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Transient Constrictive Pericarditis: A Recent 2 Countries Study

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ABSTRACT

Background: Constrictive pericarditis (CP) is a disease of the pericardium that leads to impaired diastolic filling of the heart. The treatment of such a disease entity is known to be purely surgical by pericardiectomy.

Patients and methods: This is a prospective, analytical non-randomized study conducted during the period from January 2014 to November 2020. 34 cases of constrictive pericarditis were referred to us for management; 12 of them (35.29%) had a classic picture of definite constrictive pericarditis with areas of calcifications and typical symptoms of constrictive pericarditis (group A). 22 cases (64.71%) had typical symptoms but they responded to medical treatment with complete resolution of the pathology and symptoms (group B).

Results: In group A, the mean age was 37 ± 12.3 years. They were treated with pericardiectomy via median sternotomy. 2 cases had persistent symptoms; there was no mortality operative or post-operative. 4 of them were TB positive. In group B, the mean age was 42 ± 14.1years. All were treated medically and resolved totally. All were preceded with influenza like symptoms or chest infection with bilateral pleural effusion and all were TB negative. Biopsies were taken from the pericardium revealing nonspecific reaction.

Conclusion: There was an entity of constrictive pericarditis, which is known as transient constrictive pericarditis. It is a different pathology which is mostly autoimmune. It responds to medical treatment. There was no calcification, it might be recurrent and is associated with variable amounts of pericardial effusion and bilateral pleural effusions.

Keywords: Constrictive pericarditis (CP), Transient CP, Classic CP.

INTRODUCTION

Constrictive pericarditis (CP) is a pericardial disease process characterized by the development of right sided heart failure secondary to impaired diastolic filling of pericardial etiology despite preserved right and left ventricular myocardial function. CP can be classified into three different subtypes including transient CP, effusive CP, and chronic pericardial constriction. In fact, overlap may present between these distinct subtypes. Transient pericarditis was first described in 1987 when a case series of 16 patients with pericardial constriction were proven to have permanent resolution of constrictive pathophysiology by echocardiography after an average of 2.7 months spontaneously (range of 12 days to 10 months) [(1, 2, 3)].

In 2015 the European Society of Cardiology (ESC) addressed the transient constrictive pericarditis as a variant of CP. The main effect of constrictive pericarditis is the impedance of the diastolic filling (biventricular) of the heart leading to low cardiac output (COP) and congestive heart failure, which is reversible even spontaneously, regardless of the cause [(1)]. Constrictive pericarditis is caused by fibrosis of the parietal pericardium and sometimes affects the visceral pericardium too. It might be acute, subacute or chronic but what characterizes that pathological entity is fibrosis, calcification, loss of elasticity and fixity of the pathology [(2)].

In the 1980s, **Hancock [(3)]** described that kind of pathology but within the context of the classic one, attributing this elastic form as acute or subacute reversible inflammation. In his opinion it was a step in the same pathological entity. But later in 1987 **Sagrista-Sauleda and his colleagues [(2)]** described the transient constrictive pericarditis as a separate entity not as a phase of the classic constrictive pericarditis describing it in 9%-17% of all cases of pericarditis with effusion that resolved on medical treatment only. Patients of transient CP were mostly idiopathic or attributed to viral infections. The patients they followed had no other similar attacks with no eventual constriction, fibrosis or calcification of the pericardium. They attributed the pathology to inflammation, edema and fibrin deposits. **Sagrista-Sauleda and colleagues[(2)]** did not report recurrence in 31 months follow up period but they did not emphasize on the single attack nature of this disease but they declared a three phases evolutionary pattern; phase 1, no constriction and moderate effusion, Phase 2, decreased amount of effusion and constriction, and Phase 3, normal pericardium and normal hemodynamics. Other authors reported cases following viral infection, autoimmune diseases, bacterial infection and idiopathic. All authors denied radiation therapy correlation to transient CP. Others proposed causes of transient CP might be malignancy, trauma, collagen vascular diseases or post-pericadiectomy [(4, 5)]. Despite most authors reporting good

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recovery with medical treatment yet all stated the necessity of surgical pericardiectomy if there was no response to medical therapy. The medical therapy of such cases includes non-steroidal anti-inflammatory drugs (NSAIDs), steroids, diuretics, antibiotics and chemotherapy or combination of colchicines and NSAID. It is reported also that some cases resolved spontaneously without medications. Pericardiectomy is reserved only for refractory symptomatic cases [6].

The diagnosis and follow up is usually by the echocardiography and the computed tomography (CT) scan of the chest but some authors reported magnetic resonance imaging (MRI) diagnosis as the Gadolinium contrast accumulates in the areas that have inflammations and fibrosis [7]. Multimodality imaging was recently recommended by the American society of echocardiography to diagnose transient CP. By priority they stated that echocardiography then the CT and finally the MRI. As the CP might involve many subspecialties like oncology, rheumatology, cardiology, emergency medicine (ER) and infectious diseases as the etiologies are variable and the symptoms too. Those physicians should be involved in the discussion of such cases. The treatment starts by NSAIDs with colchicine. If the case is refractory; steroids were added. Surgical pericardiectomy is better avoided as the inflammation is acute and there are exudative adhesions with no clear planes and unfavorable outcome of surgery. Triple therapy may be required some times to avoid fixed constriction or recurrence [6, 8]. Such cases might be diagnosed properly before any surgical interference with sternotomy pericardiectomy by using video assisted thoracoscopy for pleural or pericardial biopsies [9].

Objective: In our practice we faced the problem of the typical form of constrictive pericarditis (classic) and the solution was surgical, but we noticed many cases of transient constrictive pericarditis too. These cases were of an acute, not an insidious onset. Their course is different from the progression of typical constrictive pericarditis. We performed this study to delineate the difference between the 2 types.

PATIENTS AND METHODS

Data of 34 cases of constrictive pericarditis were reviewed in Saudi German Hospital, Madinah, Kingdom Saudi of Arabia (KSA), and in Cairo University Cardiothoracic Surgery Department. All the 34 patients presented with tachycardia and hypotension and congested neck veins. Constrictive pericarditis clinical and echocardiography features were elicited. Careful history taking and thorough clinical examination were primarily done. All patients were investigated for Tuberculosis (TB) by sputum culture for acid fast bacilli, tuberculin and Polymerase Chain Reaction (PCR), complete blood picture (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and kidney and liver profiles. All patients were submitted for plain chest X-ray CXR (postero-anterior and lateral views), CT chest and abdomenopelvic ultrasonography. All were investigated ECG 12 leads, transthoracic echocardiography, central venous pressure (CVP) line and invasive monitoring of the arterial blood pressure. All patients were investigated for autoimmune diseases (Anti-Cyclic Citrollinated Peptide (Anti-CCP) was normal. C-ANCA and p-ANCA were normal. Anti DNA –ABS and A.N.A. were all normal.

We classified the 34 patients into two groups. Group A (12 patients) who had clear history of gradual onset and progressive course of unresolving signs and symptoms of cardiac constriction and necessitated pericardiectomy as the clinical condition did not improve with anti-inflammatory medications. Group B (22 patients) had sudden onset of symptoms and signs with previous history of upper respiratory (mostly viral) infection or chest infection and they did not show pericardial calcifications with radiological investigations. They responded to medical treatment with relief of the clinical condition.

All patients of group A were submitted for pericardiectomy via median sternotomy. Heart lung machine was used in all patients as standard procedure. We started to dissect the aorta and the left ventricle then the right side and the SVC finally the IVC. The pericardium is a double layered sac, outer fibrous tough and inner smooth mesothelial serous two layered; visceral and parietal layers and in between the pericardial cavity. The outer parietal layer is continuous with the inner layer of the fibrous pericardium. Both the fibrous pericardium and the parietal part are attached to the surrounding structures by the sternopericardial ligaments, the vertebra-pericardial ligaments and the phrenopericardial ligaments [10].

Group B patients had history of symptoms of common cold or flu just before the emergence of symptoms. They all received medical treatment in the form of indomethacin 150 mg/day with aspirin 600mg/tds for 10 days with clinical improvement. The second line we started after no or little improvement clinically and by CT picture with steroids in the form of initial IV hydrocortisone sodium succinate (Solucortef) 100 mg/12 hours for 3 days, then regular prednisone 10 mg/8 hours then maintenance dose of 15 mg/day on divided doses. Bisoprolol 2.5 mg/12 hours and lasix 40 mg IV/24hours were also given. The steroids were taken for 2 weeks after hospital discharge then gradually tapered and replaced by colchicine 0.6 mg/day regardless the meal. Patients tolerated the colchicine with no gastrointestinal tract (GIT) problems. 14 patients of group B were submitted for thoracoscopic pericardial biopsy before start of medical treatment. Pericardial multiple biopsies from

different pericardial sites were examined histopathologically and were non-specific.

Ethical consent:

An approval of the study was obtained from Cairo University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent-samples t-test of significance was used when comparing between two means. Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters. The confidence interval was set to 95% and the margin of error accepted was set to 5%.

RESULTS

In group A (typical constrictive pericarditis), all the 12 patients were males. The mean age was 37 ± 12.3 years. They had lower limb edema, mild ascites, hepatomegaly, normal CBC, elevated liver enzymes and high bilirubin level. They had typical symptoms with raised CVP in some more than 20 cm water. 6 of them were positive for TB. All had calcified areas of the pericardium proved by X-rays and echo. Histopathological examination revealed non-specific inflammatory process with areas of calcifications. All were negative for autoimmune tests. After pericardiectomy, 10 patients immediately showed a decrease in CVP and improved cardiac output. The CVP remained relatively high in all patients (above 10 cmH_2O) even though they were well dehydrated.

Patients of group B were 22 cases. 18 cases of them were females and 4 were males. The mean age was 42 ± 14.1years. All had clinical history of recent common cold and chest infection symptoms without leucocytosis some times as shown in table (1 & 2). Mostly, the symptoms progressed to severe chest tightness and tachycardia. Initial plain CXRs were done and were normal [Fig. 1]. So the patients were reassured and went home. They came again to ER with severe respiratory distress, atypical chest pain and tachycardia with fever and mild lower limb edema. They were admitted in the cardiac care unit (CCU) and transthoracic echocardiography was done revealing thickened pericardium without being tamponading, mild pericardial effusion with diastolic filling impairment. Despite cardiac magnetic resonance (CMR) being accurate in diagnosis of CP yet it is costly and was not performed routinely, as we already diagnosed the condition by echo and CT chest. The CT chest revealed markedly thickened pericardium reaching 18 mm-22 mm with little pericardial and bilateral pleural effusions [Fig. 2]. Arterial line and CVP were inserted showing systolic BP around 90-100 mmHg. The CVP was 15-20 cmH_2O. ECG showed diffuse concave elevated ST-segment with little rise of the troponin. Later the ECG had low voltage tracing. Tuberculin was negative, PCR was negative too. Blood gases were within normal and normal electrolytes. CBC showed increased total leucocytic count (TLC) in some patients. Coagulation profile, albumin and proteins were all normal. The thyroid profile was normal. ESR was double the normal and the CRP was significantly as high as 159 mg/L (normal < 5mg/L).

Immunological investigations namely Anti-cyclic citrollinated peptide (Anti-CCP), C-ANCA, p-ANCA, Anti DNA –ABS and A.N.A were all normal.

Clinically the patients of group B improved with complete clinical and radiological remission after one to two weeks [Fig. 3]. Those patients were discharged on Bisoprolol 2.5 mg/12 hours, aspirin 300 mg/OD, colchicine 0.6 mg/day and proton pump inhibitor. The patients remained clinically free of symptoms after 2 months of follow up then 2 females of group B experienced another similar attack while they were on colchicine and aspirin [Fig. 4]. They were admitted with the same line of management. Both improved after one week of admission. Clinically, echocardiographically and CT chest were free [Fig. 5]. The patients were discharged on colchicine 1.6 mg/day divided doses plus aspirin 600 mg for 2 months then colchicine alone 0.6 mg for another 2 months. The follow up for almost one year revealed no recurrence with thin normal pericardium.

14 patients in group B were submitted to thoracoscopic pericardial biopsy as the diagnosis at the time of presentation was controversial. Results were non-specific inflammatory reaction of the pericardium. All group B patients had effusive pericarditis and bilateral pleural effusion which was mild.

Table (1): Pre-op clinical data

	Group A (12 cases)	**Group B (22 cases)**
Age (mean)	37 ± 12.3 years	42 ± 14.1 years
Sex	12 males	18 females 4 males
Chronicity	All	None
TB	6 cases	None
Uremia	2 case	None
Idiopathic	4 case	All cases
Constrictive symp. NYHA class (before) NYHA after Limb edema Ascites	All III-IV I-II All patients All patients	All II-III l 8 patients None

Table (2): Pre-op investigations

	Group A.	**Group B.**
Plain CXR	Calcifications	Not conclusive
CT chest	100% diagnostic non-effusive.	100% diagnostic All effusive
Echo	Diagnostic.	Diagnostic
Lab	Raised ESR and CRP Altered liver functions in 8 patients	Raised ESR and CRP Liver functions altered in 2 patients only
Autoimmune tests Mortality Morbidity	Not performed. None Residual constriction in 2 cases.	Negative. None Recurrence in 2 cases

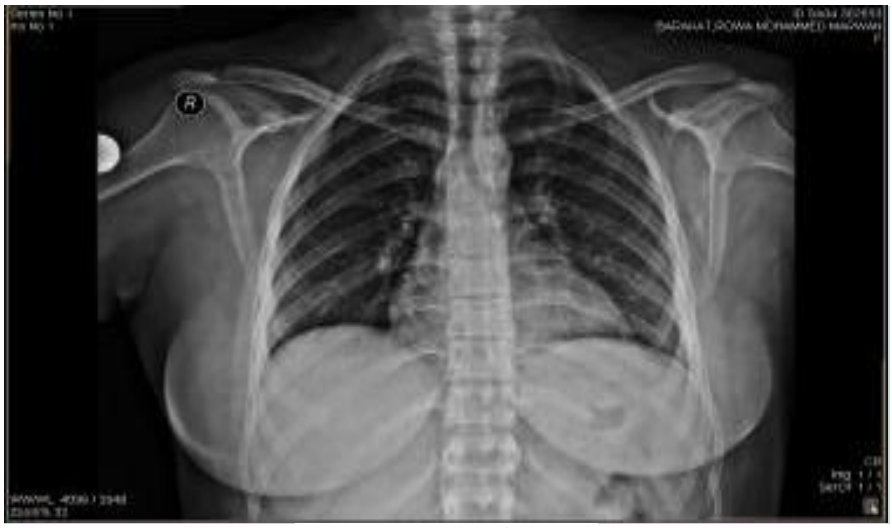

Fig. (1): Normal findings.

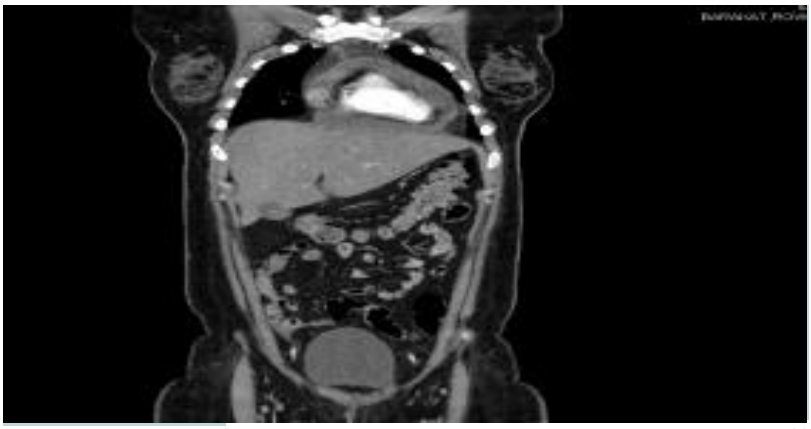

Fig. (2): Mild pericardial and bilateral pleural effusion.

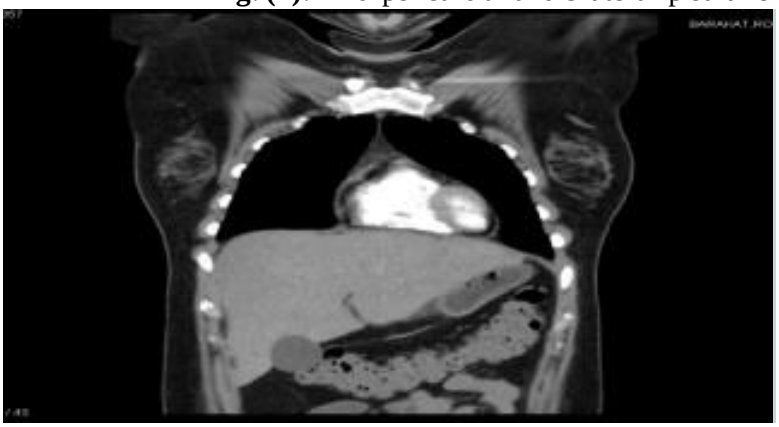

Fig. (3): Radiological remission.

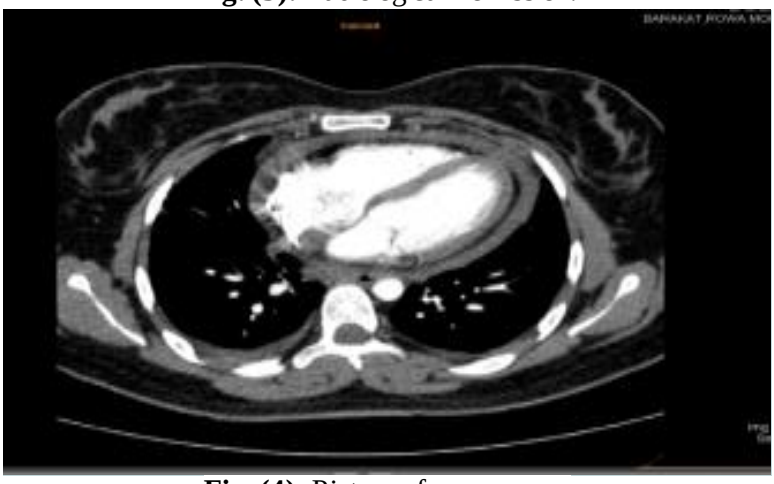

Fig. (4): Picture of recurrence.

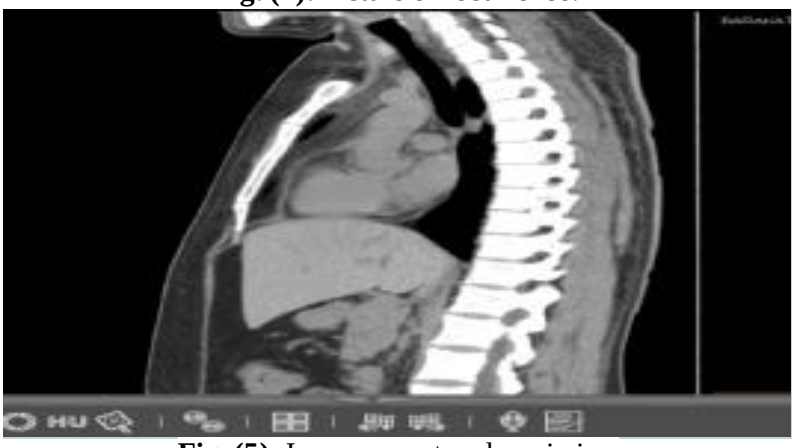

Fig. (5): Improvement and remission.

DISCUSSION

Though there are acute and subacute forms of constrictive pericarditis yet the definition states that it is a chronic inflammatory process, often characterized by chronic scarring, fibrosis and calcification of the pericardium associated with diastolic dysfunction, eventually leading to low cardiac output and heart failure [(11)]. The main etiologies of chronic CP are post cardiac surgeries (24%), idiopathic (21%) malignancy (13%), radiations (11%) and other causes (11%). The acute forms constitute 20% of cases [(12, 13, 14, and 15)].

In our study, we could identify two categories of CP, the classic type and the transient type. In our practice we could diagnose and treat 22 cases of such category over 6 years. Most of them were females (18 cases). There was no specific preferred age of this entity and it occurred in patients ranged in age between 34 and 68 years old with female preference. While in the classic type the incidence was more in males (3:1 male to female ratio), the age range was so wide from 10 to 60 years old and this was similar to work of others [(16)].

In group A 50% were tuberculous while in B, no evidence of TB. Some authors reported up to 60% tuberculous cases in the classic type [(16, 17, 18)].

The NYHA class of dyspnea was more in the classic type up to class IV, and improved to class I to II after pericardiectomy. In the transient variety the NYHA was II to III and resolved totally after complete remission with medical treatment. Other authors reported same results [(16)]. The liver functions were altered more in group A than B and this is mostly due to the chronicity and more cardiac encasement [(16)].

In the transient type, bilateral pleural effusion also disappeared after complete recovery. In all cases there was no ascites but lower limb edema was minimal and occurred in 16 patients (72.72%). While in the classic type all had ascites and significant lower limb edema. The reason may be attributed to the degree of constriction and the chronicity.

In group A (classical type), the earlier the pericardiectomy the better the results [(16)]. The technique of pericardiectomy was via median sternotomy in all patients while some other authors described different techniques with controversies of the outcome due to completeness of the resection and release of the heart, some described the left antero-lateral thoracotomy or the bilateral thoracotomy. We support the standard median sternotomy which is more reliable [(16)].

In all the cases of both groups the diagnosis was feasible by plain CXR, CT chest, ECG and echocardiography. We did not need to do cardiac MRI or cardiac catheterization. The plain CXR was conclusive in group A cases due to the calcification, which existed in all cases. While in group B it was not of any value.

Cases of group B were only diagnosed by echocardiography and CT chest. In patients of group B the pericardium was significantly swollen and there was effusion in all cases, all of them had pleural effusion and they responded to medications within 1 to 2 weeks with complete remission. The recurrence was reported in 2 cases. **Sagrista-Sauleda *et al.*** [(2)] first described this category and suggested that the mechanism responsible for the findings in these patients were transiently thickened and inelastic pericardium resulting from edema, fibrin deposition, or inflammation. They also noted a characteristic three-phase evolutionary pattern of constriction. This might explain the difference in the severity of symptoms between both groups. The 3 phases described were as follows: Phase 1; Moderate pericardial effusion with no constriction, phase 2: constrictive pathology where the effusion started to decrease, and phase 3: Normalization.

In our cases of group B, we only noticed the inter-phase between 1 and 2 at the first presentation of the patients. We had recurrence recorded while others had none reported [(2)]. We performed the possible autoimmune markers for group B patients to confirm any evidence of autoimmunity, yet all were negative. Other authors suggested an autoimmune-mediated mechanism post viral infection and we support this theory as all group B patient were preceded by viral or bacterial upper respiratory tract infection [(3)]. We followed the regimen described in other literatures for group B [(19, 20)].

It was wise before rushing to pericardiectomy, which is a considerable mortality and morbidity operation to give a chance for patients with constrictive pericarditis especially if the congestive symptoms are not massive and there were no calcifications in the thickened pericardium. The possibility of transient type in cases of constrictive pericarditis should be born in mind, especially if its features are evident and we should try medical treatment first [(4)].

CONCLUSION

Recent advancements in diagnosis and treatment have created a renewed interest in transient CP, following its recognition as a sub-type of pericardial constriction in the updated 2015 ESC Pericardial Disease guidelines. The diagnosis and management of the transient type of constrictive pericarditis gained popularity. Similar to other types of constriction, it typically presents with right heart failure secondary to pericardial-induced jeopardized diastolic filling. But, in transient CP, the mechanism of impaired pericardial function and thickening is essentially related to acute or sub-acute inflammation, rather than fibrosis or calcification. Perhaps cardiac MRI is gaining acceptance as a modality of choice in diagnosis but in our work echocardiography and CT were enough. The

management of transient type is essentially medical with favourable outcome while that of classic type is surgical pericardiectomy, which is almost always through median sternotomy.

Abbreviations:

ANA	Antinuclear antibody
Anti DNA-ABS	Anti-double stranded antibodies
CANA	Complement-fixing antinuclear antibodies
CBC	Complete Blood Picture
CCU	Cardiac Care Unit
CMR	Cardiac Magnetic Resonance
COP	Cardiac Out Put
CP	Constrictive Pericarditis
CT	Computed Tomography
CRP	C Reactive Protein
CXR	Chest X-Ray
ER	Emergency Room
ESR	Erythrocyte Sedimentation Rate
GIT	Gastrointestinal tract
KSA	Kingdom Saudi Arabia
NSAID	Non-Steroidal Anti Inflammatory Drugs
P ANCA	Perinuclear anti-neutrophil cytoplasmic antibodies
TB	Tuberculosis

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