Original Research Article

Histopathological Spectrum of Cardiac Tuberculosis on Autopsy: Series of 11 Cases

Ruchi Agarwal[1], Kulwant Singh[2], Swaran Kaur Saluja[3], Deepti Agarwal[4], Monika Gathwal[5], Sunaina Hooda[6]

[1]Professor, [2]Professor, [3]Professor, [4]Professor, Department of Pathology, BPS GMC for Women, Khanpur Kalan, Sonepat, [5]Associate Professor, [6]Assistant Professor, Department of Pathology, BPS GMC for Women, Khanpur Kalan, Sonepat.

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Abstract

Background: Tuberculosis (TB) is leading cause of morbidity and mortality worldwide. However, this endemic disease rarely involves heart. Cardiac TB can involve any structure of heart with pericarditis is most frequent manifestation.

Methods: This retrospective study was conducted at Department of Pathology from January 2012 to December 2020. Autopsy records of all cases suggestive of tuberculosis in any part of heart were selected and slides were reviewed.

Results: A total of 11 cases of cardiac TB were recorded on autopsy, including 6 cases of isolated myocarditis, 2 cases of myopericarditis 2 cases of isolated pericarditis and one case of necrotizing arteritis in left coronary artery. Concomitant pulmonary TB was present in 72.7% cases.

Conclusion: This study highlights that in all patients of pulmonary tuberculosis with appearance of any cardiovascular sign or symptom, cardiac TB should be suspected as one of the differentials.

Keywords:, Caseating granuloma, fibrinous pericarditis, necrotizing arteritis, tuberculous myopericarditis

Introduction

Tuberculosis (TB) is a communicable disease caused by *Mycobacterium tuberculosis* and is a major cause of morbidity worldwide and the leading cause of death from a single infectious agent. TB is endemic in India and has the highest burden of tuberculosis accounting for 26% of the global cases as per Global TB Report 2020.[1] This slowly developing disease may affect any organ in body and can have variable presentations that can pose diagnostic difficulties.

Cardiac tuberculosis is rarely reported and is usually seen secondary to lesions elsewhere in the

Corresponding Author: Sunaina Hooda, Assistant Professor, Department of Pathology, Bhagat Phool Singh, G.M.C. For Women, Khanpur Kalan, Sonepat, Haryana.

E-mail: docsunainahooda@gmail.com

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body. It occurs in 1 to 2 % of patients with pulmonary TB.[1] Pericardium is the most frequently affected part of heart by TB, however few cases of involvement of myocardium, endocardium, valves, aorta and coronary artery are reported in literature.[2,3,4,5]TB accounts for pericarditis in approximately <5% of cases clinically and can presents as acute pericarditis, pericardial effusion, cardiac tamponade and constrictive pericarditis.[6,7] Incidence and mortality found to be higher in cases associated with immunodeficiency states.[7,8] Tuberculosis is the most common cause of constrictive pericarditis in endemic countries, accounting for 38% to 83% of the cases.[9]

Myocarditis is exceedingly rare presentation of this endemic disease and mostly reported in association with pericardial involvement. Literature in past had reported prevalence of 0.14%, 0.2% and 2-5% in various series.[7,10,11] It was suggested that either due to continuous myocardial contractility which prevents lodgment of tubercle bacilli or the production of lactic acid through muscular activity protects heart from tuberculous infection.[12]

Autopsy studies are helpful in not only finding the cause of death, but also an opportunity to study the whole human body as a whole to fill the gaps in existing knowledge about etiopathogenesis and effect of rare diseases. Here we are presenting a series of eleven cases describing histopathological spectrum of cardiac TB on autopsy from a tertiary care center of north India.

Material and Methods

This retrospective study was conducted at Department of Pathology, Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Sonepat from January 2012 to December 2020. Routinely, post-mortem specimens of various organs were received in our department along with postmortem examination report from forensic expert. Grossing of 10% formalin fixed specimens was performed and sections were taken from various organs including heart, lung, liver, spleen, kidney and brain for histopathological examination. Sections were processed and Hematoxylin & eosin stained sections were examined. Ziehl-Neelsen (ZN) staining for acid fast bacilli using 20% H2SO4 was performed as per requirement. Records of histopathology reporting of autopsy specimens were reviewed and cases with either of the findings were included in this study: (i) caseating granulomatous inflammation in any structure of heart with/without AFB positivity with ZN stain (ii) AFB negative granulomatous inflammation in heart with AFB positive granulomatous inflammation in lung. Relevant data including demographic details, cause of death, gross and microscopic findings were noted. Histopathology slides were reviewed and findings were recorded.

Results

In the present study, a total of 11 cases of cardiac TB involving different cardiovascular structures (0.28%) were observed out of 3923 autopsy heart specimens received during 9 years. This study showed male preponderance with M:F ratio of 10:1. Age range was from 24- 65 years with mean age 39.1 years. We observed 8 cases (72.7%) in below 45 years age group while only 3 cases in more than 45 years age group. Postmortem papers mentioned cause of death as sudden death in 5 cases, chronic illness in 3 cases while TB in 2 cases.

In our study, 6 cases of isolated myocarditis, 2 cases of myopericarditis 2 cases of isolated pericarditis and one case of necrotizing arteritis in left coronary artery were reported. Concomitant pulmonary TB was present in 72.7% cases. ZN staining for AFB was positive in only 54.5% cardiac TB cases while positive in lung of all cases of pulmonary TB with heart involvement. Disseminated TB was reported in two cases with miliary tubercles in various organs.

Grossly, all four cases of pericarditis revealed that both visceral and parietal layers of pericardium are grey white, opaque, thick and adhered firmly to underlying myocardium. On microscopy, two cases reveal myopericarditis with eosinophilic fibrinous exudate and chronic inflammatory infiltrate in pericardium. Other two cases showed caseating granulomatous inflammation with fibrosis.

We observed 6 cases of isolated myocarditis and 2 cases of myopericarditis. Left ventricle was the most common area (75%) involved in myocarditis

followed by apex and interventricular septum. Grossly, grey white areas identified in myocardium ranging from 2 mm to 1.5 cm diameter in 37.5% cases. Histopathology revealed variable number of granulomas ranging from a single caseating granuloma to multiple coalescing epithelioid cell granulomas replacing large areas in myocardium along with lymphocytes, Langhans giant cells and caseation necrosis at places. In three cases, miliary myocarditis with miliary tubercles in other organs was present. Pulmonary TB was reported in 80% of cases showing myocardial involvement.

Only one and very rare involvement of coronary artery by TB was also reported in our study in a 43 years male presented with history of sudden death. Grossly, no abnormality detected in any part of heart expect for thickened left coronary artery wall with narrowing of lumen. Microscopy revealed necrotizing arteritis with presence of occasional granuloma in the arterial wall and ZN staining for AFB was positive. Lung and liver were unremarkable grossly as well as microscopically in this case (Table 1).

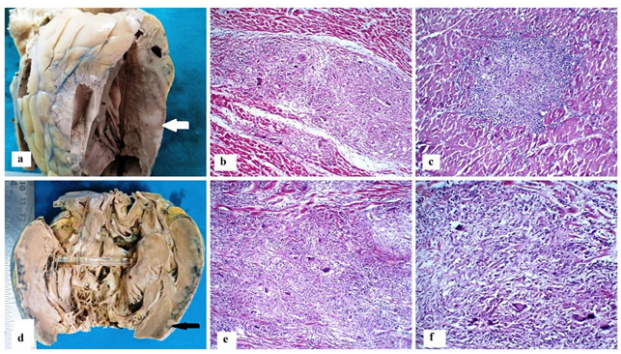

Figure 1 (a) Gross specimen of heart revealing multiple grey white areas in the left ventricular wall (thick white arrow), (b) Microphotograph from same case showing multiple epithelioid cell granulomas with multinucleated giant cells infiltrating the myocardium (H&EX40), (c) Microphotograph from another case showing occasional necrotizing epithelioid cell granuloma in myocardium (H&EX100), (d) Gross specimen of heart revealing multiple grey white areas in the left ventricular wall (thin black arrow), (e) & (f) Microphotograph from same case showing multiple epithelioid cell granulomas (H&EX100, H&EX200).

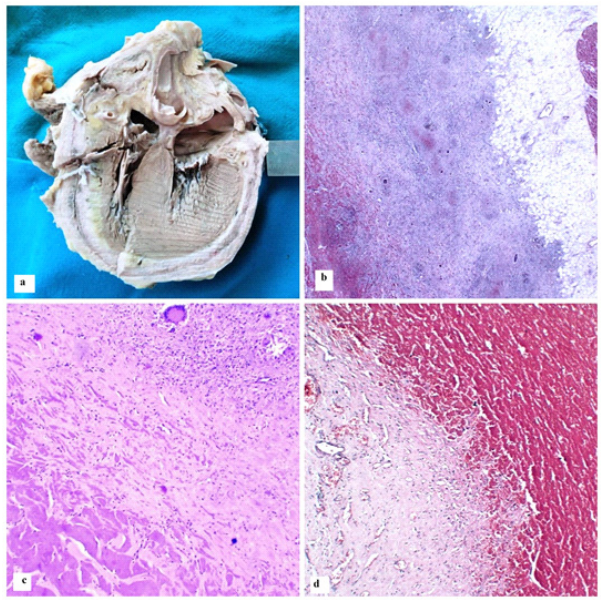

Figure 2 (a) Gross section of the heart revealing layers of pericardium thick and opaque, (b) & (c) Microsections from the heart revealing multiple epithelioid granulomas, giant cells and exudate in the pericardium(H&EX20, H&EX100), (d) Microsections revealing thick fibrinous exudate and fibrosis in pericardium (H&EX100).

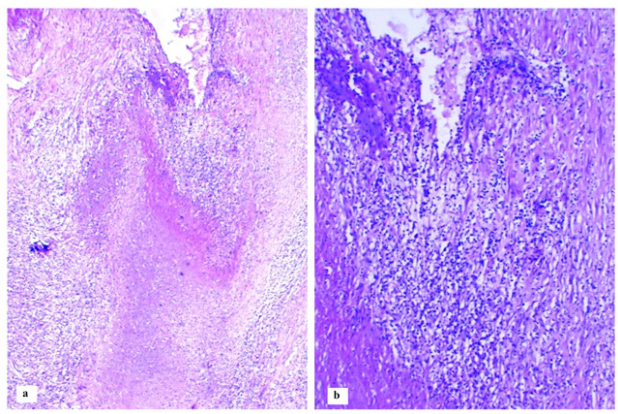

Figure 3 (a) & (b) Microsections from left coronary artery revealing caseous necrosis and epithelioid cell granulomas in the wall (H&EX40, H&EX100).

Table 1: Demographic and histomorphological findings of 11 cases of cardiac tuberculosis on autopsy.

S No.	Age (Yrs)	Sex	Cause of death (as mentioned in Post mortem papers)	Cardiac findings					Pulmonary findings	Extra pulmonary findings
				Area of heart involved	Weight of heart (gm)	Gross Features	Micros-copy	Diagnosis		
1	50	M	Chronic illness	Apex, IVS, LVW	324	Multiple grey white areas in apex and IVS	Multiple necrotizing granulo-matous inflamma-tion AFB - posi-tive	Tuberculous Myocarditis	-	-
2	35	M	Sudden death	Apex, IVS, LVW	338	Multiple grey white areas in LVW and IVS	Multiple epithelioid cell granu-lomas AFB -positive	Tuberculous Myocarditis	Multiple necrotizing epithelioid cell granu-lomas AFB -positive	Occasional granulomas in liver
3	30	M	Chronic illness	IVS	200	-	Few necrotizing epithelioid cell granu-lomas AFB - positive	Tuberculous Myocarditis	-	-
4	42	M	Sudden death	LVW	232	-	Occasional epithelioid cell granu-loma AFB-negative	Tuberculous Myocarditis	Multiple necrotizing epithelioid cell granu-lomas AFB-positive	-
5	24	M	TB	LVW	224	-	Few epithelioid cell granu-lomas AFB- nega-tive	Tuberculous Myocarditis	Multiple necrotizing epithelioid cell granu-lomas AFB- posi-tive	Multiple necrotizing epithelioid cell granulomas AFB-positive in Liver, kidney and spleen, Tubercular meningitis, AFB-positive
6	25	F	Sudden death	Apex	260	-	Ill formed epithelioid cell granu-lomas AFB-negative	Tuberculous Myocarditis	Multiple necrotizing epithelioid cell granu-lomas AFB- posi-tive	-

7	55	M	Sudden death	LVW, IVS and pericardium	620	Thick pericardium, occasional grey white areas in LVW and IVS	Few necrotizing epithelioid cell granulomas in myocardium with serofibrinous pericarditis AFB-positive	Tuberculous Myopericarditis	Multiple necrotizing epithelioid cell granulomas AFB- positive	Epithelioid cell granuloms in spleen
8	26	M	Chronic illness	LVW	276	Thick white pericardium	Few epithelioid cell granulomas in myocardium with fibrinous pericarditis AFB- negative	Tuberculous Myopericarditis	Multiple necrotizing epithelioid cell granulomas AFB- positive	-
9	35	M	Chronic illness	Pericardium	350	Thick grey white pericardium	Multiple necrotizing epithelioid cell granulomas, fibrinous exudate, fibrosis in pericardium AFB-positive	Tuberculous pericarditis	Multiple necrotizing epithelioid cell granulomas AFB- positive	-
10	65	M	TB	Pericardium	700	Thick grey white pericardium	Multiple necrotizing epithelioid cell granulomas, fibrinous exudate and fibrosis in pericardium AFB- negative	Tuberculous pericarditis	Multiple necrotizing epithelioid cell granulomas AFB – positive	Renal amyloidosis
11	43	M	Sudden death	Left coronary artery		Lumen of left coronary artery appear narrowed	Necrotizing arteritis with occasional epithelioid cell granuloma in left coronary artery AFB – positive	Tuberculous Coronary arteritis	-	-

Discussion

Tuberculosis stands top among infectious etiologies causing disease burden and death worldwide.[1] Laennec was the first to describe cardiac tuberculosis in 1826 and kept heart last in the list of organs involved by TB.[13] Tuberculous pericarditis or myopericarditis has been reported, however isolated myocarditis, tuberculoma, tuberculous endocarditis and arterial involvement are rarely reported.[10]

TB is believed to be one of the main causes of pericarditis in developing countries and its incidence is significantly rising in association with immunocompromised status like HIV.7,14 Four pathological stages of tuberculous pericarditis are recognized: (1) fibrinous exudation rich in neutrophils, early granuloma formation and abundant mycobacteria; (2) serosanguineous effusion with plenty of mononuclear cells; (3) absorption of effusion with multiple caseating granulomas and later on thickened pericardium and finally fibrosis; and (4) constrictive pericarditis due to fibrous scar around heart encasing it that reduces diastolic filling.

The first ever case of myocardial TB was reported in 1664 by Maurocadat and second by Morgagni in 1761.[10] Myocardium can contract the infection mostly through blood borne seedling and less frequently by retrograde lymphatic drainage from tuberculous mediastinal nodes or direct spread from infected structures in surrounding.[15]Three histological patterns of tuberculous myocarditis as describe by Horn and Saphirare are (i) nodular tubercles of the myocardium that varies from pea to egg size with central caseation, (ii) miliary tubercles of the myocardium complicating generalized miliary disease, and (iii) diffuse infiltration associated with tuberculous pericarditis where myocardium is infiltrated by granulation tissues containing giant cells, endothelial cells and lymphocytes.[16] Anatomical predilection of the wall of right atrium involvement has been described due of the frequent involvement of the right mediastinal lymph nodes by tuberculosis and subsequent spread to the adjoining myocardium.[17] Clinically tuberculous myocarditis can present as arrhythmias, conduction blocks, cardiogenic shock, ventricular aneurysm, right ventricular outflow obstruction or even sudden cardiac death,.[18]

Ante mortem diagnosis of this entity is challenging as many patients remain asymptomatic, rarely suspected clinically and obtaining sample for AFB staining or culture from heart is difficulty.[7]Thus, majority of the cases of cardiac tuberculosis were diagnosed incidentally on autopsy and accounts for <0.1% of TB-related deaths.[10,18]

In our study, preponderance of young individuals (below 45 years) and male gender for cardiac TB was observed. We had reported cases of pericarditis, myocarditis, myopericarditis and necrotizing arteritis caused by TB. Left ventricle was most frequently affected site with simultaneous presence of pulmonary TB was seen in 80% cases of myocarditis. In presence of caseating granulomas with or without AFB positivity, the diagnosis of TB is obvious. However, in case of occasional non caseating granulomas in heart, histological evidence of concomitant pulmonary tuberculosis is highly suggestive of cardiac TB.

Findings of our case series are similar to a systematic review of 16 cases by Michira et al. They observed that males were twice more frequently affected by tuberculous myocarditis than in females. Most of the reported cases of tuberculous myocarditis were predominantly in immunocompetent patients. Out of the reported sudden cardiac deaths, 81% occur in the 'young' patients (below 45 years). Left ventricle was commonly involved structure (68%) with concomitant pulmonary infection was reported in 56% of the cases. Concomitant pericarditis was recorded in 43% of the cases. Involvement of other extrapulmonary sites apart from the heart was recorded in 56% of the cases. Isolated cases of tuberculous myocarditis without involvement of any other organs were found in 25% of all reviewed cases.[19]

In a study conducted by Rose AG, myocardial tuberculosis was observed in 19 patients (0.14%) at autopsy over a 27-year period. Eight patients had miliary lesions and 11 had nodular lesions, most commonly observed in the ventricles. Out of the 19 cases, only in one patient diagnosis of myocardial TB was made ante mortem. Three patients developed left ventricular aneurysms.[10]

Differential diagnosis of cardiac TB includes granulomatous and giant cell rich lesions in heart.

Clinical history, radiological and serological investigations will always help in narrowing down the differentials. Differentials include sarcoidosis, fungal infections, giant cell myocarditis, systemic lupus erythematosus, syphilis, drug hypersensitivity, rheumatic fever and idiopathic granulomatous myocarditis.[20] Presence of confluent non caseating granulomas with peripheral fibrosis and asteroid bodies in giant cells may help in reaching the diagnosis of sarcoidosis. Necrotizing granulomas are seen in case of fungal carditis with Periodic Acid Schiff and Gomori Methamine Silver stain will identify the causative agent. In giant cell myocarditis, infiltration of myocardium by mixed chronic inflammatory infiltrate including lymphocytes, eosinophils, plasma cells, macrophages, many giant cells observed without any evidence of granulomas. SLE may lead to pancarditis, however pericarditis is more frequently observed than myocarditis. Diagnosis relies on presence of specific antibodies in serum with perivascular and interstitial mononuclear cell infiltrate with myocardial degeneration and fibrosis and Libman-sacks endocarditis of valves. In hypersensitivity myocarditis, poorly formed histiocytic lesions and numerous eosinophils infiltrating the cardiac muscle fibers and perivascular infiltrate are observed without any formation of giant cells or granuloma. In case of acute rheumatic fever, pancarditis may be present with aschoff nodules containing histiocytes with caterpillar like nuclear chromatin. Idiopathic granulomatous myocarditis is usually a diagnosis of inclusion and reveals non-caseating granulomas in heart without any evidence of similar lesions in any other organ of the body. As this study is based on autopsy findings of organs received, correlation with history and investigation findings is not possible.

To conclude, this case series emphasizes that although infrequent, tuberculosis can involve any cardiac structure. Histopathological spectrum of TB in heart may vary from diffusely infiltrating caseating granulomas to occasional non- caseating tubercles. Most of the cases in our series revealed presence of TB in extra cardiac organs which suggest that ante mortem diagnostic frequency can be increased by high index of suspicion in all patients presenting with cardiac symptoms with known case of TB of any organ, especially in TB endemic areas like in developing countries.

Conflict of Interest: None

Source of funding: None

Ethical Clearance with Date & Reference no. - BPSGMCW/RC 736/ IEC /22, dated 08.02.2022.

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