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Original Article

Pathology Section

Elucidation of Histological Features of Pericardium in Cases Clinically Presented as Constrictive Pericarditis: A Retrospective Observational Study

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ABSTRACT

Introduction: Constrictive Pericarditis (CP) is an uncommon but important disease characterised by impaired diastolic ventricular filling and impaired ventricular ejection as a result of thickened, fibrosed and often calcified pericardium.

Aim: To analyse histomorphological features of pericardial biopsy removed in patients with clinical and radiological features of constriction.

Materials and Methods: The present study was a retrospective observational study conducted at LPS Institute of Cardiology and Cardiothoracic Vascular Surgery and Department of Pathology, GSVM Medical College, Kanpur, Uttar Pradesh, India. A total of 108 patients with CP were studied between a time period of January 2008 to June 2019. Clinical, demographic, laboratory and operative data of patients were retrieved from record section of mentioned departments and analysed. On histology the following parameter, if present, were recorded: inflammation and its type, granulation tissue, fibrosis, extracellular collagen deposition, granuloma, haemosiderin deposition, mesothelial hyperplasia, capillary proliferation, and calcification. Data was analysed using Microsoft Office Excel spread sheet.

Results: Out of 108 cases, 98 cases (90.7%) had increased pericardial thickness and 10 cases (9.2%) had normal pericardial thickness, despite clinical and echocardiographic features of restriction. In majority of cases (96 cases, 88.9%), inflammation was of chronic type and only in 8 cases (7.4%), it was of acute nature. Tubercular pericarditis was the major cause in 46 cases (42.6%) followed by chronic non specific idiopathic in 39 cases (36.1%).

Conclusion: The current study evaluated the histological features of CP in a semiquantitative grade manner thus helping clinician and pathologists to guide for other ancillary testing and thus guide toward accurate diagnosis. The current study evaluated the histological features of CP in a semiquantitative grade manner thus helping pathologists to guide for other ancillary testing and thus guide toward accurate diagnosis.

Keywords: Collagen deposition, Fibrosis, Tuberculosis, Ventricles

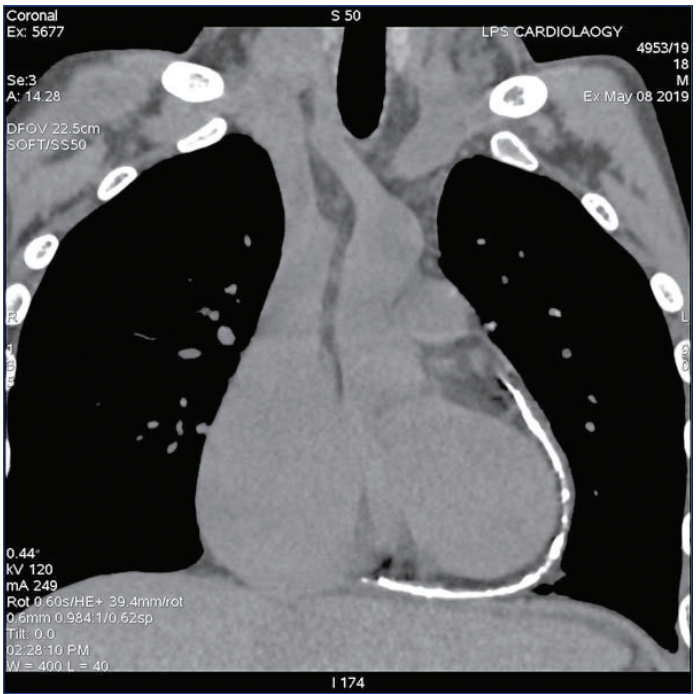
INTRODUCTION

The CP is relatively uncommon cardiac pathology known to be caused by various factors resulting in thickened, fibrosed and often calcified pericardium which limits diastolic ventricular filling and impaired ventricular ejection.

The disease is characterised by clinical signs of right heart failure subsequent to loss of pericardial compliance and initial presentation in majority of the cases is due to systemic congestion e.g., ascites, anasarca, lower extremity oedema. Later on features of decreased cardiac output predominate [1-4].

Worldwide idiopathic being the most common cause followed by tubercular which is still the leading cause in developing countries like India, Africa and many sub-Saharan countries [5-7]. In recent year, there is a change in the scenario of pericarditis as number of postcardiac interventional pericarditis is on rise leading to increase incidence of iatrogenic aetiology [2,8-13]. Other causes of CP include mediastinal trauma, irradiation, neoplasm, postmyocardial infarction and viral infections like HIV etc., [2,14].

Diagnosis can be ascertain based on clinical features along with radiologically visible thickening along with calcification which can be demonstrated by Computed Tomographic (CT) scan and Magnetic Resonance Imaging (MRI) [Table/Fig-1]. Echocardiography also a useful tool for diagnosis as it can also demonstrate effusion and haemodynamic parameter along with ejection fraction [2,15-17]. Normal pericardium is a thin relatively avascular sac with thickness of 2 mm or less and a thickness of more than 4 mm suggestive of constriction and a thickness of more than 6 mm are specific for constriction [18].



[Table/Fig-1]: Computed Tomographic (CT) Scan showing dense calcification.

In addition to the classic chronic and subacute and acute form, many other categories have been recognised such as effusive-constrictive, transient, occult and CP with normal pericardial thickness [19]. Histologically, CP is characterised by thickened pericardium with

fibrosis, increased collagen deposition, lymphoplasmacytic infiltrate with or without granuloma formation, necrosis and calcification [19-24].

A lot had been discussed about clinical and radiological features of CP but there is sparse literature on histomorphological features of CP [5,9,19-22]. The present study was a retrospective observational study where, the authors analysed histomorphological features of pericardium biopsy specimen removed surgically in 108 patients with clinical and radiological features of CP and thus identifying the cause of constriction which further aids to the management of the patient in follow-up.

MATERIALS AND METHODS

The present study was a retrospective observational study conducted on 108 patients presented between a time period approximately 10 years, from January 2008 to June 2019 at LPS Institute of Cardiology and Cardiothoracic Vascular Surgery and Department of Pathology, GSVM Medical College, Kanpur, Uttar Pradesh, India. Clinical, demographic, laboratory and operative data of patients were retrieved in the month of November and December 2019 from record section of both mentioned departments and analysed.

Inclusion and exclusion criteria: Patients who had complete clinical, radiological and histological data were included in the study. Those having incomplete data or known cases of restrictive cardiomyopathy were excluded. Patients who had incomplete clinical radiological or pathological data and known case of primary or metastatic pericardial disease were excluded from the study.

Study Procedure

Diagnosis of CP was made on the basis of clinical features supported by chest X-ray, echocardiography, CT scan or MRI where needed. Surgical and pathological findings were then reviewed for confirmation of diagnosis. The diagnostic findings include respiration related vascular septal shift, variation in mitral inflow E velocity, medial mitral annular 'e' to lateral 'e' and hepatic vein expiratory diastolic reversal ratio [25]. Other findings included atrial enlargement, pericardial thickening, calcification and abrupt relaxation of the posterior wall.

Pericardiectomy was performed through left anterolateral thoracotomy or median sternotomy approach. After surgery pericardial biopsy specimen were fixed in formalin, processed, paraffin embedded and sectioned for Haematoxylin and Eosin (H&E) staining. The maximal pericardial thickness was recorded in millimetre and the following parameters, if present, were recorded: inflammation and its type, granulation tissue, fibrosis, extracellular collagen deposition, granuloma, haemosiderin deposition, mesothelial hyperplasia, capillary proliferation, and calcification.

Inflammation both acute and chronic and extracellular collagen deposition were graded semi-quantitatively graded as 0=absent, 1=mild, 2=moderate, 3=severe/abundant. Similarly fibroblastic proliferation also graded as 0=absent, 1=few spindle shape fibroblast, 2=many spindle shape fibroblasts, 3=many plump reactive fibroblast.

STATISTICAL ANALYSIS

Data was analysed using Microsoft Office Excel software using spread sheet.

RESULTS

Total 108 cases were studied, out of which, 80 cases (74.1%) were males and 28 cases (25.9%) were females. Highest number of cases fall under age group 40-59 year [Table/Fig-2]. Almost all cases were presented with chief complaint of dyspnoea. Other presenting features at the time of diagnosis were fatigue, abdominal discomfort, ascites, hepatomegaly and raised jugular venous pressure.

Age group (in years)	Male	Female	Total
<19	03	01	04 (3.7%)
20-39	19	12	31 (28.7%)
40-59	57	14	71 (65.7%)
> 60	01	01	02 (1.9%)
Total	80 (74.1%)	28 (25.9%)	108

[Table/Fig-2]: Age and sex distribution of the cases.

Chronic pericardial effusion was present in 62 cases of which 28 cases were diagnosed as tubercular on histological follow-up. The histological features were evaluated semi-quantitatively [Table/Fig-3]. Histological features such as inflammation, both acute and chronic, fibrosis, extracellular collagen and capillary proliferation were semi-quantitatively graded as 0 to +3 depending on absent, mild, moderate and abundant respectively.

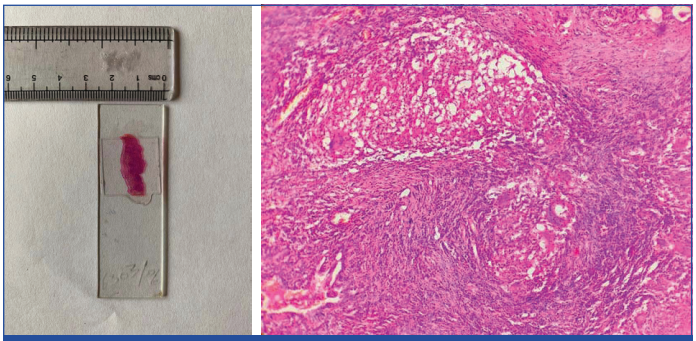
Parameters and score	Number of cases (%)
Increased thickness	98 (90.7)
Inflammation	
Acute	08 (7.4)
Absent	100 (92.6)
Mild	06 (5.6)
Moderate	02 (1.8)
Severe	00
Chronic	96 (89)
Absent	12 (11.1)
Mild	61 (56.5)
Moderate	32 (29.6)
Severe	03 (2.8)
Acute on chronic	04 (3.7)
Granuloma	
Absent	62 (57.4)
Caseating	08 (7.4)
Non caseating	38 (35.2)
Calcification	12 (11.1)
Fibrosis	
Absent	02 (1.8)
Few spindle cells	34 (31.5)
Many spindle cells	64 (59.2)
Many plump reactive spindle cells	08 (7.4)
Granulation tissue	16 (14.8)
Haemosiderin deposit	12 (11.1)
Mesothelial cell hyperplasia	03 (2.8)
Capillary proliferation	08 (7.4)
Extracellular collagen deposition	
Absent	12 (11.1)
Mild	76 (70.3)
Moderate	06 (5.6)
Abundant	14 (12.9)

[Table/Fig-3]: Histological features on biopsy and their score (absent, mild, moderate and severe were graded as 0 to +3).

Maximum pericardial thickness range from 1-22 mm with mean thickness of 7 mm [Table/Fig-4]. Thickening was present in 98 cases (90.7%) and the cause of thickening was fibrosis in all cases. Additionally, thickening was also due to extracellular collagen deposition in 14 cases (12.9%), calcification in 12 cases (11%).

Inflammation was predominantly chronic and consists of lymphoplasmacytic in 96 cases (88.9%). And was mild in 61 cases (56.5%), moderate in 32 cases (29.6%) and severe in 3 cases (2.8%). Acute inflammation was present in 8 cases (7.4%) that too

were mild in majority of cases (6 cases, 75% of total). Non caseating granulomas were seen in 38 cases (35.2%) as compared to caseating granulomas in 8 cases (7.4%) [Table/Fig-5]. Acute inflammation co-existed with chronic inflammation in 4 cases (3.7%). Haemosiderin (due to old haemorrhage) was seen in 12 cases (11.1%) and mesothelial cell hyperplasia was seen in 3 cases (2.8%). All clinical, radiological and histological features were evaluated and the final diagnosis was made. Tubercular pericarditis was the most common diagnosis in 46 cases (42.6%) followed by chronic non specific/ idiopathic in 39 cases (36.1%).



[Table/Fig-4]: Thickened pericardium showing thickness approximately 1 cm. (H&E, whole mount slide).
[Table/Fig-5]: Caseating and non caseating granuloma surrounded by dense fibroblastic proliferation. (H&E, 100X). (Images from left to right)

DISCUSSION

Although CP usually affects adults, the age range is quiet broad and affecting children as well as elderly also [26]. In present study, also the patient was as young as 12 years and as old as 73 years. Usually, males are affected more as compared to female and in the present study also male:female ratio was approximately 3:1 which is comparable to many other studies [2,22].

Tubercular pericarditis was still the major cause of constriction (42.6%) followed by idiopathic (36.1%). Other causes include chest trauma and postradiation and postmyocardial infarction in 1.8% and malignancy in 3.7% cases. The results of current study are comparable to few other reports from developing countries like Africa, sub-Saharan countries and India [6,7,27]. The data from developed countries in contrary to current study considered idiopathic as the commonest cause of CP (45-55%) followed by postsurgical (13-36%), postradiation (9-10%) and miscellaneous causes range between 9-22% in different studies [2,11,12,17,28].

Pericardial effusion was present in 62 cases (57.4%) and out of which 32 cases (51.6%) cases were diagnosed as tubercular [26].

Pericardial thickness was increased in majority of the cases (98 cases, 90.7%) with average thickness of 7 mm. The cases showing increased thickness had corresponding increased pericardial thickening in CT Scan. Similar findings were observed in other studies also [29,30]. However, 9.2% cases normal pericardial thickness both on CT Scan and histopathological examination however, on Echocardiogram (ECHO) based haemodynamic studies, features were suggestive of CP indicating increased pericardial thickness does not necessary imply constriction. These results are in concordance with reports of few other studies [20].

In all cases, the cause of pericardial thickening was fibrosis and increased extracellular collagen deposition. The maximum pericardial thickness was observed in cases where fibrosis was of grade 3 category (7.4% cases) and all these cases had abundant extracellular collagen deposition. Additionally, pericardial thickness was also due to calcification in 12 cases which was also observed in CT scan [Table/Fig-3].

Acute inflammation was absent in majority of cases and when present was of mild to moderate degree in majority of cases. The findings are consistent to those described in several other studies also [20,22,26,31-34]. Chronic inflammation was seen in 88.9% cases and when present was of mild to moderate degree (63.5% and 33.3%, respectively). Only 3.1% cases show severe lymphoplasmacytic infiltrate. The chronic infiltrate was predominant feature of idiopathic as well as tubercular CP cases. The results were similar to those described in several other studies [26,28].

Cases diagnosed as tubercular, non caseating granulomas were seen in 82.6% cases and caseating granulomas were in 17.4% cases. Along with granuloma other findings were capillary proliferation, fibrosis and calcium deposition similar results were observed by other studies also [22,26]. Other less dominant findings were granulation tissue, haemosiderin deposition and mesothelial cell hyperplasia which were also observed by other studies also [21,22,26].

It has often been difficult to establish a definite aetiological cause in cases of CP even after extensive radiological tests, pericardial biopsy therefore, provides a relatively simple and inexpensive approach in suspected cases.

Limitation(s)

There were limitations to the present study. Since this was a retrospective observational study performed only on patients who were clinically as well as radiologically proven cases of CP, hence, it poses limitation on true sensitivity and specificity of the biopsy findings for the diagnosis of CP, as there are many other cardiac diseases like restrictive cardiomyopathies, which could not entirely be ruled out by pericardial biopsy, as in few of these, patients are having a component of concomitant CP.

CONCLUSION(S)

There are many diseases which clinically and radiologically presents as constrictive pericarditis. The pericardial pathology is subtly different according to pathogenesis of disease and so is the management according to underlying pathology. The current study evaluated the histological features of CP in a semi-quantitative grade manner, thus, helping pathologists to guide for other ancillary testing and thus a guide towards accurate diagnosis and further management.

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