Cardiovascular Topics

The role of chest radiography in diagnosing patients with tuberculous pericarditis

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Summary

Aim: **To describe the abnormalities on chest X-ray (CXR) in patients presenting with tuberculous pericardial effusions.**

Methods: **One hundred and seventy patients presented to Tygerberg Hospital with large pericardial effusions (epi-pericardial separation > 10 mm). All patients had a diagnostic work-up, which included CXR, ECG, two-dimensional echocardiography and HIV serology. Echocardiography was followed by pericardiocentesis and drainage. Pericardial fluid was analysed for adenosine deaminase (ADA), Ziehl Neelsen (ZN) stain, bacterial and mycobacterial cultures. Sputum was sent for ZN stain and mycobacterial cultures. Tuberculous pericardial effusions were diagnosed according to predetermined criteria.**

Results: **The diagnosis of tuberculous pericarditis was made in 53% (*n* = 90) of patients with pericardial effusions. Forty-one of the subjects (45.5%) were HIV positive. All patients had an enlarged cardiac silhouette and in the majority of cases, the cardiac shadow was globular with distinct margins. The cardiothoracic ratio (CTR) exceeded 0.55 in all patients. The amount of fluid drained correlated with the radiographic finding of cardiac enlargement.**

Conclusion: **In developing countries where TB is very prevalent, CXR plays an important role in the identification of large pericardial effusions. Although sonography will still be required for a definite diagnosis, the results of this study show that CXR is a useful screening tool.**

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Most pericardial disease in sub-Saharan Africa is caused by tuberculosis (TB).[1] This is especially so in the Western Cape Province of South Africa where the prevalence of TB is among the highest in the world and TB is one of the leading causes of morbidity and mortality.[2] The epidemic of human immunodeficiency virus (HIV) infection has also increased the incidence of TB,[3] most notably of extrapulmonary TB.[4] Studies in several sub-Saharan countries have shown a close association between pericardial effusions and HIV infection.[5,6] It has also been demonstrated that TB is the predominant cause of large pericardial effusions in HIV-infected patients in this region.[1] Significant pericardial effusions have been identified by echocardiography or autopsy in up to 46% of patients with acquired immunodeficiency syndrome (AIDS).[7]

Three investigations are commonly used to diagnose pericarditis: electrocardiography (ECG), echocardiography and chest radiography (CXR). Twelve-lead ECG is of supportive but not diagnostic value in cardiac tamponade.[8] Echocardiography is the most useful test, but it may be unavailable in areas where the disease is most common. The classical finding on CXR is an enlarged globular cardiac shadow with a clear margin due to impaired movement of the distended pericardium.[9] It is not clear how the CXR assists in diagnosing the underlying cause in a patient in whom a large pericardial effusion has been confirmed. According to the literature, less than one-third of patients with tuberculous pericardial effusions have any evidence of active pulmonary TB on CXR.[10,11]

Aim

The aim of this study was therefore to describe the abnormalities noted on CXRs in patients presenting with tuberculous pericardial effusions, in particular with regard to cardiac silhouette and features suggestive of active pulmonary TB.

Methods

A prospective study was carried out at Tygerberg Academic Hospital, Western Cape, South Africa. A total of 170 patients presented to the Echocardiography Unit with large pericardial effusions (defined as epi-pericardial separation of more than 10 mm) between February 1995 and June 1999. These patients were enrolled in the study and followed up for a minimum of 12 months. All patients gave

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written informed consent to participate in the study, which was approved by the Ethics Committee of Stellenbosch University.

All patients underwent a comprehensive diagnostic work-up, which included a full medical history, physical examination, CXR, 12-lead surface ECG, two dimensional echocardiographic studies and HIV serology.

The admission CXRs were studied in detail by a radiologist and two physicians, all of whom were blinded to the clinical diagnosis. The following radiological parameters were noted: cardiothoracic ratio (CTR), presence of pericardial or pleural calcifications, presence of pleural effusions, mediastinal lymphadenopathy, features of disseminated TB, alveolar infiltrates and evidence of cavitatory lesions.

Echocardiography was used to determine the location of the pericardial effusion, the epi-pericardial distance, amount of epicardial thickening, presence of fibrin strands, signs of tamponade, and presence of and localisation of constriction. Echocardiography was followed by pericardiocentesis and drainage by an indwelling pigtail catheter. The amount of drained pericardial fluid was measured and patients were accordingly divided into one of four groups: < 500 ml, 500–999 ml, 1 000–1 499 ml or > 1 500 ml. Pericardial fluid was analysed for the following: total protein, lactate dehydrogenase (LD), adenosine deaminase (ADA), cytology, differential cell count, Ziehl Neelsen (ZN) stain, and bacterial and mycobacterial cultures. In addition, sputum was also sent for ZN stain and mycobacterial cultures. Pericardial biopsies were performed in 17 patients in whom an aetiological diagnosis could not be made within seven days after admission, or in whom adequate drainage could not be achieved by closed pericardiocentesis. The biopsies were sent for histopathological examination and TB culture.

Pericardial effusions were considered to be tuberculous in origin when diagnosed by one or more of the following criteria: (i) isolation of *Mycobacterium tuberculosis* (*M. tuberculosis*) from the drained pericardial effusion or pericardial biopsy specimen; (ii) demonstration of granulomatous inflammation on histopathological examination of the pericardial biopsy sample; (iii) presence of a lymphocytic pericardial exudate together with measured ADA level ≥ 40 IU/l; (iv) presence of a lymphocytic pericardial exudate associated with compatible clinical features and a good response to anti-tuberculous chemotherapy; and/or (iv) presence of a lymphocytic pericardial exudate with a positive sputum ZN stain and/or TB culture.

Statistical analysis

Statistical analysis of interval variables was done using the Mann-Whitney U-test and expressed as mean (standard deviation, ± SD). Non-parametric data were analysed using the Kruskall-Wallis one-way ANOVA and Chi-square tests. These data were expressed as median (range). A p-value < 0.05 was considered statistically significant.

Results

The diagnosis of tuberculous pericarditis was made in 90 of the 170 patients with pericardial effusions (53%). Forty of the subjects were female and 50 were male. Forty-one of the subjects were HIV positive, with a median (range) CD4 lymphocyte count of 296 (34–1 006) cells/µl. The mean (± SD) ages of the TB/HIV-positive (n = 41) and TB/HIV-negative (n = 49) subjects were 31.9 (± 8.4) and 39.7 (± 16.0) years, respectively. The echocardiographic data are presented in Table I. There was no significant difference between the HIV-positive and -negative patients with regard to the amount of pericardial fluid drained or the echocardiographic findings.

The CXR findings are presented in Table II. All patients had an enlarged cardiac silhouette and in the majority of cases, the cardiac shadow was globular with distinct margins. The CTR exceeded 0.55 in all patients. In 10 patients, the CTR was > 0.75. Forty-five patients (50%) had radiological evidence of pleural effusions, with no significant difference between HIV-positive and -negative individuals. Twelve patients presented with bilateral effusions, compared to 15 patients with left-sided and 18 with right-sided pleural effusions. In HIV-positive patients, the median (range) CD4 count was significantly higher in patients with pleural effusions than in those without pleural effusions [312 (34–1 006) cells/µl versus 144 (39–445) cells/µl, respectively; $p < 0.05$].

It was difficult to evaluate the hilar regions for evidence of pulmonary TB, especially on the left side, due to the cardiac enlargement and displacement of anatomical

TABLE I. ECHOCARDIOGRAPHIC DATA OF PATIENTS PRESENTING WITH TUBERCULOUS PERICARDIAL EFFUSIONS (n = 90).

Parameter	*TB/HIV+ (n =41)*	*TB/HIV– (n = 49)*	*Total (n = 90)*
Presence of tamponade	37	44	81
Pericardial thickness (mm)	6.7	6.8	6.7
Presence of fibrin strands	26	32	58
Effusive constriction	2	3	5
Volume of pericardial effusion (ml)* [median (range)]	816 (250–1 800)	832 (250–2 700)	825 (250–2 700)

*Pericardial volumes were not available for three patients (HIV+: n = 1, HIV–: n = 2).
HIV+: human immunodeficiency virus positive; HIV–: human immunodeficiency virus negative; TB: tuberculosis.

TABLE II. SUMMARY OF CHEST RADIOGRAPH FINDINGS OF PATIENTS PRESENTING WITH TUBERCULOUS PERICARDIAL EFFUSIONS (n = 90).

Variable	*TB/HIV+ (n = 41)*	*TB/HIV– (n = 49)*	*Total (n = 90)*
CTR > 0.55 and ≤ 0.75	39	41	80
CTR > 0.75	2	8	10
Left-sided pleural effusion	7	8	15
Right-sided pleural effusion	8	10	18
Bilateral pleural effusion	5	7	12
Mediastinal lymphadenopathy	5	2	7
Disseminated TB	2	2	4
Alveolar infiltrates with cavitation	2	5	7
Alveolar infiltrates without cavitation	2	2	4
Bronchopneumonia	1	2	3
Consolidation pneumonia	2	0	2

CTR: cardio-thoracic ratio; HIV+: human immunodeficiency virus positive; HIV–: human immunodeficiency virus negative; TB: tuberculosis.

TABLE III. CARDIO-THORACIC RATIO AND AMOUNT OF PERICARDIAL ASPIRATE IN PATIENTS PRESENTING WITH TUBERCULOUS PERICARDIAL EFFUSIONS (*n* = 87).

Amount of pericardial aspirate (ml)			
Range	*Mean (± SD)*	*Mean (± SD) CTR*	*Sample size (n)**
< 500	398.8 (82.6)	0.68 (0.12)	21
500–999	703.6 (124.8)	0.69 (0.17)	38
1 000–1 499	1 223.1 (96.7)	0.72 (0.16)	19
> 1 500	1 770.0 (226.4)	0.77 (0.18)	9

*Pericardial volumes not available for three patients (HIV+: *n* = 1, HIV–: *n* = 2).
CTR: cardio-thoracic ratio; SD: standard deviation; HIV+: human immunodeficiency virus positive; HIV–: human immunodeficiency virus negative.

structures. Many of the CXRs were also of poor quality due to poor inspiratory efforts and the compression of lung tissue. Four patients were identified with right-sided mediastinal lymphadenopathy and three had bilateral mediastinal node enlargement; five of these seven patients were HIV positive. Four patients had evidence of disseminated TB, 11 had evidence of alveolar infiltrates compatible with active TB, three presented with a bronchopneumonic picture and two patients had radiological features of consolidation. In seven of the 11 patients with alveolar infiltrates, there was evidence of cavitatory disease and six of these were found to be sputum-smear positive for *M. tuberculosis*. In addition to these 27 patients (30%) with features of active pulmonary TB, a further six individuals with tuberculous pericardial effusions had radiological features of pulmonary fibrosis suggestive of previous TB (6.7%) and four patients had calcified nodules suggestive of a healed Ghon focus (4.4%).

The amount of fluid drained correlated with the radiographic finding of cardiac enlargement (Table III). In patients with a CTR between 0.55 and 0.75, the median (range) amount of fluid drained by pericardiocentesis was 795 (250–1 800) ml, whereas in those with a CTR > 0.75, it amounted to 1 605 (1 400–2 700) ml. Two of the HIV-infected patients had a CTR > 0.75 compared with eight TB patients not infected with HIV. No pericardial calcifications were noted on CXR.

Discussion

Enlargement of the cardiac silhouette on CXR does not usually occur until at least 250 ml of fluid have accumulated in the pericardial space.[11] Classically, the presence of a pericardial effusion is suspected when a rapid increase in the size of the cardiac silhouette is seen in the presence of clear lung fields. In some cases, the heart may assume a globular or 'water bottle' shape, blurring the contours along the left cardiac border and obscuring the hilar vessels.[11,12] The parietal pericardial and epicardial fat layers are normally 1–2 mm apart. The presence of an effusion may result in more marked separation of the pericardial fat lines, apparent on high-quality frontal or lateral chest films in about 25% of patients with pericardial effusions.[13] The fact that all our patients had enlarged cardiac silhouettes confirms that there is a good correlation between the sonographically confirmed diagnosis of large pericardial effusions and CXRs. A study conducted in Harare, Zimbabwe also found that 100% of patients with tuberculous pericarditis had a CTR > 55%.[14]

The 50% proportion of patients in this study with radiological evidence of pleural effusions is higher than the 30% previously reported.[10] In our study, right-sided pleural effusions occurred slightly more frequently than left-sided effusions. These results differ from previous studies in which it was found that pericarditis is more strongly associated with left-sided pleural effusions.[15,16] These studies were, however, not confined to patients with TB. The effusions seen in the present study could have developed either as a result of congestion or as part of a pleural immune response against tubercular antigens. In addition, mycobacteria were cultured from the pleural fluid of six individuals and it is therefore likely that a certain proportion of pleural effusions result from a cellular immune response against tubercular proteins without viable bacilli entering the pleural space.[17]

The finding that CD4 lymphocyte counts in HIV-positive patients were lower in those patients presenting with pleural effusions may imply that the cellular immune response in these individuals is less likely to respond vigorously to the invasion of the pleural space by tubercular bacilli (or proteins), due to advanced immunodeficiency. In a similar study, the prevalence of pleural effusion in tuberculous HIV patients with CD4 T-lymphocyte counts greater than 200 cells/µl was 27%, while it was only 10% in HIV patients with TB and CD4 counts of less than 200 cells/µl.

The radiological evidence of active TB in 30% of our patients confirms previous results.[10] The correlation between cavitatory TB and smear positivity is well documented.[19] Four of the six patients with mediastinal lymphadenopathy were HIV positive. Generalised lymphadenopathy was noted in more than half of the HIV-positive patients in the current study and is related to B-cell and CD8 T-cell hyperactivity caused by HIV.[20] Individuals with dual infection of TB and HIV are particularly prone to significant mediastinal lymphadenopathy.[18,21-24]

Conclusion

In developing countries, where TB is usually more prevalent than in industrialised nations, CXR plays an important role in the identification of large pericardial effusions. This study demonstrated that the degree of radiographic cardiomegaly correlates well with the amount of pericardial fluid aspirated at the time of pericardiocentesis. CXRs also contribute to the diagnosis of active TB. The presence of mediastinal lymphadenopathy indicates the possibility of co-infection with HIV. Although sonography will still be required for a definite diagnosis, the results of this study show that CXR is a useful screening tool.

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