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Severe calcific constrictive pericardiectomy operation: 'Hearts of stone'

Tuğra Gençpınar¹, Çağatay Bilen², Gökmen Akkaya³, Hasan Hepağuşlar⁴, Kıvanç Metin⁵, Hudai Çatalyürek⁶, Öztekin Oto⁷

Abstract

Background: Dense constrictive pericarditis, 'Hearts of stone' is a rare condition characterized by limitation of myocardium due to a massive fibrosis and calcification of the pericardium. The aim of this study was to research the literature to discuss the surgical intervention and management of densely calcified constrictive pericarditis.

Methods: Over a seven-year period, 19 consecutive patients who underwent pericardiectomy operation for severe constrictive pericarditis reviewed to determine reasons, surgical techniques, mortality and morbidity rates, and improvement of functional capacity. We freed the anterior pericardium from phrenic nerve to phrenic nerve. In two cases, we used a rongeur to break down the dense calcification. The indications for pericardiectomy were tuberculous in 4 cases (21%), idiopathic-fibrous in 11(57.8%), rheumatic in 2(10.5%), uremic in 1(5.2%), and neoplastic in 1(5.2%).

Results: Inpatients mortality ratio was 5.2% in case of isolated severe calcified pericardiectomy. Ascites in 3 patients (15.7%), hepatomegaly in 4 (21%) and peripheral edema in 15 (78.9%) were found on their physical examination. In the 1st postoperative month follow up, dramatically improvement of preoperatively functional capacity were the number of cases in New York Heart Association class IV (worse general condition) moved from 14 to II; in class III from 4 to II; in class II from to I in one case. In our all series, idiopathic-fibrous was the most frequent cause of chronic severe constrictive pericarditis, but the second most common tuberculous pericarditis was increasing overall. Postoperative and neoplastic pericarditis were rare.

Conclusion: The preoperative clinical conditions and functional status at follow-up was improved in all cases. We recommended that the orthopedic surgical instrument, 'rongeur', is very useful to cut that totally calcified tissue.

Keywords: Constrictive pericarditis, pericardiectomy, heart failure, calcification

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Introduction

Chronic calcific constrictive pericarditis is caused by massive fibrosis and calcification of the pericardium, processes that inhibit diastolic filling of the heart.[1-3] It may be idiopathic or frequently caused by viral infections, radiotherapy, thoracic and/or heart surgery. The clinical features are non-specific. Therefore, limitation of myocardium due to a rigid pericardium result to chronic heart failure. Surgical pericardiectomy is an effective intervention for dense calcific constrictive pericarditis. After surgical removal of the pericardium, diastolic filling of the heart returns into normal. Patients are potentially curable by a pericardiectomy from phrenic nerve to phrenic nerve. Yetkin et al.[2] recommend that the median sternotomy approach for chronic constrictive pericarditis and consider cardiopulmonary bypass safe to use in indicated cases.

Diagnosis can made by chest X-ray and computed tomography (CT), magnetic resonance imaging (MRI), echocardiogram (ECHO) and heart catheterization that can showed anterior chest wall calcification like calcified pericarditis. Goel et al [1] have demonstrated that standard chest CT-scan allows a nice anatomic delineation of the pericardium and its calcifications. Furthermore, computed tomography best defines the often asymmetric degree of pericardial thickening or calcification, which may be important in determining the optimal surgical approach for pericardial resection.

Methods

We reviewed the cases of 19 patients who underwent pericardiectomy operation via median sternotomy for severe constrictive pericarditis, "Hearts of stone" between January 2008 and July 2015, to determine causes, treatment options of surgical techniques, mortality and morbidity rates, and improvement of functional capacity. In all patients who has admitted to our clinic for the surgical therapy, cardiac evaluation confirmed constrictive pericarditis. All cases presented with dyspnea on exertion and easy fatigability.

In all cases, the operation was performed thorough median sternotomy. We freed the anterior pericardium from phrenic nerve to phrenic nerve. In two cases, the severe calcified pericardium around both ventricles was so hard to contract because of dense calcified tissue which adhered to the myocardium. Different seizers failed to cut due to severe calcification and adhesion. Therefore, we employed a rongeur to peel off the calcified pericardium gently around the right and left ventricles which performed without the usage of extracorporeal circulation.

The primary outcomes were the risk factors including advanced age, sex, smoking status, hypertension, hyperlipidemia, carotid disease, diabetes mellitus, prior cardiac events, chronic obstructive pulmonary disease, peripheral vascular disease, neurological events, HbA1c levels, and serum creatinine levels. The secondary outcomes were of preoperative New York Heart Association (NYHA) heart failure functional class and left ventricular ejection fraction. Other outcome measures were perioperative death (in hospital) and intensive care unit vital follow up. In all calculations and statistical analyses, "Statistical Package for Social Sciences" (SPSS-Chicago, IL, USA) 16 and Software Excel (Microsoft-USA) programs were used. The statistical results are presented as mean values.

Results

During the 7-year period between January 2008 and July 2015, we performed pericardiectomy operation thorough median sternotomy on 19 cases with a diagnosis of constrictive pericarditis. The cases consisting of 9 female (47.3%), 10 male (52.2%) were found. 19 cases with an average age of 56.57 years (min: 35, max: 85) (11.23 SD) have been observed.

Ascites in 3 patients (15.7%), hepatomegaly in 4 (21%) and peripheral edema in 15 (78.9%) were found on their physical examination. The cases operated on within 2 months after the onset of symptoms. Laboratory results found hyponatremia, hypoproteinemia and hypoalbuminemia in all cases. The mid-term survival was satisfactory. There was no any neurological complication (postoperative major adverse cardiovascular and cerebral event (MACCE) during pericardiectomy operation. Comorbidities related to the patient group were the diabetes mellitus in 1 case (5.2%) (Insulin dependent-HbA1c median ratio 7.78) and the hypertension in 3 cases (15.1%). There was 1 case (5.2%) with atrial fibrillation. None of the cases had concomitant coro-





nary artery disease. Chronic Obstructive Pulmonary Disease was observed in 1 case (5.2%). Alcohol use was not found. Smoking was observed in 8 patients (42.1%). Preoperatively, four of the 19 patients (21%) had needed pericardiocentesis. These patients had taken diuretics and digitalis at optimal doses for heart failure.

Inpatients mortality ratio was 5.2% (1 case in tuberculous pericarditis, 85 years old) with multiple organ failure and low cardiac output. No patients had required a mechanical circulatory support or dialysis. Prolonged ventilatory use (≥24 hours), mediastinal re-operation for hemorrhage, sternal wound infection, or mediastinitis had not been put forth. The average intubation time was found to be 1.05±5.1 hours. Postoperative periods were uneventful. Computed tomographies and chest X- rays were normal (Figure 1-2) Normal cardiac functions were revealed by serial echocardiography that showed left ventricular ejection fractions were about 50% globaly and left and right ventricular hypokinesia in all cases.

There founded none evidence of phrenic nerve injury. We had not used to placed emporary pacing wires or Intra-aortic balloon counter-pulsation (IABP). There was no need ventricular defibrillation. The patients maintained normal life activities and discharged in five days. In the 1st postoperative month follow up, dramatically improvement of functional capacity were the number of cases in NYHA class IV (worse general condition) moved from 14 (preoperatively) to II; in class III from 4 to II; in class II from to I in one case. The

Table 1. The demographic characteristics of the cases (n=19)

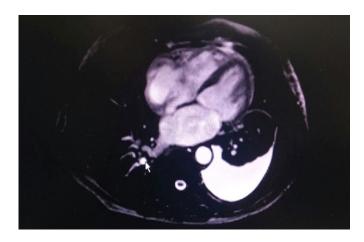
	56.57±11.23			
Mean Age (yr)	(min: 35, max: 85)			
Female	9 (47.3%)			
Mortality	5.2%			
	n	%		
Current Smoker	8	42.1		
Hypertension	3	15.1		
Diabetes (HgA1c ≥7 mg/dl)	1	5.2		
History of Myocard Infarction	-	-		
Chronic Obstructive Pulmonary Disease	1	5.2		
Peripheral Vasculary Disease	1	5.2		
Coronary Artery Disease	-	-		
Atrial Fibrillation	1	5.2		
Neurological complication (MACCE)	-	-		
Ascites	3	15.7		
Hepatomegaly	4	21		
Peripheral edema	15	78.9		

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Figure 1. CT angiography image of dense constric- Figure 2. Post-operative X-ray image tive pericarditis





chronic constrictive pericarditis were tuberculous in 4 cases (21%), idiopathic-fibrous in 11 (57.8%), rheumatic in 2 (10.5%), uremic in 1 (5.2%), and neoplastic in 1 (5.2%) (Table-2).

Standard anticoagulant therapy (acetyl - salicylic acid 100 mg/day) was given. Mean duration of intensive care unit (ICU) was 3.9/day, and the duration of hospital stay was 5.2 days. Blood drainage was about 3.31/liter. Both erythrocyte replacement (average 2.89/ liter) and fresh frozen plasma were used for bleeding. There was no need for early repeat pericardiectomy or re-exploration.

Discussion

Dense chronic constrictive pericarditis was previously described in 1842 by Cheever. [2] Severe calcific constrictive pericarditis give rise to increase both ventricular end-diastolic pressures and a decrease in out-

Table 2. Comparison of pre-post operative NYHA class

NYHA Class	Preoperatively (%)	Postoperatively (1st month) (%)		
I	-	1 (5.2)		
II	1 (5.2)	18 (94.7)		
III	4 (21)	-		
IV	14 (73.6)	-		
NYHA: New York Heart Association Class				

flow volume.[1-5] Pericardiectomy is the only treatment option for calcified pericardium.^[3-7] Pericardiectomy is a safe surgical approach with available techniques. [6-8] Cases typically present with symptoms of both sided heart failure which including dyspnoea, orthopnoea, easy fatigability, hepatomegaly and ascites. Most common causes are tuberculosis, viral infection, previous cardiac surgery, radiotherapy, idiopathic, sarcoidosis and rheumatic diseases.^[7-10] In approximately 50% of cases, chest X-ray and computed tomography are used to demonstrate dense calcification of the pericardium. [2-4] The echocardiogram and heart catheterization are important for diagnosis that visible pericardial calcification on chest region.[10-12]

During the 7-year period, anterior pericardium was resected from phrenic nerve to phrenic nerve. We freed the anterior pericardium first from the aorta and the left ventricular outflow tract as supported by literature.[12-15] After that, the both ventricles and finally venae cavae was resected. None of patient required cardiopulmonary bypass. In two cases, the calcified pericardium around both ventricles was so hard to contract because of calcified tissue which adhered to the myocardium. Different seizers failed to cut; therefore we used a rongeur to break down the calcification (Figure 3). This orthopedic surgical instrument was very useful to cut that totally calcified tissue which is of about 8 mm thickness. Rongeur was applied to gouge out pericardium in small pieces. The tricky point is not to create sharp ends during step by step biting of pericardium in order to avoid penetration. We offer that a rongeur is very useful for peeling off the





densely calcified pericardium.

We avoided electrocauterization to prevent thermal dysfunction. Also, phrenic nerves protected. Surgical loops (Design for Vision *3.5, US) were used during dissection and the operation. For an excellent exposure, an additional deep pericardial retraction suture was used. The pericardiectomy field was irrigated with 0.1 ml/sec flow %0.9 saline solution to aspirate microparticles. All patients were followed up by serial echocardiography which showed improvement. Also, nor late recurrence or mediastinal re-exploration was found.

In our research series, idiopathic-fibrous is the most frequent reason of chronic constrictive pericarditis (57.8%), but the second most common tuberculous pericarditis (21%) is soaring overall. Postoperative and neoplastic pericarditis are rare. Yetkin et al.^[2] have demonstrated that in developed western countries cases of uremic, postoperative, and neoplastic pericarditis are increasing. In order to maintain hemodynamic stability, we recommend early surgical intervention. Also, tuberculosis or neoplastic cases must be continued their specific medical treatment.

Hirai et al.^[8] detected that using an 'Ultrasonic Scalpel' is a useful method for treatment of chronic constrictive pericarditis, and advocate the use of the Ultrasonic Scalpel for a safe and easy pericardiectomy. The scalpel,

Figure 3. CT angiography image of dense constrictive pericarditis



curette, and rongeur are used for gouging out bone in neurosurgery and orthopedic surgery. Regarding the surgical treatment of severely calcific constrictive pericarditis, a rongeur can also be used in dissection of severely calcified pericardium. Another difficulty in cases, we used rongeur previously. We offer that a rongeur is very useful for peeling off the densely calcified pericardium. Phrenic nerve-during pericardiectomy must be protected. Global left ventricular regional wall motion should be observed carefully during the surgery.

Also, experienced surgical approach is essential for successful severe calcific pericardiectomy. In order to maintain hemodynamic stability; careful manipulation of the heart and pericardial incision, intra-aortic balloon pump and pacing wires preparation, pharmacological interventions, and anesthesia monitoring are very important. Inotropic agents are essential to maintain cardiac output during the manipulations. In addition, the availability of heart-lung machine and perfusionist are necessary for temporary support. The follow-up is required with a great experience. Fluid and electrolyte balance must be protected during the operation and intensive care unit.

Conclusion

Surgical treatment of severely calcific constrictive pericarditis has been shown to improve hemodynamic stability and can safely improve heart function. The preoperative functional status at mid-term follow-up was improved in all cases. Difficulty in cases, a rongeur may useful to gently peel off the calcified pericardium around the right and left ventricles. The article highlights the importance of considering different instruments in those research.

Study Limitations: The primary limitation of our study is the lack of access to patient records before 2008. Long-term follow-up and large-scale prospective studies are needed to determine the frequency of severely calcific constrictive pericarditis.

Research Article





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Importance of renal dysfunction in the mortality of acute coronary syndrome patients

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Abstract

Background: Ischemic heart disease is an important death cause in Brazil. The Acute Coronary Syndrome is a subset of signs and symptoms which represents an acute complication of ischemic heart disease. Many of these patients have common risk factors, including renal dysfunction. The analysis of the importance of this commitment in the event of outcomes is still little explored in our midst.

Objective: To study the associantion between renal dysfunction and the occurrence of deaths in patients with Acute Coronary Syndrome, Methods: This is a analytical study, with patients admitted to the Coronary Care Unit of a Tertiary Hospital (Salvador / BA) diagnosed with acute coronary syndrome, in the period from 2011 to 2014. The patients were divided into three groups according to renal function and two groups according to clinical diagnosis.

Results: We identified six hundred seventy-four (n = 674) individuals. Mean age was 69.6 ± 12.4 years and 50.7% (n = 342) were male. Regarding the clinical diagnosis, 49% of patients (n = 331) were diagnosed with Unstable Angina and 50.9% (n = 342) with Acute Myocardial Infarction. The average value of creatinine clearence rate was 63.2 ± 29.3 ml / min (p = 0.001). Conclusion: The severe renal dysfucntion is an important prognostic factor for development of coronary artery disease and was associated with bad prognosis of patients with ACS. The variables DM, hypertension and dyslipidemia were often associated in theses patients.

Key words: Acute coronary syndrome; renal insufficiency; glomerular filtration rate.

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Introduction

Recently, cardiovascular diseases (CVD) are an important cause of mortality and disability in the World^[1], in Brazil^[2, 3] and Bahia.^[4] Ischemic heart disease can develop multiple outcome.^[5] It can remain asymptomatic for a lifetime, can evolve for an Acute Coronary Syndrome (ACS), a chronic disease or sudden death.^[2, 6]

Epidemiological data demonstrated that SCA is an endemic disease.^[7] It is estimated that about 83 million adult United States population develop at least one type of cardiovascular disease.^[5] Of this total, about 15 million had coronary heart disease and in 2010 and of the total number of deaths recorded, 32% were cases related to cardiovascular disease.^[5,8] On Brazilian scene, the figures reveal that the situations are similar. The prevalence of coronary artery disease in Brazil adult population is around 5 to 8% and about 32% of the population died due to cardiovascular problems.^[4]

Kidney disease (KD) is a major systemic condition and constitutes common final pathway of many different diseases of the kidney and urinary tract, [9] characterized by the renal failure function.[10] Based on creatinine clearance values (CrCl), renal function can be divided into mild impairment (CrCl> 60 mL / dL), moderate (CrCl 30-60 ml / dL) and severe (CrCl \leq 30 mL / dL), with a subgroup represented dialytic patients dialíticos. [10] Kidney disease is associated with risk factors that include: advanced age, male gender, hypertension, diabetes mellitus (DM), smoking and family history of CVD,^[5] which are similar to the factors risk for ACS. [1] Thus it is not unusual that there is an association between ACS and kidney disease. The KD is associated with increasing mortality, since patients with mild to moderate degrees of renal impairment is showing worse prognosis of ACS when compared to those with preserver normal renal function.[11]

ACS is responsible for high costs in health care and the implementation of public and private politics that reduce these numbers depend on the understanding of studies to accurately reflect the strategy diagnoses and therapeutic.^[12] Knowledge about interventions that promote reduction in the incidence of CVD is a constant challenge.^[13] Risk factors for ischemic heart disease are not properly documented in Brazil^[14] and

analysis of the clinical outcome of these patients is varied and there are few studies done on the subject.

Methods

Study design and sample selection

Consecutive patients admitted to the Emergency Ward and thereafter admitted to the Coronary Care Unit of the Hospital Português (Salvador, Bahia, Brazil) with a diagnosisof unstable angina (UA) or acute myocardial infarction (AMI) with ST segment elevation (SSE) and without SSE, from January 2011 to December 2014, participated in the study. We included those patients with chest pain or equivalent ischemic condition within 48 hours of admission and at least one of the three following characteristics: 1) ischemic electrocardiographic changes (T-wave inversion or ST segment depression), 2) serum markers of myocardial necrosis above the upper limit of normal, and/or 3) documentation of prior coronary artery disease.

We excluded patients with: ST-segment elevation ≥1 mm in two or more leads on the admission ECG, normal coronary angiogram, hemodynamically significant primary valvular disease (mitral and aortic insufficiency or stenosis), hypertrophic cardiomyopathy, cancer, infectious diseases, autoimmune diseases and patients suffering from recent trauma or surgery.

This study was approved by the Ethics and Research Committee of Portuguese Hospital (n°1074369). Patients information were recorded in electronic medical records. The identification information had been saved on the digital platform with the code numbers guaranteeing the anonymity of these.

Statical analysis

The baseline characteristics of the patients were summarized in four mutually exclusive groups of renal function and the types of diagnosis. For descriptive analysis, quantitative variables were represented by mean and standard deviation, where their distribution were normal, and represented by medians and interquartile ranges when the distribution was not normal. The definition of normality was made by graphical analysis and Shapiro-Wilk test. Categorical variables were represented by frequencies and percentages. In-





clusion of variables have been carefully chosen, taking into account the number of monitoring events, to ensure parsimony of the final models. Statistical analysis was performed using the chi-square test, Test T student and Mann-Whitney test.

In order to identify which factors are associated with the combined events, we used the model of logistic regression. The variables with p <0.10 were included in the model. Those that remained significant (p <0.05) were considered independent for the occurrence of the outcome in question. Any p values <0.05 were considered statistically significant. Data were aggregated using the Statistical IBM software package for Social Sciences (SPSS ®, Chicago, IL, USA), version 20.0, and presented in numbers and informative graphics.

Results

Were identified six hundred seventy-four (n = 674) patients with ACS. The mean age was 69.6 ± 12.4 years and 50.7% (n = 342) were male. Regarding the clinical

diagnosis, 49% of patients (n = 331) were diagnosed with UA and 50.9% (n = 342) with AMI. The mean (standard deviation) of the general creatinine clearance was 63.2 ± 29.3 (p = 0.001). Forty-nine percent of the patients (n = 330) had normal renal function, 39% (n = 266) moderate renal impairment and 12% (n = 79) severe renal impairment. The analyzed comorbidities, 82.9% (p = 0.004) and 57.6% (p = 0.107) of the subjects had hypertension and hyperlipidemia, respectively, whereas only 10.1% (p = 0.859) had a family history of CAD.

Among the total sample, 3% (n = 20) died during follow-up in the CCU. These subjects had mostly age (80.2 \pm 9.3; p <0.001) and showed the lowest creatinine clearance values (41.8 \pm 26.0, p <0.005). The most common diagnosis in this population was AMI without ST elevation followed by myocardial infarction with ST elevation. Hypertension and DM showed, respectively, 75% and 45% (p <0.05) among these patients. Demographic and clinical characteristics of patients are shown in Table 1.

Table 1. Demographic characteristics of ACS patients of Tertiary Hospital CCU, Salvador, Bahia - 2011 a 2014

Variable	General (n=674)	Death		P value
		No (n=654)	Yes (n=20)	
Age (years) ^a	69,6 ± 12,4	69,3 ± 12,3	80,2 ± 9,3	< 0,001
Gender (M)a	342 (50,7)	332 (50,8)	10 (50)	0,946
Hypertensio ^a	558 (3)	543 (2,1)	15 (2,7)	0,004
DM ^a	255 (3)	246 (1,8)	9 (3,5)	0,001
Smoking ^a	151 (3)	149 (3)	2 (1,3)	0,011
Dyslipidemia ^a	388 (3)	380 (2,8)	8 (2,1)	0,107
CVD familiar historic ^a	68 (3)	66 (2,4)	2 (2,9)	0,859
Admission dyagnosis ^c				0,005
Unstbale Angina	331 (49,1)	327 (50,0)	4 (20,0)	
AMI withou SSE	264 (39,2)	253 (38,7)	11 (55,0)	
AMI with SSE	79 (11,7)	74 (11,7)	5 (25,0)	
Creatinine clearance (ml/min) ^b	$63,2 \pm 29,3$	63,8 ± 29,1	41,8 ± 26,0	0,001

Data presented as mean \pm standard derivation or ou n(%); a Pearson Chiq-square Test; b T de student test;c U de Mann-Whitney test; **DM**: Diabete Mellitus; **CVD**: cardiovascular disease; **SSE**: ST segment elevationnt





Creatinine clearance values median 60mL /min (IQR 40-80) and 35ml/min (IQR 20-55) - p = 0.005 for the sample control and non-control, respectively - **Figure 1**. The lowest median CrCl values found was on the sample of patients diagnosed with SSE > 12hours and whose died (20 ml / min; p <0.005) - Figure 3. Hypertension was present in 89.9 % of individuals with severe KD and 80% mild KD (p = 0.094). Dyslipidemia was the second most frequent comorbid affecting 57.6% (p = 0.164). DM ranged from 32.9% in individuals with severe KD to 40.9% in those with mild KD (p = 0.250).

Independent predictors analysis of outcome occurring combined, the variables hypertension, diabetes mellitus, smoking and the degrees of renal function composed of losgistic regression model. The variables were selected for present value of P <0.10 or clinical relevance well documented. Logistic regression analysis identified that the clearance rate of creatinine is a significant independent predictor of combined outcomes (OR: 3.44; 95% CI: 1.827 to 6.493; p <0.001) Table 2.

Discussion

Renal dysfunction (RD) and cardiovascular disease are strongly associated and currently the RD is being considered important risk factor for ACS (15). Kidney disease, as well as ACS are commonly associated with factors such as age, sex and other clinical conditions, and lifestyle habits. One should not, therefore, fail to consider the influence of these clinical conditions in the outcome of these patients.

Corroborating previous studies^[2, 6] the prevalence of age was observed in the total sample, averaging 69.6 years (p <0.001). The prevalence between the sex-

es was not significant (p = 0.946). This finding goes against previous research findings as in Rio de Janeiro and Porto Alegre in which highlight the prevalence of males in their results. The clinical diagnosis was observed prevalence of AMI (p = 0.005) and between it the most common, regardless of evolution, was AMI without SSE, similar to that found in a study conducted in Brazil southern, but differs from study conducted in cardiac emergency, in which achieved a 60% prevalence of patients with UI. [16]

In this study, the RD was considered a factor regardless of the outcome of patients, but moderate and severe disorders were associated with worse prognosis (p = 0.001). The values documented creatinine clearances revealed that the lowest rates were among patients who progressed to death. Thus, this study complements the findings of previous studies that have shown that severe RD is an independent predictor of cardiovascular events, [15, 17] suggesting increased RD frequency in mor-

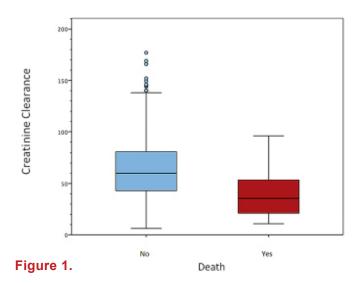


Table 2. Logistic regressino for outcome combined events. Tertiary Hospital, Salvador, Bahia, 2011 a 2014.

Variable	OR	I.C.95%		P value	
Hypertension	0,56	0,19	1,6	0,270	
DM	1,74	0,7	4,350	0,233	
Smoking	0,19	0,06	0,59	0,004	
CICr	3,44	1,83	6,493	<0,001	
DM: Diabete Mellitus; CICr: creatinine clearance; OR: odds ratio					





bidity and mortality of patients with ACS^[15, 17, 18, 25] and therefore, patients with renal impairment severe usually have worse prognosis.^[19] Patients who progressed to death had increased kidney damage, among themselves, and between the control sample was greater frequency of normal kidney function.

It is believed that some factors that compromise renal function may contribute to adverse outcomes in ACS patients. Among these factors are included insulin resistance, extracellular changes, oxidative stress and endotelial dysfunction,[18] so the RD is directly or indirectly involved in the development of hypertension, dyslipidemia, and neuroendocrine disorders important contributors to the advancement of acute coronary disease. [15] Analysis data showed that among the risk factors highlighted the massive presence of hypertension, which affected about 90% (p = 0.004) of the sample, being prevalent in the two study groups. Then, it was noted that dyslipidemia was also quite common such. DM, however, was present in most patients who died and a little less in the control group. Smoking was not so frequent in the study because most of the individuals denied the habit, but, however, the rate was similar in both groups. Another clinical condition was researched family history of CVD who remained not significant because the vast majority of patients were not aware of this information.

This study demonstrates the hypertension as the most prevalent risk factor for ACS. In the 90s, the Framingham,^[20] study's found the prevalence of hypertension were as follows: patients without disease 38%; patients who had sudden death from heart disease 63%; and patients with non-sudden death from heart disease

79%. Similarly, the study FRICAS case-control showed an association with hypertension of 53.4% among cases and 20, 8% of the controls (P = 0.000). These results confirm the importance of hypertension as a risk factor for the occurrence of ACS.

In earlier descriptive and retrospective studies, in Brazil south^[1] such as in Bahia,^[22] DM was present in about 40% of patients. In the present study, DM was recorded at 37.8% (p = 0.001) of patients going against the expectations.

In this study, smoking was found in 22.4% of patients (p = 0.011), since about 74% of patients denied the use of tobacco. This result was not expected since previous studies, such as Interheart it demonstrated that smoking, with a consumption of one to five cigarettes / day increases the risk of AMI in 40%,^[23] similar to the study data made in Porto Alegre.^[1]

The limitations on the present study relate to observational and retrospective nature of research with interpretation of clinical data. In addition, this study was a single center; so your results may not be fully extended to other populations.

It is essential to understand that many patients with ACS are also carriers of RD and the association of these two conditions can increase the mortality rate. Moreover, despite universal issues it is possible that regional variations related to demographic conditions, can influence differently, so varying from place to place. Thus, the analysis of the importance of complications in patients with ACS, allows investigation and treatment strategies are applied correctly.





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Repair of coarctation of the aorta, bicuspid aortic valve, subaortic membrane and ascending aotic aneurysm in a single session

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Abstract

10% of the coarctation of the aorta (COA) cases are diagnosed higher than 40-year of age and other cardiac pathologies accompany to 40% of these cases. The cause of mortality in 20% of undiagonised cases is the aortic rupture of ascending aorta. Aneurysm of the ascending aorta (AAA), COA, bicuspid aortic valve (BAV)and subaortic membrane were observed in a young male patient referring to our medical center with dispnea. The patient was operated and all pathologies were repaired in one single session. AAA or aortic dissections (AD) accompanying with other cardiac pathologies like BAV, ventricular septal defect (VSD) can be repaired in one single operation by an accurate surgical approach.

Keywords: Fungal endocarditis, myxoma, aspergillus

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Introduction

Coarctation of the aorta (COA) is characterized by narrowing in the descending aorta distal to the left subclavian artery. It is very common and almost accounts for 5-7% of congenital heart diseases. Nearly 85% of patients with COA have a bicuspid aortic valve (BAV).(1) Most of the patients having COA remain asymptomatic until adulthood and are diagnosed mostly on investigation for systemic hypertension. 10% of COA cases are diagnosed higher than 40-year of age and other cardiac pathologies accompany to 40% of these cases. (2,3) The cause of mortality in 20% of undiagonised COA cases is the aortic rupture of ascending aorta, and in 75% of instances, rupture occurred in the ascending aorta. (4) Although the association between COA and aneurysm of the ascending aorta (AAA) or aortic dissections (AD) has been wellknown, surgical treatment of accompanying pathologies of the ascending aorta in patients with COA have been uncommon.

Figure 1



Case History

A 19-year old male patient was referred to our clinic with a dispnea. On the physical examination 1/4 aortic diastolic murmur was auscultated. Bilateral lower extremity pulses were non-palpable. Tension arterial was 147/80 mmHg. On transthoracic echocardiography (TTE) ejection fraction was 62%, minimaly aortic insufficiency, BAV, subaortic membrane were observed and left ventricule output tract gradient was 41/18 mmHg. Aortic root diameter was 36 mm and ascending aorta diameter was 53 mm in TTE. A computerized tomographic angiography (CTA) was planned and aortic root diameter was 38 mm, ascending aorta diameter was 55 mm, arcus aorta diameter was 24 mm and distal part was 16 mm and a coarctation was observed just after the left subclavian artery origin on CTA (Figure 1,2). The patient was operated and all pathologies were repaired in one single operation. A control CTA was applied and the patient was discharged on the postoperative sixth day (Figure 6).

Figure 2







Operating Procedure

Right axillary artery and right common femoral ven were cannulated. After median sternotomy, the patient was cooled to 26 oC. The ascending aorta was aneurysmatic (Figure 3). Cardiac arrest was obtained after antegrade and retrograde cold crystalloid cardioplegia. The aorta was clamped on the distal part of the aneurysm and after aortotomy bicuspid arotic valve, subaortic membrane and aneurysmatic aorta was resected. Coronary ostiums were prepared in button shape and Benthall procedure was applied with a 25 mm mechanic prosthetic aortic valve (SJM RegentTM Mechanical Valve) and 30 mm Dacron graft. Spontaneous beat after warm blood cardioplegia and declamping was observed. The proxi-

mal part of a 14 mm Dacron graft was anastomosed to the ascending aorta graft and then the graft was passed under the left pulmonary hilus and left side of the heart and anastomosed to the distal of the coarctation (Figure 4, 5c). Total aortic x-clamp time was 160 minutes and total cardiopulmonary bypass time was 227 minutes.

Discussion

Ascending aorta and aortic valve diseases are mostly associated with COA. The main point in the pathology of COA should be the developmental abnormality of neural crest tissue causing medial degeneration and aortic dilatation. The systemic hypertension originating from COA ends up with the gradual weakening of the arterial wall and may cause AAA or AD.

Figure 3

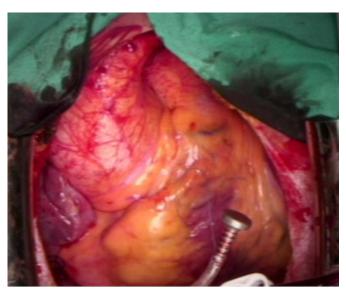


Figure 4

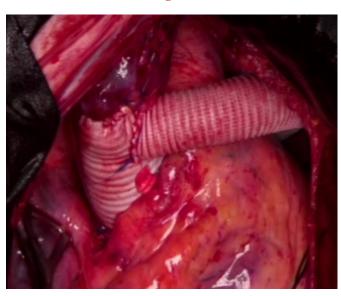


Figure 5

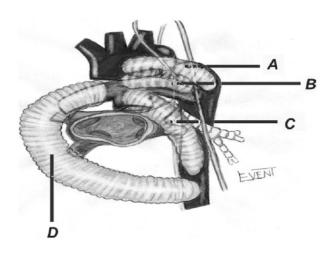


Figure 6



Demirdaş E., Atılgan K., Taşdemir O. Repair of Coarctation of The Aorta, Bicuspid Aortic Valve, Subaortic Membrane and Ascending Aotic Aneurysm in A Single Session EJCM 2016; 04 (4): 89-92. Doi: 10.15511/ejcm.16.04089.





Surgical treatment of accompanying pathologies of the ascending aorta in patients with COA have been uncommon. Lawson et al described the first successfull repair of COA and chronic AD association, which was managed with a two stage operation. In the first stage COA was repaired in order to reduce the proximal hypertension and prevent the progression of the AD, since ascending aorta replacement without the repair of COA may cause congestive heart failure and perioperative bleeding through the suture lines due to high afterload pressure. On the other hand, the increased afterload might be the cause of bleeding and haemodynamic instability in patients whose cardiac lesions are operated in the first stage.

After cross-clamping due to the increase of afterload and wall strain, atrial fibrillation and ischaemia might occur in the dilated ventricle. Also, in the distal segment of the coarctation, ischaemia might be seen due to the low cardiac output. Thus, the repair of COA and AAA or

AD in one single operation may have better results.

Another important point in the repair of COA is the extraanatomic bypass procedure. The first extraanatomic bypass was described by Siderys et al in 1974. They bypassed ascending aorta and the distal of the renal artery of the descending aorta by using a 22 mm Dacron graft. Figure 5 shows the four main procedures of the repair of COA. Using a side-clamp for the proximal and distal anastomoses of the graft for the extra-anatomic correction of coarctation prevents paraplegia, allowing the blood flow to the branches of the aorta and the intercostal arteries. (2)

In this case, we prefered to place Dacron graft above the phrenic nerve through the lateral pericardium and paid attention to avoid vagal and phrenic nerve injuries. As a result; the repair of COA accompanying with cardiac pathologies like AAA or AD, BAV, ventricular septal defects in one single operation can be managed safely.

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An useful complication of emergent pericardiocentesis procedure in cardiac tamponade: Case report

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Abstract

We present a case of 19-years-old patient was admitted to emergency service with abdominal pain, nausea, dyspnea and loss of appetite for one week and had prodromal symptoms for ten days. He was hypotensive, tachycardic and dyspneic. CT scan indicated large amount of peritoneal, pericardial and bilateral pleural fluid. With the diagnosis of cardiac tamponade; emergent pericardiocentesis (PC) was implemented by apical approach and quick hemodynamic relief was observed. It was understood that rapid haemodynamic response was a result of complication characterized by increase in left pleural fluid and decrease in pericardial effusion.

Keywords: Useful complication, pericardial effusion, pericardiocentesis procedure, cardiac tamponade.

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Case Report

A 19 years old man with a history of migraine and smoking, was admitted to emergency service with abdominal pain, nausea, dyspnea and loss of appetite for one week. The abdominal pain was worsening by standing and it was relieving by lying down. He had prodromal period symptoms for ten days. Chest x-ray revealed minimal cardiac silhouette enlargement. As computerized tomographic (CT) scan of abdomen and thorax revealed large amount of free peritoneal, 30 mm pericardial, 30 mm pleural effusion in left lung as well as 20 mm effusion in right lung, he was consulted to our department. Electrocardiogram showed sinus tachycardia. Transthoracic echocardiography (TTE) showed large circumferential pericardial effusion (PE) with right atrial (RA) and right ventricular (RV) diastolic collapse and >30% variation in mitral inflow pattern suggesting cardiac tamponade (Figure 1). He was hypotensive and tachycardic during examination; pulsus paradoxus was observed at the same time. It was concluded that the most convenient way for PC was apical approach. However collecting very small amount of pericardial fluid (15 cc), his hemodynamic profile was rapidly improved. A CT scan of thorax was taken immediately and 15 mm residual pericardial effusion was implemented; but 20 mm effusion at right and 45 mm at left lung was identified. (Figure 2). Thoracal drainage tube was inserted left pleural cavity and 500 cc hemorrhagic fluid drainage was collected. Tube was removed 2 days after, and no residual or recurrent effusion existed in his control radiologic examination. Increase in acute phase reactants like, CRP:93(0-5mg/l) fibrinogen:744 (200-400mg/dl), ESR: 53mm/h and neutrophilic leucocytosis was established in blood tests. However pericardial effusion was exudative quality; aerob- anaerob blood, urine and fluid culture was negative, no acid fast bacilli was seen in fluid, ANA, Anti-CCP, Anti-DNA and ENA profile were also normal. Colchicum 2*5mg and brufen 3*600 mg without antibiotic regimen applied as the treatment strategy. 10 days after beginning of the treatment, only 10 mm pericardial effusion at posterior wall and 8 mm at RV neighbouring found in TTE (Figure 3). He was on treatment for two months without any symptoms; rheumatologic and genetic tests are still having been done.

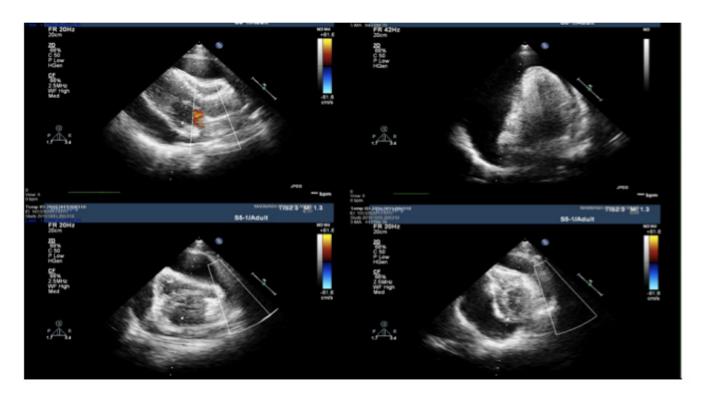


Figure-1: Echocardiographic images before procedure shows right ventricular collapse during diastole





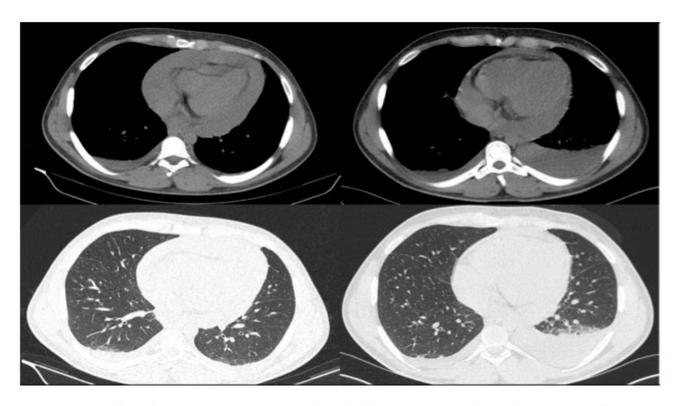


Figure-2: <u>Left side CT images were taken before PC</u>; in <u>right side images after PC</u> representing increase of <u>left pleural effusion</u>

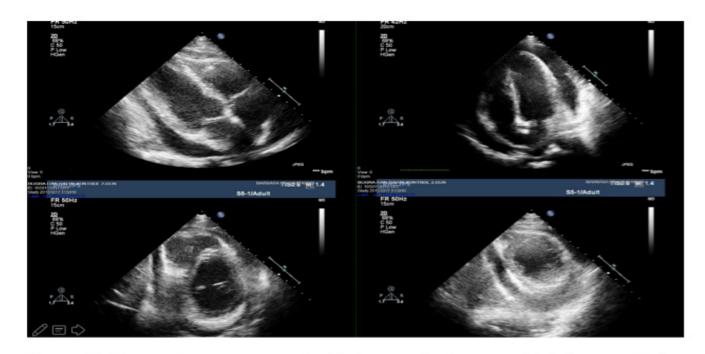


Figure-3: Decreasing amount of effusion and absence of right ventricular diastolic collapse were seen in echocardiographic images after PC





Discussion

Cardiac tamponade is a life-threatening condition and requires emergent treatment. A variety of percutaneous or surgical therapeutic methods have been applied. Pericardiosyntesis is a minimally invasive, easy to perform procedure and has relatively shorter inhospital stay and lower complication rate than surgical operation. Apical, subxiphoid and other sides are area of interest in procedure. In our clinic, most of the PC are done by apical approach with lower complication rates. In this case, a complication happened during emergent

PC which is likely to occur. Despite symptomatic and haemodynamic relief of patient, immediate echocardiographic study and CT scan was taken due to continuing of clinical suspicion. Thoracal drainage tube inserted fastly as a result of increase in left pleural effusion.

We think that increase in the amount of pleural fluid is an acceptable result confronting with the life threatening feature of tamponade. Mutual result of tamponade, haemodynamic parameters, clinical backround of patient as well as collaborative assessment of imaging techniques are contributing to the outcome.

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Right atrial aspergilloma mimicking atrial mixomax

İsmail Balaban¹, Kemal Baysal¹, Fersat Kolbakır²

Abstract

Infective endocarditis is a serious but relatively rare infection that is associated with high morbidity and mortality rates. Aspergillus endocarditis is an uncommon entity and invasive cardiac aspergillosis is a severe and extremely life threatening disease. Prolonged use of intravascular catheters, anatomical cardiac conditions, exposure to multiple broad-spectrum antibiotics, intravenous drug abuse, and previous history of surgery are the most common risk factors of fungemia and fungal endocarditis. Diagnosis is based on the isolation of etiologic agents from cardiac and blood samples or specimens from other sterile sites or positive histopathological findings of pathologic specimens. Echocardiographic findings of endocardial involvement can lead to diagnosis. Echocardiographically, differencial diagnosis of tumor extensions, especially myxoma, atipically located bacterial vegetations, thrombus or fungal masses is very difficult as thrombi and infective verrus can mimic myxomas. Treatment of fungal endocarditis only with antifungal agents is generally unsuccessful and additional surgical intervention is usually required. In this case report we present an fungal endocarditis caused by Aspergillus species that mimicked an atrial myxoma echocardiographically in a patient who had a history of treatment with wide spectrum antibiotics for a long time. We suggest that patients who had broad spectrum antibiotic treatment for a long time should be scanned for fungal infections and if intracardiac mass is determined, fungal endocarditis should be considered in differential diagnosis.

Keywords: Fungal endocarditis, myxoma, aspergillus

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Introduction

Aspergillus species may cause severe invasive infections in almost every major organ system, including sinuses, lungs, central nervous systemand heart. Aspergillus endocarditis is an uncommon entity.^[1] Invasive cardiac aspergillosis is a severe and extremely life threatening disease. The most common predisposing conditions include underlying anatomical cardiac condition, prosthetic cardiac devices, central venous catheters, previous antibiotic use, malignencies, solid organ and bone marrow transplants, prior surgery- cardiac or not- and immune suppressive therapy.^[1, 2, 3]

Myxomas are most common type of primary cardiac tumors and may be seen at any age but rarely in child-hood period. Approximately 12.7% of all myxomas originate from right atrium.^[4] We present a case with fungal endocarditis which mimics an atrial mixoma in echocardiographic examination.

Case Report

A 2 months and 10 days old male patient was referred to our hospital because of heart murmur. He was born 1360 gr with vaginal delivery at 26 weeks gestational age. He was treated with broad spectrum antibiotics in another medical center for two months. No additional information about central venous catheterization could be obtained. In physical examination at admission, he had growth retardation (weight 2000 gr, < 3%; height 42 cm, <3%) and 3/6 degree systolic ejection murmur which was best heard in left middle side of sternum.

Hemogram test revealed anemia, leucocytosis and thrombocytopenia. Biochemical laboratory tests were all in normal ranges. C- reactive protein was 90.7 mg/dL. In echocardiographic evaluation an atrial septal defect and a 17x8.2 mm sized mass originating from right side of atrial septum and extanding to right ventricular cavity through tricuspit valve, which was considered to be a thrombus, vegetation or right atrial mixoma, was determined (Figures 1 and 2).

Antibotic treatment was arranged and antifungal treatment was initiated in consultation with pediatric infection department. Blood samples for culture test was obtained. Surgical treatment was considered. A 1x1cm sized mass was excised from right side inferior vena cava region of interatrial septum with right atriotomy. In patologic examination of this mass, a group of fungal hyphae showing 45 degrees angulations was discovered and diagnosed as aspergilloma histologically (**Figure 3**). The patient deceased because of early surgical complications in the first day of surgery.

Discussion

Invasive aspergillosis (IA) has a wide spectrum of clinical presentations and is associated with high mortality rates and has a wide spectrum of clinical presentations. Clinical manifestations include, but not limited, central nervous system, catheter ascociated, eye, cutaneus, pulmonary, renal, gastrointestinal aspergillosis and osteomyelitis, endocarditis, pericarditis, arthtritis caused by Aspergillus species.^[5] Infective endocarditis

Figure 1

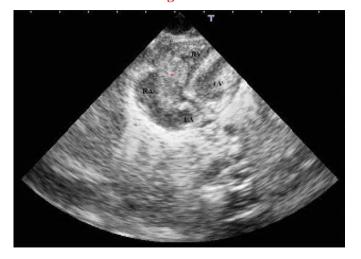
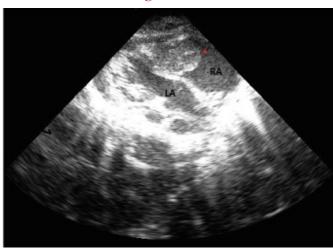


Figure 2





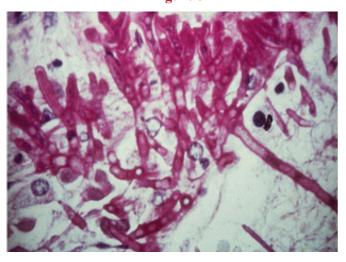


(IE) is a serious but relatively rare infection that is associated with a high morbidity and mortality rates and predominated by causal agents that are bacterial in origin. Fungal endocarditis (FE) is reported less frequently than bacterial endocarditis in both adults and children, with an incidence in children of between 0 and 12% of total pediatric IEs. [6] Fungal endocarditis is a life-threatening infection with a poor prognosis, has been characterized by excessive mortality (50%) and morbidity, regardless of treatment, so early diagnosis and treatment is important. [7,3]

Many factors, including prolonged use of intravascular catheters, anatomical cardiac conditions, exposure to multiple broad-spectrum antibiotics, intravenous drug abuse, and previous history of surgery, have been implicated as possible causes of fungemia and FE. In addition, prosthetic heart valves are the most frequent risk factor for these infections, and a few cases have been reported after heart transplantation.^[7]

In pediatric patients although there are several risk factors associated with developing FE, including congenital heart defects, corrective or palliative surgery for heart defects, central indwelling venous catheter and other lines, parenteral hyperalimentation, exposure to multiple broad-spectrum antibiotics, chronic immunosuppression, premature infant with a low birth weight, candidemia in the neonate, bone marrow or lung trans plantation, rheumatic heart disease, leukemia; there are two main risk groups^[1] the premature neonate, in whom the primary factors are due to inser-

Figure 3



tion of central venous catheters, total parenteral nutrition, and prolonged exposure to broad-spectrum antibiotics^[2] and children with congenital heart defects in whom palliative or corrective surgery using vascular patches and grafts is a risk factor.^[6]

Our patient was in the first group, as he was premature and received wide spectrum antibiotics for a along time. Unfortunately we could not obtain information about usage of intravascular catheter.

The diagnosis of endocarditis and particularly FE in children is difficult, because these children are often extremely ill and the signs of IE may not be clear. [6] Patients with Aspergillus endocarditis may present with fever, multiple embolic strokes, valve abnormalities, and arrhythmias. [8] But, as in other fungal infections, clinical signs are often nonspecific, so the diagnosis of FE is still challenging. Diagnosis is based on the isolation of etiologic agents from cardiac and blood samples or specimens from other sterile sites or positive histopathological findings of pathologic specimens. [7]

It is a fact that, it is difficult to grow fungi, particularly filamentous fungi, in automated blood culture systems. ^[6] Conventional direct microscopy, histopathology, and culture methods are the only available techniques in most centers to diagnose invasive fungal infections due to lack of adequate laboratory techniques like galactomannan or beta-glucan tests assay which can be useful for detection of fungal infections. ^[8, 7] However, echocardiographic evidence of endocardial involvement can throw suspicion on endocarditis and lead to diagnosis. ^[9] Transthoracic and transesophageal echocardiography has been shown to be useful in diagnosing fungal infections of the heart and sensitivity of these methods are quite similar, 88.9% and 92%, respectively.

There are several cases reported with echocardiographic findings of FE.^[10, 11, 9] In most cases, diagnosed as FE, clinical presentations are large vegetations seen in echocardiography and the absence of positive blood cultures for typical bacterial agents.^[5] In our case, an evident mass in right atrium, originating from right side of atrial septum and extanding to right ventricular cavity through tricuspit valve was detected in transthoracic echocardiography. Because of the right atrial origin and





existance in atrial cavity, the mass looked like an atrial myxoma. Cardiac myxomas may occur at any age, but mostly present between the ages 30 to 60, usually as sporadic cases and usually in left atrium. Familial forms have been reported and sometimes recurrences can be seen.^[4,12,13] Differential diagnosis of such an atrial mass mostly can not be obtained completely with only echocardiographic study.

The differencial diagnosis included tumor extension, especially myxoma, atipically located bacterial vegetation, thrombus or fungal mass. Thrombi and infective verrus can mimic myxomas.^[14, 15] So the nature of the mass, medical history of the patient about especially for coagulation disorders and risk factors for developing infective endocarditis can be very important for management of the mass.

Treatment of pediatric FE only with antifungal agents is generally unsuccessful and surgery in addition to antifungal treatment is usually required. [6] Surgery in the management of FE aims to remove endocardial vegetations, as they are responsible for the complications and contribute to the high mortality rates especially in Aspergillus endocarditis. Also surgical removal of the mass provides material for diagnosis.

As reported in many previous studies early surgical debridement is crucial and should be followed by long-term antifungal therapy.^[5] We suggested that the mass in atrial cavity seen in echocardiography may reveal an infective mass because of the risk factors of exposure

to wide spectrum antibiotics for a long time and our patient's being premature. But certain differential diagnosis was impossible only with echocardiographic findings, as blood culture tests were all negative.

So the excision of the mass surgically was necessary for treatment and diagnosis, especially for the possibility of fungal endocarditis. The mass obtained by surgical intervention was examined pathologically and was diagnosed as Aspergilloma histologically. Unfortunatelly the patient deceased because of early surgical complication, atelektasis.

Conclusion

Fungal endocarditis is a rare but increasing entity causing mortality and morbidity. Aspergillus endocarditis in patients who have no had cardiac surgery is extremely rare. With this case we present a patient with big cardiac mass in right atrium extanding to right ventricle in initial echocardiographic evaluation, considered as an atrial myxoma or infective mass and finally diagnosed as Aspergillus endocarditis.

The patient was treated with broad spectrum antibiotics for a long time and this is a predisposing factor for invasive fungal infections. We suggest that patients who had broad spectrum antibiotic treatment for a long time should be scanned for fungal infections and if intracardiac mass is determined, fungal endocarditis should be considered in differential diagnosis.

Case Report





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Conflicts of interest were not reported.

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Short Reports are accepted when the research topic, aim and results of the study are in limited in scope and in cases that do not require writing a full original article. Short Reports can be described as a summarized version that have been prepared according to the structure of research articles. Publishing an article as a short report does not reflect a lower quality. The same rules as relevant to original articles apply to preparing a short report, but structured abstracts are not mandatory references and tables should not exceed 6 and 2 in number, respectively. Abstracts should not exceed 100 words and the text should be restricted to a maximum of 1000 words.

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Reviews are evidence-based articles about a specific topic using relevant citations from the most recent literature with the authors' conclusions on this subject. The author is expected to have conducted research on the subject and to have experience in order to discuss and analyze the subject. There is no obligation to follow a particular format and may contain subtitles depending on the subject. The text should not exceed 4000 words excluding the title, abstracts, references and tables. E Journal of Cardiovascular Medicine, only publishes review articles solicited by the editors.

Letters to Editor and Comments

Letters to the editor or comments can be sent to provide commentary and analysis concerning an article published in the journal, to give information about ongoing research, to provide informa-

Reviewer Instructions





tion in cardiology and cardiovascular-vascular-endovascular surgery, cardio-metabolic and vascular sciences. Letters to the editor or comments may include an optional title, tables and references. These articles should not exceed 1000 words.

What Would You Do?

These are brief articles discussing cases and situations encountered in cardiology and cardiovascular surgery with a biopsychosocial approach. If necessary, photographs (with permission from the patient/owner) may be added. Sections should consist of a title, case report, discussion, questions and answers. Brief comments can be sent to provide commentary on previous articles and case reports written by other authors. Comments should include the number of the journal the article was published in. The text should not exceed 1000 words.

International Reprots

Translations of important documents, declarations and guidelines prepared by international organizations in the field of cardiology and cardiovascular surgery, may be published in the journal. Presubmission Inquiry to the Editorial Board of the Journal before submitting the article is recommended. It is the translator's responsibility to obtain permission from the owner of the original manuscript for publication and translation.

News

These articles focus on advances and innovations in clinical topics relevant to cardiology and cardiovascular surgery. There is no obligation to follow a particular format. The text should be limited to 1000 words.

Editorials

Editorials usually provide information about the editorial policy of E Journal of Cardiovascular Medicine, give commentary and feedback on articles published in the journal, draw attention to topics of current interest and give information related to and discuss the development of cardiology and cardiovascular surgery in the world. They are mainly written by the members of the Editorial Board. Editorials are limited to 2000 words with some exceptions and may include a title and references when necessary.

MANUSCRIPT FORMATTING

Manuscripts should be designed in the following order:

Title page

Abstract

Main text

References

Tables, figures and illustrations

Title Page

The title page of the manuscript should include: The title, first

and last names of each author. Complete affiliation and title for each author, with the name of department (s) and institution (s) to which the work should be attributed.

The corresponding author should be clearly identified with name, address, telephone- facsimile number and email address for correspondence about the manuscript. Authors should clearly indicate if the article has previously been presented at a congress or scientific meeting. The title should be concise and informative without abbreviations and not exceed 10 words.

Abstract

Abstracts hould be exact in English, with a minimum of 150 and maximum of 350 words. Abstracts of original research articles should be structured under subheadings as follows: objectives, methods, results and conclusion. A maximum of 3 key words should be added to English abstracts.

Text

The text contains the rest of the manuscript. It is structured differently according to the type of manuscript (original research article, review, etc.). For example, original research articles should consist of aim and objectives, methods, results, discussion and conclusion.

References

References should be cited in consecutive numerical order as first mentioned in the text and designated by the reference number in parentheses. If the number of authors for the reference is more than 6 authors, list the first three authors and add "et al".

Journal names should be abbreviated as used in Index Medicus. References should be cited in the Vancouver style. For detailed information please visit the relevant link

Examples:

For research articles follow the example below:

 Verschuren WM, Jacobs DR, Bloemberg BP, et al. Serum total cholesterol and long-term coronary heart disease mortality. JAMA 1995; 274(2): 131–6.

For book chapters follow the example below:

Rakel RE. The family physician. In: Rakel RE, editor. Text-book of family practice. 5th ed. Philaldelphia: W.B. Saunders; 1995.
 p. 3-19.

For web pages follow the example below:

- Guidance for clinicians. An International Benchmarking Study. http://www.who.int/topics/surgery/accessed: 29/09/2002.

Tables and Figures

Legends should take place on the top of the page for tables, and bottom of the page for figures and placed on separate pages. Explain all nonstandard abbreviations in footnotes.



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