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A STUDY OF DIFFERENTIATION OF BENIGN AND MALIGNANT PERICARDIAL EFFUSION BY CT FINDINGS

General Medicine

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ABSTRACT

Background: Pericardial effusion develops as transudate (hydropericardium), exudate, blood (hemopericardium), or a mixture of these substances. Echocardiography is an excellent initial imaging tool for evaluating the pericardium, particularly pericardial effusion. Antituberculosis chemotherapy dramatically improves survival among patients with tuberculosis pericarditis. **Objectives:** To Study the differentiation of benign and malignant pericardial effusion by CT findings. **Methods:** Apart from clinical examination, patients were selected after confirmation of pericardial effusion by transthoracic echocardiography. CECT was performed and CT images reviewed for the presence of pericardial thickening, pattern of pericardial thickening, and mediastinal lymphnode enlargement. Omnipaque (Iohexol Injection) 350mgI/ml was used for contrast. Cytology was done only where pericardiocentesis was indicated. **Results:** CT scan findings were suggestive of abnormal pericardial thickening in 34.3% patients, mediastinal lymphadenopathy in 27.1% patients and pleural effusion in 72.9% patients. Pattern of abnormal pericardial thickening was smooth in 58.3% patients while as it was irregular in 41.7% patients. Benign pericardial effusion was observed in 62.9% patients while as 37.1% patients had malignant pericardial effusion. CA lung was seen in 21.4% patients, lymphoma in 5.7%, CA breast in 4.3%, leukemia in 2.9%, CA esophagus and renal cell carcinoma in 1.4% patient each. **Conclusion:** CT scan has an increasingly important role in decision making, particularly in determination of the optimal treatment for patients with constrictive pericarditis.

KEYWORDS

Pericardial effusion, antituberculous chemotherapy, echocardiography, lymphnode.

INTRODUCTION

Pericardial effusion develops as transudate (hydropericardium), exudate, blood (hemopericardium), or a mixture of these substances. The presence of a large pericardial effusion generally suggests the patient has more serious disease and is commonly associated with Malignancy, hypercholesterolemia, uremic pericarditis, myxoedema, and parasitosis[1]. Development of techniques of sampling and analyzing pericardial fluid and tissue has improved the etiologic classification of the disease and increased the likelihood of identifying a specific cause, reducing the number of idiopathic cases[2,3]. Echocardiography is an excellent initial imaging tool for evaluating the pericardium, particularly pericardial effusion, but it can be limited by the intrinsic properties of the technique, such as small or limited field of view, occasionally poor acoustic windows, and problems related to anatomic factors, such as severe emphysema[4]. Cross-sectional imaging techniques such as CT, however, can display the detailed anatomic features of the entire pericardium more clearly than can echocardiography and CT has been found to be an excellent tool for detecting pericardial effusion[5,6]. In addition, associated thoracic changes can be evaluated because of the larger field of view inherent in CT. Previous reports[5-9] have suggested that malignant pericardial effusion and tuberculous pericardial effusion may be associated with nodular or uneven pericardial thickening. To the best of our knowledge, however, the diagnostic performance of CT in differentiating malignant and benign pericardial effusion has not been fully elucidated in the clinical literature.

The differential diagnosis of pericardial effusion in patients with malignant disease includes malignant pericardial effusion, radiation-induced pericarditis, drug-induced pericarditis, and idiopathic pericarditis[10]. Metastatic pathways to the pericardium can be lymphatic or direct extension[11]. The presence of effusion and an irregularly thickened pericardium or pericardial mass suggest metastatic involvement of the pericardium, and effusion is the most common manifestation of metastatic pericardial disease[9,12,13]. Metastatic involvement of the pericardium has been frequently found in autopsy series; however, visualization of metastatic deposits with any imaging method is unusual[14]. In addition, nonmalignant pericardial effusion is found at postmortem examination of as many as 6% of patients with cancer[12,15]. Tuberculous pericarditis can be lethal because of the difficulty of early diagnosis and ready progression to constrictive pericarditis[16]. As described in previous reports[8,17,18], tuberculous pericardial effusion can manifest as abnormal pericardial thickening. Seven of 11 cases (63.6%) of benign pericardial thickening in their study were associated with tuberculous pericarditis (six cases of smooth and one case of irregular thickening). The incidence of tuberculous pericarditis ranges from 8% to 17% among HIV-negative persons[16,19,20] but from 17% to 34% among HIV-positive persons[21]. Antituberculosis chemotherapy dramatically improves survival among patients with tuberculosis pericarditis.

Aims and Objectives

- To validate the relevance of CECT chest findings of pericardium especially abnormal thickening, pattern of thickening and mediastinal lymphadenopathy.
- To investigate the value of CECT chest findings in predicting the presence of malignant pericardial effusion.

MATERIAL AND METHODS

The present observational study was conducted in the Postgraduate Department of Medicine, Government Medical College, Srinagar over a period of one and a half years. Patients with transthoracic echocardiography proved pericardial effusion were included in the study.

Initially apart from clinical examination, patients were selected after confirmation of pericardial effusion by transthoracic echo-cardiography. CECT (transthoracic) was performed and CT images reviewed for the presence of pericardial thickening, pattern of pericardial thickening, and mediastinal lymphnode enlargement. Omnipaque (Iohexol Injection) 350mgI/ml was used for contrast. Cytology was done only where pericardiocentesis was indicated.

Calculation of mean pericardial thickening was made for both benign as well as malignant pericardial effusion and a p value of <0.05 was taken significant using independent student's t test. Chi-Square (c^2) test was used to evaluate the significance of associated pleural effusion or mediastinal lymphnode enlargement in predicting the presence of benign or malignant pericardial effusion. All the patients underwent transthoracic echocardiography and Contrast-Enhanced Computed Tomography (CECT). Normal pericardial thickening ranges from 0.7 to 2.0mm on CT images. 2 mm to 3 mm is considered equivocal whereas 4mm thickness at any point is abnormal. Lab facilities: Cytology and microbiology (AFB staining).

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 22.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and categorical variables were summarized as percentages. Diagnostic accuracy (sensitivity, specificity, positive predicted value and negative predicted value) of CECT in diagnosis of abnormal pericardial thickening and mediastinal lymphadenopathy,

was seen by taking histopathology and cytology as gold standard.

RESULTS

The present observational study was conducted in the Postgraduate Department of Medicine, Government Medical College, Srinagar over a period of one and a half year on 70 patients of pericardial effusion. Mean age of patients in our study was 56.1±7.82 years. 54.3% were males and 45.7% were females. Most common presenting symptoms were dyspnea in 61.4% patients, chest pain in 28.6% patients, palpitations in 15.7% patients and fever in 7.1% patients. CT scan findings were suggestive of abnormal pericardial thickening in 34.3% patients, mediastinal lymphadenopathy in 27.1% patients and pleural effusion in 72.9% patients. Pattern of abnormal pericardial thickening was smooth in 58.3% patients while as it was irregular in 41.7% patients. Benign pericardial effusion was observed in 62.9% patients while as 37.1% patients had malignant pericardial effusion. CA lung was seen in 21.4% patients, lymphoma in 5.7%, CA breast in 4.3%, leukemia in 2.9%, CA esophagus and renal cell carcinoma in 1.4% patient each. Tubercular pericardial effusion was observed in 12.9% patients, pneumonia in 7.1% patients, renal failure in 4.3% patients, myocardial infarction in 2.9% patients, systemic lupus erythematosus (SLE) and hypothyroid in 1.4% patient each. Abnormal pericardial thickening was present in 46.2% patients with malignant pericardial effusion and in 27.3% patients with benign pericardial effusion. Diagnostic accuracy of CECT in diagnosis of abnormal pericardial thickening with sensitivity of 46.2, specificity of 72.7, positive predictive value of 50, negative predictive value of 69.6 and accuracy of 62.9. Mediastinal lymphadenopoathy was present in 61.5% patients of malignant pericardial effusion and 6.8% patients of benign pericardial effusion. Diagnostic accuracy of CECT in diagnosis of mediastinal lymphadenopathy with sensitivity of 61.5, specificity of 93.2, positive predictive value of 84.2, negative predictive value of 80.3 and accuracy of 81.4.

Table 1: Different parameters of study patients

		No. of Patients	Percentage
Age distribution	< 40	3	4.3
	40-49	15	21.4
	50-59	19	27.1
	60-69	26	37.1
	≥ 70	7	10.0
	Mean±SD (Range)=56.1±7.82 (17-90)		
Gender distribution	Male	38	54.3
	Female	32	45.7
Clinical symptoms at presentation	Dyspnea	43	61.4
	Chest pain	20	28.6
	Palpitations	11	15.7
CT Findings	Abnormal pericardial thickening	24	34.3
	Mediastinal lymphadenopathy	19	27.1
	Pleural effusion	51	72.9
Pattern of abnormal pericardial thickening	Smooth	14	58.3
	Irregular	10	41.7
Final diagnosis	Malignant pericardial effusion	26	37.1
	Benign pericardial effusion	44	62.9
Etiology of malignant pericardial effusion	CA lung	15	21.4
	Lymphoma	4	5.7
	CA breast	3	4.3
	Leukemia	2	2.9
	CA esophagus	1	1.4
	Renal cell carcinoma	1	1.4
Etiology of benign pericardial effusion	Tubercular pericardial effusion	9	12.9
	Pneumonia	5	7.1
	Renal failure	3	4.3
	Myocardial infarction	2	2.9
	Systemic lupus erythematosus (SLE)	1	1.4
	Hypothyroid	1	1.4
	Idiopathic	23	32.9

Table 2: Data on pericardial thickening and mediastinal lymphadenopathy

		Malignant pericardial effusion		Benign pericardial effusion	
		No.	%age	No.	%age
Abnormal pericardial thickening	Present	12	46.2	12	27.3
	Absent	14	53.8	32	72.7
	Total	26	100	44	100
Mediastinal lymphadenopathy	Present	16	61.5	3	6.8
	Absent	10	38.5	41	93.2
	Total	26	100	44	100

Table 3: Diagnostic accuracy of CECT

	Parameter	Value	95% CI
Diagnostic accuracy of CECT in diagnosis of abnormal pericardial thickening to detect malignant pericardial effusion	Sensitivity	46.2	28.7-64.5
	Specificity	72.7	58.2-83.7
	Positive predictive value	50	31.4-68.6
	Negative predictive value	69.6	55.2-80.9
	Accuracy	62.9	51.2-73.2
Diagnostic accuracy of CECT in diagnosis of mediastinal lymphadenopath to detect malignant pericardial effusion	Sensitivity	61.5	38.9-74.5
	Specificity	93.2	78.8-96.4
	Positive predicted value	84.2	56.7-91.5
	Negative predicted value	80.3	65.4-87.5
	Accuracy	81.4	67.6-86.6

DISCUSSION

The present study was conducted to determine whether CT findings are useful for differentiating malignant and benign pericardial disease in patients with pericardial effusion. Most cases of pericardial effusion can be managed safely with an echocardiographically guided percutaneous approach if there is a need for pericardiocentesis[22]. Mean age of our study patients was 56.1±7.82 years range (17 years to 90 years) with majority i.e. 26 (37.1%) belonging to 60-69 year age group followed by 19 (27.1%) belonging to age group of 50-59 years age group and 15 (21.4%) patients being 40-49 years of age. There were 38 (54.3%) males and 32 (45.7%) females. Gibbs CR et al (2000)[22] determined the aetiology of large and symptomatic pericardial effusions and to review the management and subsequent outcome. In their study patients age ranged between 16 to 92 years with males age of 54 years. Their study patients consisted of 24 males and 22 females. Another study done by Seferovic PM et al (2003)[2] had 66.7% males and 33.3% females. Sun JS et al (2010)[23] validated the usefulness of a CT finding of abnormal pericardial thickening and to investigate the value of associated thoracic changes in predicting the presence of malignant pericardial effusion. The age of patients in their study ranged between 23 to 82 years with mean age of 54 years. Males outnumbered females with 55.4% males versus 44.6% females. In a study done by Razek AAKA and Samir S. (2019)[24] age of the patients ranged between 22-68 years with mean age of 39 years with 29 men and 12 women.

In our study, symptoms at presentation included dyspnea in 43 (61.4%) patients, chest pain in 20 (28.6%) patients, palpitations in 11 (15.7%) patients and fever in 5 (7.1%) patients. Similar findings were observed by Gibbs CR et al (2000)[24] in their study most common presenting complaint included breathlessness (90%), chest pain (74%), cough (70%), abdominal pain (61%) and unexplained fever (28%). Sun JS et al (2010)[23] conducted a study in which dyspnea was the most common presenting symptom in 41 (55.4%) patients and chest pain in 20 (27%) patients. Cully M et al (2019)[25] conducted a study in which presenting complaints included shortness of breath (65%), followed by fever (52%), fatigue (44%), and chest pain (44%). Most common presenting complaints were dyspnoea (n = 37), and chest pain (n = 34) in a study done by Razek AAKA and Samir S (2019)[24]. So dyspnea seems to be the commonest symptoms in pericardial effusion. Computed tomography (CT) scan findings were suggestive of abnormal pericardial thickening in 24 (34.3%) patients, mediastinal lymphadenopathy in 19 (27.1%) patients and pleural effusion in 51 (72.9%) patients. Benign pericardial effusion was observed in majority of patients i.e. 44 (62.9%) while as 26 (37.1%) patients had malignant pericardial effusion. Abnormal pericardial thickening was present in 12 (46.2%) patients with malignant pericardial effusion and 12 (27.3%) patients with benign pericardial effusion. Mediastinal lymphadenopoathy was present in 16 (61.5%) patients of malignant pericardial effusion and 3 (6.8%) patients of benign pericardial effusion respectively. Sun JS et al (2010)[23] conducted a study in which

CT findings of pericardial thickening was observed in 24 patients. In their study thirteen cases (46.4%, 13/28) were associated with malignant pericardial effusion, and 11 cases (23.9%, 11/46) were associated with benign pericardial effusion.

In our study, pattern of abnormal pericardial thickening was smooth in 14 (58.3%) patients while as it was irregular in 10 (41.7%) patients. Sun JS et al (2010)[23] conducted a study in which pattern of abnormal pericardial thickening was smooth in 13 of 74 patients and irregular pattern was observed in 11 of 74 patients. When compared of the 13 patients with smooth pericardial thickening 3 (23.1%) had malignant pericardial effusion while as 10 (90.9%) had benign pericardial effusion. In patients with irregular pattern 10 (76.9%) and 1 (9.1%) had malignant and benign pericardial effusion. Out of 26 (37.1%) malignant pericardial effusion patients, CA lung was seen in 15 (21.4%) patients, lymphoma in 4 (5.7%), CA breast in 3 (4.3%), leukemia in 2 (2.9%), CA esophagus and renal cell carcinoma in 1 (1.4%) patient each. Out of 44 (62.9%) patients with benign pericardial effusion, tubercular pericardial effusion was seen in 9 (12.9%) patients, pneumonia in 5 (7.1%) patients, renal failure in 3 (4.3%) patients, myocardial infarction in 2 (2.9%) patients, systemic lupus erythematosus (SLE) and hypothyroid in 1 (1.4%) patient each.

Malignant pleural effusion (MPE) is an effusion, characterized by the presence of malignant cells[26]. It is most common in lung cancer (LC), followed by breast cancer (BC), lymphoma, gynecological cancers and malignant mesothelioma[27]. Contrast enhanced computed tomography (CECT) in diagnosis of abnormal pericardial thickening with sensitivity of 46.2, specificity of 72.7, positive predictive value of 50, negative predictive value of 69.6% and accuracy of 62.9. CECT in diagnosis of mediastinal lymphadenopathy with sensitivity of 61.5, specificity of 93.2, positive predictive value of 84.2, negative predictive value of 80.3 and accuracy of 81.4. Sun JS et al (2010)[23] even though abnormal (smooth or irregular) pericardial thickening was a significant finding of malignant pericardial effusion, the sensitivity, specificity, positive predictive value, and negative predictive value were 48.3%, 76.1%, 56%, and 70%. Therefore, abnormal pericardial thickening is not a suitable finding in screening for malignant pericardial effusion. However, irregular pericardial thickening (not smooth thickening) had high specificity (97.8%) and positive predictive value (91.7%) and has the potential to be a reliably specific finding suggesting the presence of malignant pericardial effusion although the sensitivity was low (37.9%). Razek AAKA and Samir S (2019)[24] conducted a study to differentiate malignant from benign pericardial effusion with diffusion-weighted magnetic resonance imaging (MRI). The cut-off values of the Apparent diffusion coefficient (ADC) used for differentiating malignant from benign pericardial effusion were 3.25 and 3.0510-3 mm2/s with areas under curve of 0.839 and 0.791, sensitivities of 88.2% and 70.6%, specificities of 69.6% and 73.9%, and accuracies of 78% and 72.5% for both observers, respectively.

CONCLUSION

Although pericardial disease often represents a diagnostic challenge, CT imaging have notably contributed in the demonstration of pericardial pathologic conditions and greatly improved understanding of this enigmatic part of the heart. Since pericardial diseases have substantial morbidity and mortality, CT scan has an increasingly important role in decision making, particularly in determination of the optimal treatment for patients with constrictive pericarditis.

Therefore in the presence of above findings in a patient of pericardial effusion, we should consider seriously the possibility of malignant pericardial effusion and make diligent efforts to rule out malignancy like performing cytology and or biopsy so that we can perform a cause based specific management of such cases because it can become important where tuberculosis is endemic and malignancy is suspected.

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