy, with a typical X-ray diffraction pattern and an affinity for congored with concomitant apple green birefringence in polarised microscopy¹.

Virchow introduced the term Amyloid to the medical literature in 1854 to describe cerebral cortical red homogenous material and since then knowledge about amyloid composition has accumulated^{2,3}.

Restrictive cardiomyopathy is the major finding in cardiac amyloidosis which results from the replacement of normal myocardial contractile elements by infiltration and interstitial deposits of amyloid which lead to change in cellular metabolism, calcium transport, receptor regulation, and cellular edema

A few post-mortem studies carried out in the United State of European countries reported that the prevalence of senile systemic amyloidosis was 22-25% in patients older than 80 years. But the prevalence of senile systemic amyloidosis in other Asian countries need further clarification.

Histopathological examinations have a critical role in obtaining direct evidence of amyloid deposits and determining the type of amyloid. As the heart is the most commonly affected organ, myocardial biopsy is thought to be the most sensitive method for detecting amyloid deposits in patients with senile systemic amyloidosis, but this type of biopsy is too invasive and carries a risk of complications, especially for elderly patients.

In this study, the clinicopathological features of senile cardiac amyloidosis and the distribution of cardiac amyloid deposits in autopsy cases were investigated. Amyloid deposits in SA node, AV node and infra-His pathway will lead to arrhythmia and coronary artery blockage. Cardiovascular amyloidosis may be primary or it may be secondary to systemic diseases.

Aim & Objectives:

The aim and objective of the present study is to investigate the frequency of cardiac amyloidosis in the hearts of deceased persons

by Hematoxylin and Eosin Stain and congo-red Stain.

Material and Methods:

The study was conducted in the department of Pathology in collaboration with department of Forensic Medicine and Toxicology(FMT) of SCB Medical College and Hospital, Cuttack Odisha,

India, from November 2012 to October 2014 after institutional ethical committee approval from S.C.B. Medical College, Cuttack

Inclusion Criteria:

The heart of autopsy cases of persons more than 50 years of age were taken from the department of FMT, SCB Medical College and Hospital, Cuttack were included in this study.

Exclusion Criteria:

Primary liver disease

Study sample:

54 cases that fulfilled the above criteria were taken up for the study.

Microscopy and interpretation

Hematoxylin & Eosin Stain:

On light microscopy amyloid deposits appear as extracellular homogeneous structureless eosinophilic hyaline material.

Results:

Nucleus – Stained blue
Cytoplasm – Stained pink.

Congo Red Stain: On light microscopy amyloid appear as red to pink colour.

Results:

Amyloid – Red to pink
Nuclei – Blue

Grossing:

Formalin fixed specimen of heart with multiple sections were taken from ventricular and atrial wall (subendocardial surface), myocardium, valve leaflet, coronary artery, aorta etc.

Statistical analysis:

Statistical analysis was done using percentage and chi-square test. P < 0.05 is considered as the level of significance

Observation:

A total of 54 post-mortem cases were taken. The hearts were collected in these cases from the department of FMT, SCB Medical College. The post-mortem number, cause of death were recorded followed by histopathological examination using Hematoxylin and Eosin stain being carried out in the department of Pathology of SCB Medical College, Cuttack. Subsequently special stain, i.e. congo-red stain was done. The results were studied in relation to age and sex distribution, sitewise amyloid deposition and cause of death with relation to location of amyloidosis.

Table -1
Age distribution

Age group	No. of cases	Percentage
51-60 yrs.	31	57%
61-70 yrs.	20	38%
71-80 Yrs.	03	5%
Total	54	100%

Out of 54 cases thirtyone (31) cases (57%) were in the age group 51-60 yrs, 20 no. of cases (38%) in the age group of 61-70 yrs and 03 nos. of cases (5%) were in the age group of 71-80 yrs of age.

Table -2
Sex distribution

Sex	No. of cases	Percentage
Male	46	85%
Female	08	15%
Total	54	100%

Out of 54 no. of cases 46 (85%) were males and 08 (15%) were females.

Table -3
Age distribution of Cardiac Amyloidosis

Age group	Total no. of cases	Amyloid +ve cases
51-60 yrs.	31	2 (18%)
61-70 yrs.	20	8 (73%)
71-80 Yrs.	03	1 (09%)
Total	54	11

Table 3 shows distribution of cardiac amyloid according to various age groups. In our study three groups of age were taken like 51-60 yrs, 61-70yrs and 71-80 yrs age group. The majority of cases showing amyloid deposition belonged to 61-70 years age group, constituting (73%) of all positive cases, followed by 51-60 years age group (18%).

Table -4
Sex distribution of Cardiac Amyloidosis

Age group	Male	Female	Total
51-60 yrs.	2	0	2
61-70 yrs.	7	1	8
71-80 Yrs.	0	1	1
Total	9 (82%)	2 (18%)	11

Table 4 shows out of 11 positive cases of amyloidosis.9 (82%) were male and 2 (18%) were female and most of them were in 61-70 years of age group.

Table -5
Location of Cardiac Amyloidosis

Location of amyloid deposit	No. of cases	Percentage	P Value
Lt. Ventricular wall	7	64%	< 0.05
Rt. Ventricular wall	1	09%	
Lt. Atrium	2	18%	
LVW+RVW+LA+AORTA+Coronary artery	1	09%	

Total	11	100%
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Our study showed out of 11 positive cases, 7 cases showed amyloid deposition in left ventricular wall (64%), 2 cases in left atrium (18%) 1 case in right ventricular wall (09%) and 1 positive case in multiple sites like, left ventricular wall, right ventricular wall, left atrium, coronary artery and aorta (09%).

Table -6
Cause of death in relation to location

Cause of death	Location of amyloidosis	No. of +ve cases
Cardiac arrhythmia	LVW	6 (55%)
Acute MI	LVW, RVW, LA, AORTA	1(09%)
DCM	LA	1 (09%)
Sudden Death	LVW+RVW+LA	3 (27%)

Table 6 showed in 55% of cases amyloid deposition was in left ventricular wall and the cause of death was due to cardiac arrhythmia. 27% of cases showed amyloid deposition in left ventricular wall along with right ventricular wall and left atrium. Only 1 case (9%) showed location of amyloid was in left atrium and cause of death was dilated cardiomyopathy. Similarly another case where amyloid deposition was found in left ventricular wall, right ventricular wall, left atrium, coronary artery and aorta and the cause of death was acute myocardial infarction.

Table -7
Gross abnormality in relation to cause of death

Gross abnormality	No. of cases	No. of cases
LVW thickness	Cardiac arrhythmia	6
Narrowing of aortic lumen	Sudden death	3
Thickened valve leaflet	Acute MI	1
Gross enlargement	DCM	1
Total		11

Table 7 shows out of total positive cases, 6 showed left ventricular wall thickness and cause of death was cardiac arrhythmia, 3 cases showed narrowing of aortic lumen and cause of death was sudden death. Rest two cases showed thickened valve leaflet with gross enlargement of heart and death due to acute myocardial infarction and dilated cardiomyopathy.

DISCUSSION :-

Fifty four cases of autopsy heart were studied .They were studied with regards to frequency and distribution, age, sex, gross abnormalities and cause of death in senile cardiac amyloidosis. In previous hospital based series senile cardiac amyloidosis (SCA) has been seen in 25-28% of autopsied subjects aged 80years or over^{4,5}. Post mortem studies carried out in the United States and European countries reported that prevalence of senile systemic amyloidosis is 20-25% in patients more than 80 years of age^{4,5}. In the present study the prevalence of SCA was 21% confirming SCA is common in the elderly population. In the present study standard myocardial sample was taken from the subendocardial surface of ventricular walls, left atrium, valve leaflet and coronary artery which are commonly used biopsy site for general autopsy. Image 1, 2, 3 and 4 showed cardiomegaly and section revealed enlarged heart with left ventricular wall thickness, left atrial wall thickness and occluded aortic lumen. In other studies the samples were taken from the left ventricle or as one large transverse section of ventricles .In our study it was found that in majority of cases subendocardial surface of left ventricle was the most common site followed by right ventricle and atrium for amyloid deposition .Image 5 and 6 showed microscopic picture of amyloid deposits in left atrium and in the wall of coronary artery.

In our study (table 3) cases range from 51 to 80 years of age. Majority cases showing amyloid deposition belongs to 61 to 70 years of age group constituting 73% of all positive cases, followed by 51 to 60 years age group (18%) .The result revealed that the SCA associate with age is statistically significant (p< 0.05).According Tanskanen M et al senile cardiac amyloidosis

affects 25% of the elderly population .⁶ The severity of SCA was associated with male gender although the overall frequency of SCA did not significantly differ between genders .In our study (Table 4) SCA is more observed in males (82%) in comparison to females (18%) which is not statistically significant (P=0.07).In previous study SCA has been observed more often in men than in women ⁷ . Out of 11 positive (Table 5) cases seven (64%) showed amyloid deposition in left ventricular wall,2((18%) cases in left atrium ,1(9%) cases in right ventricular wall and 1positive case in multiple sites which was statistically significant (P.023) .In our study (Table 6 and 7) it has been seen that death due to cardiac arrhythmia account for 55% of cases with gross abnormalities lying within the LV wall and sudden death accounts for 27% of cases with gross abnormalities in both right and left ventricular wall and left atrium.

SUMMARY :

Senile cardiac amyloidosis (SCA) common age related amyloidosis the highest number of cases showing amyloid deposition in 61-70 years age group in our study.The study also showed the occurrence of amyloidosis is more in males (82%) than the females (18%) .The cardiac amyloidosis commonly involved the left ventricular wall (64%), followed by left atrium (18%) and gross abnormality was found to be left ventricular wall thickening (12%) followed by aortic lumen narrowing (6%) and 1% of each showing thickened valve leaflet and gross enlargement of heart .Also in the majority of cases we found, cause of death was due to cardiac arrhythmia (55%) and sudden death due to acute myocardial infraction (9%) and dilated cardiomyopathy (9%) which is similar with other studies .^{8,9}

CONCLUSION :

Senile cardiac amyloidosis is a very serious disabling or life threatening condition. MRI,ECHO can detect amyloid deposits. Tofamedis ,a novel therapeutic drug is now available for treatment of SCA .Our study concludes that early detection of SCA in our elderly and emergence of newer drugs will help the clinicians to treat the condition to prevent the amenable fibrils and enables the amyloid deposits converted into non pathogenic constituents. Further studies are needed to focus on the earliest detection and treatment of this condition.



IMAGE 1: 65yr male with cardiomegaly(m)16x10x8cm, PM No2011



IMAGE 2: Cut Section of enlarged heart with left ventricular thickness



IMAGE 3: Cut Section of of enlarged heart with left atrial wall thickness



IMAGE-4 Aortic lumen narrowing

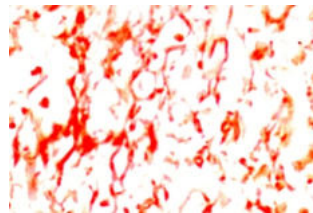


IMAGE-5 Amyloid deposit in left atrium

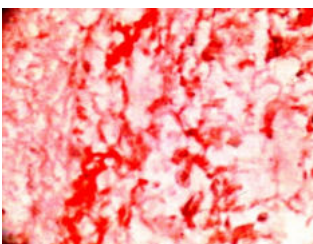


IMAGE-6 Amyloid deposits in the wall of coronary artery

LIMITATION OF THE STUDY :

- 1.The sample size accounted for the discrepancies with other studies which had been observed during the comparison of various parameters.
- 2.Less number of senile post-mortem heart were included in this study.
- 3.Congo red slide should have been examined under polarised light to observe apple green birefringent deposits, considered to be diagnostic of amyloid.

CONFLICT OF INTEREST : Nil

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