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Research Articles

Review Article

Case Report

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The effect of enoxaparin on in vitro stimulated platelet aggregation by elective percutaneous coronary intervention patients

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Abstract

Aim: The aim of the present study was to investigate the effects of enoxaparin on in vitro stimulated platelet aggregation by elective percutaneous coronary intervention patients.

Method: Twenty-two patients that scheduled for elective percutaneous coronary angioplasty (PTCA) were enrolled in the present study. The patients who had not been taking any antiaggregant agent other than aspirin and normal platelet account received enoxaparin (1mg/kg IV bolus) as anticoagulant agent during PTCA. Two blood samples were obtained for every patient via femoral arterial sheath during the intervention before and 10 minutes after enoxaparin administration and stimulated platelet aggregation responses are investigated.

Results: The decrease in platelet aggregation responses to adenosine diphosphate (ADP), collagen and epinephrine before and after enoxaparin administration were statistically significant ($p<0.05$). The decrease in platelet aggregation response to ristocetin before and after enoxaparin was not statistically significant ($p>0.05$).

Conclusion: Enoxaparin may reduce platelet aggregation in elective PTCA patients pretreated with aspirin only. With the knowledge of the importance of the platelet inhibition, choice of the anticoagulant agent during PTCA may be beneficial.

Keywords: Enoxaparin, stimulated platelet aggregation, elective PTCA

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Introduction

Subcutaneous (SC) enoxaparin has been shown to be better choice than unfractionated heparin (UFH) in the medical treatment of unstable angina (UA) and non-ST- elevation myocardial infarction (NSTEMI).[1-4] Combined analysis of two studies, the Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-Wave Coronary Events (ESSENCE) and Thrombolysis In Myocardial Infarction (TIMI) 11B, showed that enoxaparin reduced the risk of death and MI by 20% at 43 days without any significant increase of major hemorrhage.[5] ESSENCE and TIMI 11B trials demonstrated superiority of enoxaparin over UFH at 43 days for end points death or myocardial infarction (MI) and death or MI or urgent revascularization in patients who did not undergo percutaneous coronary intervention (PCI).[5]

In this analysis, excluding events that occurred before PCI, there was also superiority of enoxaparin treatment over UFH measured at 1 year for both end points in patients who underwent PCI.[5] Several studies have shown good outcomes with SC enoxaparin anticoagulation of patients with UA/NSTEMI underwent PCI on SC enoxaparin treatment.[6-8] Intravenous (IV) low-molecular-weight heparins (LMWH) in elective PCI have been evaluated and shown to be safe and effective in various registries.[3,9-11]

There are several studies that measure platelet reactivity in stable PCI patients using different methods .[12-14] The aim of the present study was to investigate the effect of enoxaparin on in vitro stimulated platelet aggregation by using % aggregation test to certain agonists in elective coronary intervention patients and the clinical significance of aggregation response to enoxaparin.

Materials and Methods

Study Population

Study population comprised patients older than 30 years with stable angina pectoris and documented ischemia (positive treadmill exercise test or positive myocardial perfusion scan for ischemia), who underwent coronary angiography and scheduled for elective PCI.

Exclusion criteria were:

1. unstable state or acute coronary syndrome,
2. stable angina with an identified precipitating factor (e.g. severe anemia, heart failure, tachyarrhythmia, thyrotoxicosis, severe uncontrolled hypertension),
3. myocardial infarction or PCI in previous month or coronary bypass surgery in 2 months,
4. treatment with UFH or LMWH >24 hours of any cause before enrollment,
5. treatment with any other anti-platelet agent than aspirin (e.g. clopidogrel, ticlopidin, dipridamol),
6. refusal of patient

22 patients, 16 males and 6 females were enrolled to the study. Mean age was 56.8 ± 1.6 years. Mean age for female patients was 57.4 ± 2.1 and for male patients 56.7 ± 1.4. Seventeen patients (14 of males and 3 of females) were smoker. Only 3 patients (2 of males and 1 of females) had diabetes mellitus and none were under insulin treatment. Fifteen patients (11 of males and 4 of females) had hypertension and were under treatment. Seventeen patients (12 of males and 5 of females) were under statin treatment since their coronary angiography procedures.

Concomitant medication was similar in male and female patients. All of patients received daily aspirin (ASA) > 100 mg more than 7 days before procedure. Fifteen of males and 5 of females were taking beta-blockers. Fourteen of males and 5 of females were using nitrates. All hypertensive patients were taking ACE-inhibitors and all of hyperlipidemic patients were taking statins.

Blood Collection

Immediately after femoral sheath replacement the first blood sample was drawn through the sheath to determine the basal (before anticoagulant) platelet aggregation response. Enoxaparin was given 1 mg/kg (100IU/kg) IV bolus after PTCA-wire crossed the lesion as a single dose. Ten minutes after the administration of enoxaparin the second blood sample was drawn through the sheath.

In vitro Platelet Aggregation Measurement

Immediately after blood collection, platelet aggregation measurements were made. All blood samples were studied into 2 hours after their collection. In vitro platelet functions were evaluated in the hematology laboratory with agregometer. Stimuli were adenosine diphosphate (ADP), collagen, epinephrine and ristocetin. PAP-4CD Bio-Data was used for platelet aggregation.

Statistical Analysis

A student-paired t-test was applied to assess the differences between pre- and post-enoxaparin platelet aggregation responses. Results are expressed as mean ± standard error (SE). The level of significance was set at $p < 0.05$. SPSS 10.0 software was used for the statistical analysis.

The alteration in the platelet aggregation response with certain stimuli before and after enoxaparin is investigated in order to explore if enoxaparin has an additional antiaggregant effect.

Results

Baseline clinical characteristics of study population and concomitant medications are described in **Table 1 and 2**. Baseline platelet counts were within normal limits in the study population and were unchanged after the intravenous administration of enoxaparin (212 ± 48x106 before and 210 ± 42x106 after enoxaparin). Not any major bleeding complication occurred. None of patients had required blood transfusion. Only 3 of patients had small hematoma on the femoral access site. In this study not any in-hospital complication (such as ischemic complications or infection) was experienced.

Stimulated platelet aggregation responses before and after enoxaparin are summarized in **Table 3**. Values are given as mean ± SE of % aggregation. Platelet aggregation responses to ADP were 36.2 ± 4.6 before and 29.3 ± 3.4 after enoxaparin (p=0.005) and to epinephrine 41.4 ± 5.3 before and 30.5 ± 4.7 after enoxaparin (p=0.02). The difference was statistically significant. Platelet aggregation responses to collagen were 57.8 ± 5.0 before and

Table 1. Patient Demographics

Demographics	Male (N=16)	Female (N=6)
Age	56.7 ± 1.4	57.4 ± 2.1
Smoker	14	3
Diabetes Mellitus	2	1
Hypertension	11	4
Hyperlipidemia	12	5

N indicates number of patients. Age is given mean ± SE in years.

Table 2. Concomitant medications of the study patients

Medication	Male (N=16)	Female (N=6)
ASA>7 days	16	6
β -blocker	15	5
Nitrate	14	5
ACE-I	11	4
Statin	12	5

N indicates number of patients.

Table 3. Stimulated Platelet Aggregation Responses

Stimuli	Before Enoxaparin (N=22)	After Enoxaparin (N=22)	P value
Adenosine diphosphate (ADP)	36.2 ± 4.6	29.3 ± 3.4	0.005
Collagen	57.8 ± 5.0	45.7 ± 6.0	0.05
Epinephrine	41.4 ± 5.3	30.5 ± 4.7	0.02
Ristocetin	75.0 ± 3.0	67.0 ± 4.3	0.07

N indicates number of patients. Data are given mean ± SE of % aggregation. A value of P < 0.05 is considered statistically significant.

45.7 ± 6.0 after enoxaparin (p=0.05); to ristocetin 75.0 ± 3.0 before and 67.0 ± 4.3 after enoxaparin (p=0.07).

Discussion

Despite of new tools, new drugs and new techniques, clot formation remains still as an important issue in interventional cardiology. The UFH has been the primary anticoagulant agent for more than 30 years, but the optimal dosage, the monitoring of anticoagulation level and the interaction between UFH and platelets remain controversial.[15-17] LMWHs offer a stable and predictable anticoagulant response and do not need for coagulation monitoring.[18]

Enoxaparin has shown its superiority to UFH in the medical treatment of UA and NSTEMI.[1,2] There is also a meta-analysis revealing a better evolution in ST-segment elevation acute myocardial infarction patients, who received enoxaparin instead of UFH as an adjunctive therapy to the thrombolytic regimen. [4] Several studies have also shown good results with enoxaparin on UA/NSTEMI patients who underwent PCI.[6-8]

There are some potential mechanisms, which may explain beneficial effects of enoxaparin.[18] Because of the molecular features enoxaparin may permit more suppression of thrombin generation than UFH with a higher antifactor Xa: antifactor IIa (thrombin) ratio (3.8:1).[18] Enoxaparin has a prolonged antifactor Xa activity and higher antifactor IIa activity than UFH because of better bioavailability, is less sensitive to the inhibitory effects of platelet factor 4, may release the tissue factor pathway inhibitor with greater capacity, has a lower tendency to increase activation and aggregation of platelets and shows potential antiplatelet effects while suppressing von Willebrand factor greater degree.[18, 19-28]

The aim of this study was to investigate the aggregation response of stable patients to enoxaparin via platelet functions beyond its anticoagulation activity. To the best our knowledge, this is the first study that compared parameters of platelet aggregation before and after administration of enoxaparin during elective PCI in patients pretreated only with aspirin. All unstable patients were excluded to avoid the interaction between activated aggregation and coagulation cascade and platelet aggregation response. In the present study, enoxaparin showed a slight decrease of % aggregation on platelet aggregation responses stimulated with collagen and ristocetin but it was statistically not significant. Enoxaparin significantly decreased platelet aggregation responses stimulated with ADP and with epinephrine in elective PCI patients. None of our patients experienced any ischemic or hemorrhagic complications neither in 72 hours nor in 30 days in follow-up.

Platelets play a key role in the development of thrombotic events during and after PCI.[29-31] There are multiple pathways of platelet activation and aggregation. Thrombin is the most potent agent, which activates platelets in subnanomolar concentrations via protease-activated receptors (PARs).[31,32,33] PAR activation results ADP release from dense granules, which acts in an autocrine way on the platelet ADP receptors.[31,34]

This endogenous ADP release may be reduced via enoxaparin resulting in significant decrease of ADP induced platelet aggregation. In a previous study Xiao et al. investigated platelet aggregation response to enoxaparin in patients taking only aspirin with UA and found a modest but not statistically significant increase in platelet aggregation with enoxaparin.[25] The conflict may be related to the study population. While UA patients have been included to the study of Xiao et al, all UA patients were excluded from the present study.[25] In another study, Aggarwal et al. have found that anticoagulation with enoxaparin during hemodialysis is associated with less platelet reactivity in a different study population.[35]

The limitations of the present study were small number of patients and lack of unstable patients. In acute coronary syndromes and unstable patients, especially by the site of thrombus, antiaggregant effect of enoxaparin may be more critical, but further studies are needed. In conclusion, enoxaparin may reduce platelet aggregation in elective PCI patients treated with aspirin only. With the knowledge of the stronger the platelet inhibition, the lower the incidence of ischemic complications,[36-39] choice of the anticoagulant agent or additional antiaggregant agents during PCI may be beneficial.

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Isolated ventricular septal defect in infants

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Abstract

Ventricular septal defect is a hole in the interventricular septum and may be isolated or associated with other major defects involving patency of the arterial duct, coarctation of aorta, pulmonary stenosis, tetralogy of Fallot, double-outlet right ventricle, truncus arteriosus, and transposition, and account for over half of the patients with congenital heart disease. Isolated ventricular septal defect is the most commonly recognized congenital heart anomaly in children and accounts for about one-fifth of all congenital heart disease. In this chapter, we'll cover isolated ventricular septal defects.

Key words: Ventricular septal defect, isolated, infant.

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Classification

The interventricular septum (IVS) is commonly divided into four parts—the membranous septum and the inlet, trabecular, and outlet portions of the muscular septum. Depending on their location in the IVS, isolated ventricular septal defect (VSD) can be divided into four types;[1,2,3]

Type I VSDs (Doubly commited/ Subarterial/ Outlet/ Infundibular/ Conotruncal/ Conal/ Juxtaarterial/ Supracristal) account for 5% to 10% of isolated VSDs. They are located below the semilunar valve and above the crista supraventricularis. The right aortic leaflet most commonly is sucked into the defect, resulting in aortic incompetence in 40% to 50% of conal defects. Atrioventricular conduction tissue is far away from the borders of this type of VSD.

Type II VSDs (Perimembranous/ Conoventricular) are the most common isolated VSDs, comprising about 70% to 80% in most series. These defects are located in the membranous septum and may extend into the inlet or outlet. They are usually bordered cranially by aortic valve and posteroinferiorly by anteroseptal commissure of the tricuspid valve and they can undergo partial or complete closure by apposition of the septal leaflet of the tricuspid valve, forming a tricuspid valve "pouch" or "aneurysm of the ventricular septum". Less commonly the noncoronary aortic leaflet may prolapse through the defect, resulting in decrease of the defect as well as progressive aortic incompetence. Atrioventricular conduction axis penetrates directly through the posteroinferior border of the defect. These type of VSDs can be associated with malalignment of the aortopulmonary septum, as in the setting of tetralogy of Fallot (anterior malalignment) or interrupted aortic arch (posterior malalignment). A Gerbode-type defect is a communication between the left ventricle and right atrium through the membranous IVS.

Type III VSDs (Atrioventricular canal/ Inlet type) account for about 5% of isolated defects. They are situated beneath the septal leaflet of the tricuspid valve, with the tricuspid valve annulus forming their posterior border. They can be associated with primum type atrial septal defects and left atrioventricular valve clefts. The conduction tissue is closely related to the posteroinferior border of the defect. They have a remarkably high prevalence in genetic conditions such as trisomy 18 and trisomy 21.

Type IV VSDs (Muscular/Trabecular) account for 10% to 15% of isolated VSDs. They have a rim totally made up of muscle and are divided into midmuscular (most common), apical (trabecular), and anterior muscular defects. The presence of multiple muscular defects is known as the "swiss cheese" septum. The conduction tissue is generally remote from the edges of a muscular defect.

The defects in the neonate are devided into 3 subgroups depending on their size;[1,4]

- Small (restrictive) VSD is < 4 mm (or less than the 33% of cross-sectional diameter of the aortic root in catheterization), the pulmonary to systemic blood flow ratio (Qp:Qs) < 1.5.

- Moderate VSD is 4-6 mm (or between the 33-75% of cross-sectional diameter of the aortic root in catheterization), Qp:Qs = 1.5 - 2.3.

- Large (non-restrictive) VSD is > 6 mm (or larger than the 75% of cross-sectional diameter of the aortic root in catheterization), Qp:Qs > 2.3.

Patophysiology

In non-restrictive VSDs, the magnitude of the shunt depends on the relative pulmonary (PVR) and systemic vascular resistance (SVR). Since in a normal individual SVR is greater than PVR, in smaller defects, the blood flow is from the left to right ventricle. In patients with a large VSD, the systolic pressure in both ventricles is the same, with right sided pressures elevated to the same levels as those normally present on the left side of the heart. Large VSDs place two major hemodynamic loads upon the ventricles; increased pressure load on the right ventricle and increased volume load on the left ventricle.

PVR is high at birth and little flow across the defect may exist during this period. When PVR shows a sharp fall by 2-8 weeks of age, in patients with large VSD, pulmonary blood flow increases secondary to increased left-to-right shunt. The augmented blood flow returns through the left atrium to the left ventricle. To acco-

modate the increased pulmonary venous return, the left ventricle dilates. If the left ventricle becomes greatly dilated, the myocardium can not develop sufficient tension to maintainn the pressure volume relationship, causing congestive cardiac failure. Patients with large VSD, develop congestive heart failure and its symptoms of tachypnea, slow weight gain and poor feeding by 2 to 3 months of age.

As pulmonary vascular disease develops, PVR increases and left to right shunt reverses and the presence of a right to left shunt will result in cyanosis (Eisenmenger syndrome). Congestive heart failure lessens. These rarely present in children below age 5 with isolated VSDs and is usually seen in adolescents and adults. In a patient with high fixed PVR, the defect should not be closed.[1,2,3]

Diagnosis

Patients with small VSDs usually are asymptomatic. A loud holosystolic murmur may be heard best at the left sternal border. Pulmonary arterial pressure and pulmonary vascular resistance is near normal. The normal decline in PVR can be delayed in infants with moderate and large VSDs. Thus, murmurs may not be detected in such infants until several weeks postnatally.

Infants with moderate or large VSDs may present with pallor, tachypnea, increased work of breathing, poor weight gain, or failure to thrive, and diaphoresis particularly with feeding at approximately two to eight weeks of age. Right ventricular impulse, felt at the lower left sternal border is prominent. A precordial trill may be palpable. As the degree of pulmonary hypertension increases, the intensity of the pulmonary component of S2 will increase. There will be holosystolic, midfrequency murmur. In patients with large VSDs, in addition to the systolic murmur, there will be a middiastolic mitral flow murmur as a result of increased volume of blood flowing from the left atrium to the left ventricle. As the PVR rises, the holosystolic murmur may disappear entirely, leaving a loud second heart sound due to closure of the pulmonary valve which is indicative of severe pulmonary hypertension.

The electrocardiogram; may be normal in small VSDs. Moderate sized VSD's may be commonly associated with hypertrophy of right, left or both ventricle. In patients with large VSDs, left atrial dilatation, manifested by biphasic P waves in leads I, AVR, and V6 associated with right ventricular hypertrophy and left or right axis deviation may be seen. Patients with pulmonary hypertension, will exhibit evidence of right ventricular hypertrophy in electrocardiography

In chest radiography; patients with small defects often will have a normal cardiac silhoutte and normal pulmonary markingsy, while moderate and large VSD patients will have increased pulmonary vascularity and cardiomegaly with biventricular enlargement. Lateral projections may show upward deviation of the left main bronchus due to left atrial dilatation in large defects. In patients with Eisenmenger syndrome, the heart may not be enlarged and the pulmonary vascular markings may not be increased. Only the main pulmonary artery is enlarged.

Transthoracic echocardiography is the mainstay for the definitive diagnosis of VSD. It allows delineation of the anatomic site of the VSD, associated cardiac lesions, pulmonary artery pressure, degree of cardiac dilatation. *Cardiac catheterization* is only indicated to determine; quantification of the ratio of systemic and pulmonary flows, the pulmonary artery pressure and accurate identification of smaller defects.[1]

Natural history

The incidence of spontaneous closure of VSDs is highest during the first year of life (40%) but continues to a lesser degree up to about 5 years, after which spontaneous closure is rare. Most VSDs are restrictive and frequently become smaller or undergo spontaneous closure. Defects located in the muscular septum close with the growth and hypertrophy of the surrounding muscular septum. Small membranous defects may close through apposition of the septal leaflet of the tricuspid valve secondary to negative pressure created by the jet through the defect.

In patients with nonrestrictive VSD, congestive heart failure symptoms develop soon after birth, concomitant with the fall in the elevated neonatal pulmo-

nary resistance. Patients are at risk of developing irreversible pulmonary vascular disease after 1-2 years of age (earlier in children with trisomy 21). Generally, outcome is good in patients of all ages when preoperative PVR is only mildly or moderately elevated. Large VSDs in such children should be repaired by three to four months of age. Eisenmenger syndrome, appearing most frequently in the second and third decade of life and typically leading to death by the age of 40.

Some patients with isolated VSD develop subpulmonary stenosis due to right ventricular infundibular hypertrophy. These patients are not at risk of pulmonary vascular destructive disease. Prolapse of the leaflets of the aortic valve occurs most frequently with the defects opening directly into the outlet of the right ventricle, muscular outlet, or perimembranous defects opening to the right ventricular outlet with malalignment of the muscular outlet septum. Untreated prolapse of the aortic valvar leaflets results first, in a decreased left-to-right shunt because the involved leaflet often prolapses into the defect and reduces the shunt, and second, worsening aortic insufficiency.[2,3]

Indication for VSD repair

- Large VSDs presenting in the first few months of life with severe congestive heart failure or inlet (AV canal) and outlet (supracristal) defects which do not generally close spontaneously are the VSD's in which surgical closure is indicated.

- An undesirable mechanism of spontaneous occlusion is prolapse of an aortic valvar leaflet into the defect, often causing aortic insuffiency. This is also an indication for surgical repair. It is preferable to identify the defects associated with this potential complication and close them before its development.

- Bacterial endocarditis is a rare complication. Following antibiotic treatment of the active infection, closure of VSD regardless of its size is indicated.

- All VSDs irrespective of size, if associated with another reason for cardiac surgery,

- All residual VSDs >3 mm or those associated with elevated pulmonary artery pressures have also indication for closure.[2,5,6]

Early repair of congenital cardiac lesions with improved postoperative care is the best strategy to prevent the development of severe pulmonary vasculopathy in CHD. However, even in developed nations, some infants/children are older at presentation or have yet-undiscovered genetic abnormalities that predispose to increased pulmonary vasoreactivity or early development of pulmonary vascular remodeling. The decision to operate on these patients with an acceptable risk of early and late postoperative complications is not easy, and the current view is that it should be not be based on single parameters.

During the 5th World Symposium on Pulmonary Hypertension of the World Health Organization (Nice, France, February 2013), a PVR of 4Wood units m2 and PVR:SVR ratio < 0.3 was proposed as a limit for considering surgery, and a PVR of 4–8 Wood units m2 as the range in which patients should be discussed case by case. The PVR of 6 Wood units m2 and a PVR:SVR ratio of 0.3 as limits for considering operation in PAH-CHD was proposed and a 20% decrease in PVR from baseline during the acute vasodilator test is considered sufficient to define a positive response but not to characterize operability. There has been debate about what to do with patients with elevated PVR (e.g., PVR > 8–10 Wood units m2 and PVR:SVR > 0.5), in particular since the answer will not be the same for patients at different ages.[7,8,9]

Technique of surgical repairing of VSD

The progress in cardiopulmonary bypass, myocardial protection, improved skill, and surgical techniques and in the perioperative care has advanced so that standard corrective operation for ventricular septal defect closure in infant patients is now obtained with almost no mortality or major morbidity. Today pulmonary artery banding is not preferred except for only a very few specific lesions like multiple muscular (Swiss cheese) VSDs, multiple VSDs with coarctation, single ventricle with large VSD, for preparing left ventricle in late (after 6 weeks of age) presented transposition of great arteries (TGA) and for training left ventricle for a double switch in congenitally corrected transposition of great arteries.

The corrective operative approach varies according

to the type of VSD. Perimembranous and inlet VSDs are usually repaired through a right atrial approach. Doubly commited VSD's are approached through the pulmonary artery, aorta or right ventricle. Muscular VSDs are usually approached through right atrium or through limited right or left ventriculotomy.

Following aorting and bicaval cannulation, moderate hypothermia (28-32C°) is constituted. The aorta is clamped and the heart is arrested with cardioplegic perfusate. The right atrium is opened to expose the tricuspid valve orifice. The pump sump sucker is placed in the left ventricle through interatrial septum to keep the operative field dry. If atriotomy is not required, the sucker is placed via the right superior pulmonary vein or left atrial appendage.

The perimembranous VSD is identified by retracting the septal and anterior leaflets of tricuspid valve. In some instances, the VSD perimeter cannot be completely identified because of the overlying tricuspid valve tissue (tricuspid valve pouch). Tricuspid valve detachment may be required by incision on the septal leaflet, parallel to the tricuspid valve annulus. The next step is to inspect the VSD. The aortic leaflets may prolapsed into the defect and must be avoided during suture placement.

The technique of VSD closure that we have been using at Ankara University, Department of Cardiovascular Surgery, is to encircle the perimeter of the VSD with multiple, interrupted, pledget-based 5-0 polypropylene sutures **(Figure-1)**. To avoid injury to the conducting system, the sutures should be placed superficially and carefully along the inferior and posterior margins of the defect and stay on the right ventricular side of the VSD. This closure begins from the area of the insertion of the muscle of Lancisi (medial papillary muscle of the conus) to the annulus of the tricuspid valve near the region of yhe triangle of Koch. Care must be taken when placing these sutures to avoid the aortic valve cusp.

The sutures are then sequentially placed through an appropriately sized patch (1.5 times the size of the actual hole in the septum), the patch is lowered into the defect, and the sutures are tied and cut. We commonly use Dacron patch. Alternatively, autologous pericardium, or polytetrafluoroethylene (Gore-Tex) patch material may be used. After the patch has been anchored by tying all the sutures, the tricuspid valve is repaired (usually with 6-0 prolene) if detachment was performed. The right ventricle can be irrigated with saline to identify tricuspid valve regurgitation. The completion of the VSD closure is accomplished by closing the atrium. Transesophageal echocardiography (TEE) is very important to assure the integrity of the repair after the closure by evaluating for residual intracardiac left-to-right shunting.

Figure 1. Dacron patch repair with interrupted sutures

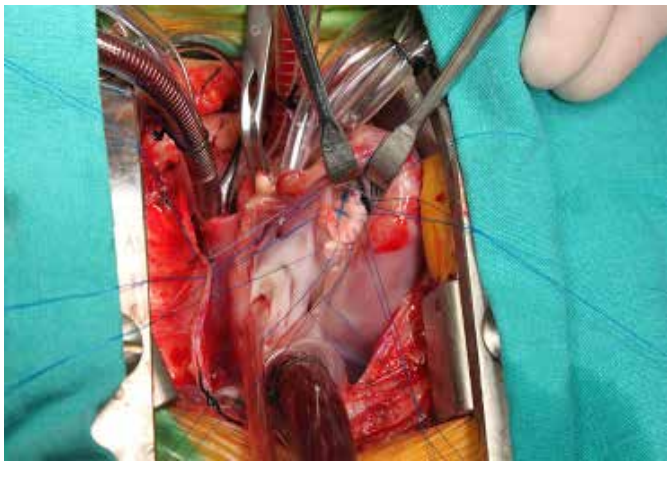
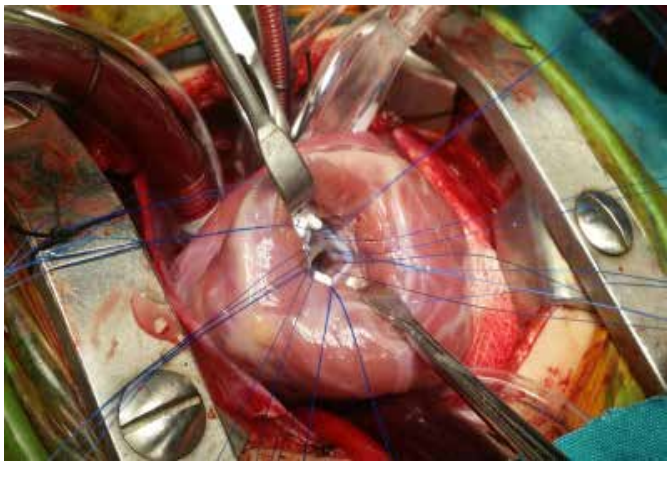


Figure 2. Left ventricolutomy for muscular VSD closure



The exposure of doubly commited VSD is usually accomplished through a vertical incision in the pulmonary artery. Pulmonary valve is gently retracted. A critical part of the closure involves placing sutures directly in the base of the pulmonary valve cusp. Pledgetted sutures are placed circumferencially around the perimeter of the VSD.

Certain muscular VSDs (Swiss cheese) may be easier to patch on the left ventricular side because of the relatively smooth septum. Left ventricular incisions, however is associated with significant long-term ventricular dysfunction and should be avoided whenever possible **(Figure-2)**. Multiple anterior muscular defects may be closed through short vertical right ventriculotomy. The defects are sandwitched between two strips of felt or pericardium, one placed inside and the other outside the right ventricle paralel to the left anterior descending coronary artery. Interrupted horizontal matress sutures are used. Midmuscular septal defects may be closed using a single composite patch to avoid injury to the conduction tissue.[2,6,10,11,12]

If the PVR is moderately elevated: (1) partial closure of the communication; (2) leaving a small ASD open while repairing posttricuspid defects; (3) placing a band on the pulmonary artery should be considered.

Over the past decade or so, transcatheter techniques for closure of ventricular septal defects have been developed. These methods have been especially useful for muscular defects, which can be the most difficult to Access surgically. Much interest has been generated in development of transcatheter approaches to close perimembranous defects. At present, this technique is not undertaken in most units because of the unacceptably high rate of post-procedure heart block associated with currently available devices.[13]

Complications

Premature rate death occurs in less than 2.5% of patients.when pulmonary resistence is low preoperatively. Repair of VSD during the first 1 or 2 years of life is curative for most patients, resulting in full functional activity and normal or near-normal life expectancy. Complications of surgical closure of VSD are generally related to injury to the anatomic structures, inadequate exposure and cardiopulmonary bypass.

Conduction system and the leaflets of tricuspid and aortic valves are at risk during VSD closure. Transient arrhythmias may be seen. Right bundle branch block (RBBB) is present late postoperatively in many patients in whom VSDs are repaired via right ventriculotomy. RBBB is less prevalent when the right atrial approach is used for VSD repair. Serious ventricular arrhythmias and sudden death late after repair of VSDs have been rare. Complete heart block requiring a pacemaker has been reported in 1-2 % of cases. Prevalence is slightly higher in patients undergoing repair of multiple VSDs. Inlet VSDs extending posteriorly to the crux, associated with straddling tricuspid valve, also have increased prevalence of heart block after repair.

During suture placement, aortic valve injury can ocur and cause aortic insufficiency. Perimembranous VSD (rather than VSDs in the right ventricular outlet) and older age at operation contribute to presence of important aortic regurgitation after repair. VSD patch may rarely cause hemolysis. Tricuspid insuffiency can ocur if the leaflets are retracted inappropriately or after tricuspid detacment for exposure. In experienced centers, reoperation for residual VSD should be 2% or less. Late postoperative cardiac function is essentially normal when repair is done during the first 2 years of life by modern techniques through the right atrium.[2,10,14]

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Transcatheter successful palliation of a newborn with ductal-dependent pulmonary circulation

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Abstract

We report a newborn who have congenital heart disease with duct-dependent pulmonary circulation and hypoplastic peripheral pulmonary arteries, was successfully palliated with ductal multiple stent implantation.

Key words: Pulmonary atresia, pulmonary hypoplasia, ductal stent implantation.

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Introduction

Conventional management of neonates with ductal-dependent pulmonary flow entails maintaining ductal patency using prostaglandin E1 infusion followed by surgical palliation with Blalock-Taussig shunt (B-T shunt). Nowadays, percutaneous transcatheter placement of a stent to maintain ductal patency has been used as an alternative method to provide a source of pulmonary blood flow.[1,2] The potential advantages of ductal stenting include reduced procedure-related risks and improved distribution of pulmonary artery blood flow.[3] Ductal stenting could be used as a bridge toward corrective surgery in neonates.[4]

Case Report

A two-day-old boy was referred to our hospital for cardiac evaluation moderate to severe cyanosis (percutaneous oxygen saturation 60%). Echocardiography showed, situs solitus, levocardia, concordant atrioventricular connection, large outlet ventricular septal defect, pulmonary atresia, hypoplastic pulmonary artery branches, right aortic arch and vertical arterial duct. Cardiac catheterization was performed via right femoral vein. Pulmonary artery branches were hypoplastic (right and left pulmonary artery 3 mm) and supplied by a vertical, tortuous ductus with distal narrowing which arises from the inner curve of a right sided aortic

Figure 1. *Vertical, tortuous ductus with distal narrowing.*

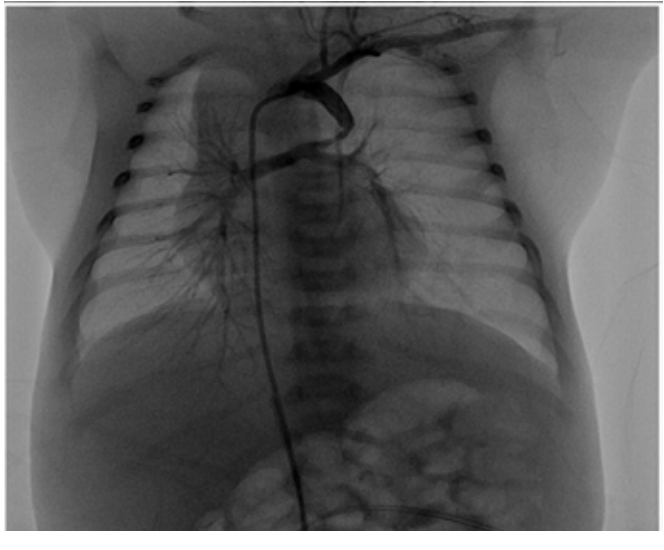


Figure 2. *First stent implantation*

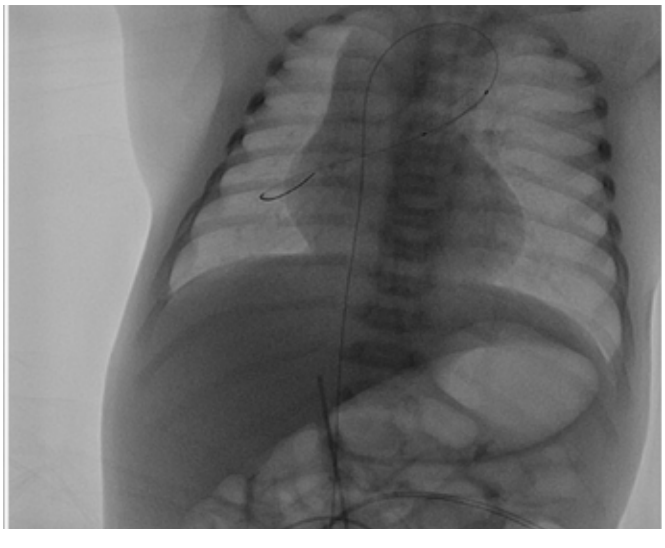


Figure 3. *Second stent implantation*

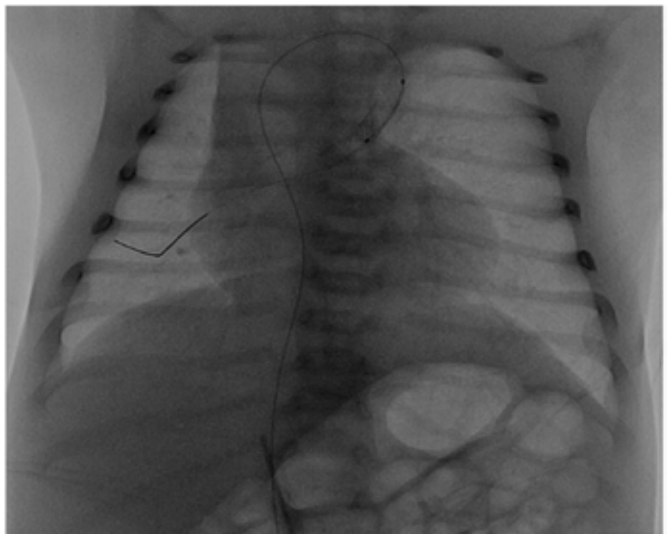
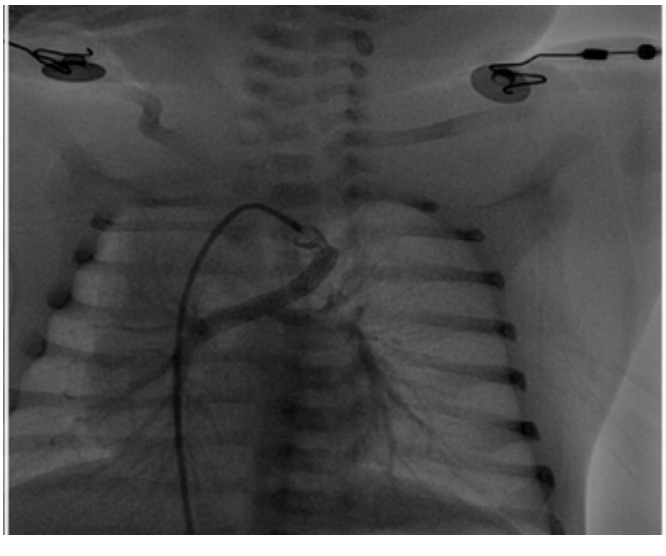
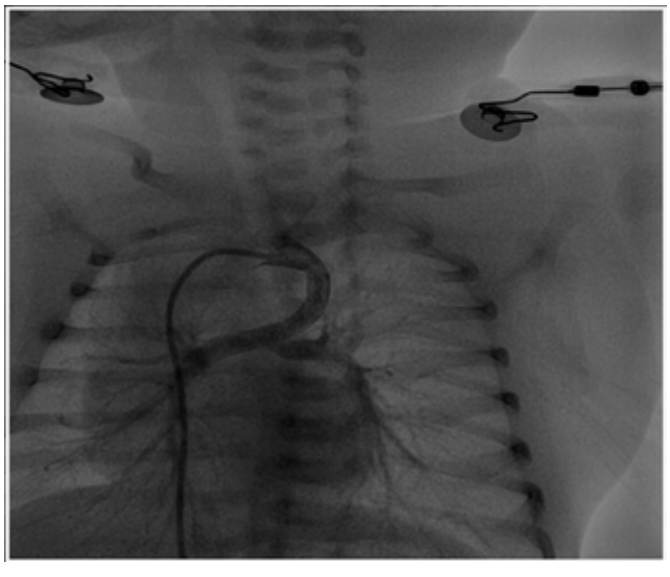


Figure 4. *Critically stenotic aortic end of ductus arteriosus*



(Figure 1). Firstly distal narrowed part of ductus arteriosus was stented with a coronary stent (4×15 mm) (Figure 2). After that a second coronary stent (4×15 mm) was implanted to cover most of the duct (Figure 3). The final oxygen saturation was 90% after two stent implantation. After cessation of prostaglandin infusion the patient' oxygen saturation gradually decreased up to the 55%. Second cardiac catheterization showed critically stenosis in aortic end of ductus (Figure 4). A third coronary stent (4×15 mm) was placed to cover the aortic side entirely (Figure 5). The oxygen saturation was increased to 85% after third stent implantation. The patient was discharged with %85 oxygen saturation in the following days. During follow-up periods of to three months he had no problem clinically, weight gain and %88 percutaneous oxygen saturation.

Figure 5. Ductus arteriosus after three stent implantation



Discussion

Ductal stenting a reliable and more physiologic alternative to surgical systemic to pulmonary shunt in neonates. But the lack of stent coverage of the entire ductus (especially in long and tortuous duct) results duct constriction and cyanosis of the patient and causes reintervention in most cases. It is well known that passing a catheter through the stent is technically very difficult and increases the risk of thrombosis and hemodynamic destabilization when compared with the primary intervention. Therefore stent long must be enough to cover entire ductus. But in some cases a small segment of the duct may be left uncovered and necessitating use of second or third stent. The full-length stenting of the duct without leaving any ductal tissue is important.

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Dead sea like giant negative t wave associated with subarachnoid hemorrhage

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Abstract

Subarachnoid hemorrhage is a catastrophic neurological event. Rupture of an aneurysm results it. In addition to neurological signs and symptoms ECG abnormalities reported. These ECG findings reported are prolonged QTc, ST segment abnormalities, T wave inversion, abnormal U wave, bradicardia, tachicardia, Premature ventricular complex, Premature atrail complex, atrial fibrilation, VT, AV blocks. We described a patient with subarachnoid hemorrhagae showed giant inverted T wave.

Keywords: Subarachnoid hemorrhage, T wave inversion

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Introduction

Subarachnoid hemorrhage is a catastrophic neurological event. Rupture of an aneurysm results it. In addition to neurological signs and symptoms ECG abnormalities reported. These ECG findings reported are prolonged QTc, ST segment abnormalities, T wave inversion, abnormal U wave, bradicardia tachicardia, Premature ventricular complex, Premature atrail complex, atrial fibrilation, VT, AV blocks. We described a patient with subarachnoid hemorrhagae showed giant inverted T wave. Generally inverted T waves are related with acute coronary syndromes. Addionally, T wave inversion occurs in patients with left ventricule hypertrophy, acute myocarditis, WPW sydnrome, acute pulmonary embolism, pericarditis, electrolit disturbances, on treatment with digoxin and Yamaguchi syndrome.

Case Report

64-year old woman admitted to the emergency department with sudden loss of consciousness and left hemiparesis. The blood pressure was 180/120 mmHg with a heart rate of 78 bpm. Her ECG showed global very widely splayed and very deeply inverted T-waves with prolonged QT (QTc: 640 ms) **(Figure 1)**. Cranial CT showed subarachnoid hemorrhage.

Standard biochemical parameters were in normal limits except serum potassium level of 3.1 mg/dL and leukocytosis on complete blood count. Bilateral basal crackling rales in the lungs were detected but the echocardiography, cardiac markers and the renal parameters were all in normal limits. The patient was entubated after a short period after admission and she died after a short time of deterioration.

Discussion

T wave is the electrocardiographic manifestation of ventricular repolarization. Any reason disrupting ventricular repolarisation just like acute coranary syndromes, left ventricular hypertrophy, pulmonary embolism, electrolyte disturbances and cerebrovascular events eventuate T wave abnormalities. Subarachnoid hemorrhage is usually accompanied by electrocardiographic abnormalities including the T-wave abnomalities he and it's thought that these changes are caused by increased sympathetic and vagal tone leading to aberrant repolarisation, probably secondary to myocyte injury and contraction band necrosis.[1]

Neurogenic ECG alterations are often transient. It causes diagnostic problems, ECG findings in neurogenic problems can mimic acute myocardial infarction. It is important to avoid inappropriate therapies. An imbalance of autonomic cardiovascular control and increased

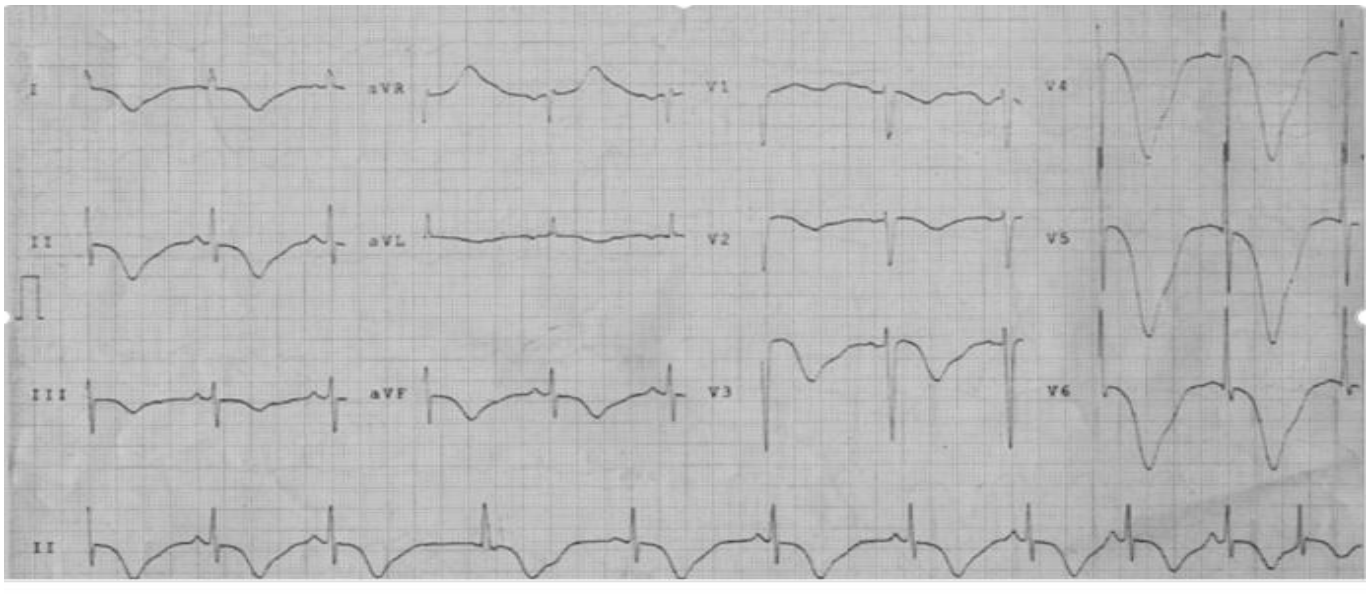

Figure 1: *Her ECG showed global very widely splayed and very deeply inverted T-waves with prolonged QT*

circulating local myocardial tissue catecholamines. Several experience investigation reported that a sudden increase in intracranial pressure occurs that a massive sympathetic discharge.[2,3] Experimental studies suggest that a large amount of norepinephrin is released during sudden neurologic problems. Alterations in cardiac depolarisation and repolarisation reported 74% of patient with cerebrovascular events.[4] Experimental studies impilicates that insular cortex is responsible in cardiovascular control and heart chronotropik organisation.

Studies suggest that its involvement occurs neurogenic ECG alterations.[5] Porter et al.[6] found that stimulation of the posterolateral hypothalamus not only induced rhythm abnormalities but also caused repolarisation changes. Attar and collegues found that stimulation of the anterior hypothalamus produced ST elevation and deepening of T waves.[7] Thus, hypothalamic stimulation is capable of causing both arrhythmias and a variety of ECG changes which mimic acute myocardial injury or ischemia. In a study by Estanol et al.[8] rhythm and repolarisation changes were created in dogs by introducing blood into the subarachnoid space.

Rudehill et al.[9] ECG s were prospectively studied on 406 patients with subarachnoid hemorrahagiae. Three hundred thirty one patients (82%) had an abnormal ECG. The predominant findings were U wave changes (47%). T wave abnormalities (32%), prolonged QTc interval (24%), and ST segment depression.(15%). Stober et al.[10] showed that ECG abnormalities in patients with subarachnoid hemorrahagiae were interested in arterial spasm on the brain. Several studies revealed electrocardiographic abnormalities related with subarachnoid hemorrahagiae.[11-13]

In conclusion; acute ischemic cardiac events show electrcardiographic abnormalities. T wave abnormalities also can often seems as a result of acute cardiac problems. On the other hand acute cerebrovascular events can mimic electrocardiographic abnormalities in patients with acute cardiac problems. As a result phsician must be aware about these ECG similarities. Otherwise, these ECG abnormalities can cause inappropriate therapies.

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Aortic valve replacement due to lactococcus lactis infective endocarditis

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Abstract

Infective endocarditis characterized by microbial infection of the endothelial surface of the heart,has an estimated annual incidence of 3 to 9 cases per 100.000 persons in industralized countries. Although common species causing infective endocarditis include streptococci, staphylococci, enterococci and fastidious gram negative coccobacilli, aortic valve replacement due to lactococcus lactis infective endocarditis seen in the literature, even if rarely. In this study we presented a 34 year old male patient underwent surgery, diagnosed with lactococcus lactis infective endocarditis.

Keywords: Infective endocarditis, Lactococcus lactis, Complication

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Introduction

Endovascular, microbial infection of intracardiac structures facing the blood including infections of the large intrathoracic vessels and of intracardiac foreign bodies, called infective endocarditis. The early characteristic lesion is a different sized vegetation, although destruction, ulceration or abscess formation may be seen earlier by echocardiography.[1]

The highest rates of the infective endocarditis are observed among patients with prosthetic valves, intracardiac devices, unrepaired cyanotic congenital heart diseases or a history of infective endocarditis, although 50% of cases of infective endocarditis develop in patients with no known history of valve disease. Other risk factors include chronic rheumatic heart disease, age-related degenerative valvular lesions, hemodialysis and coexisting conditions such as diabetes, human immunodeficiency virus infection and intravenous drug use. Diagnosis of endocarditis is usually based on clinical, microbiologic and echocardiographic findings.[2]

Indications for cardiac surgery are; heart failure, no control of infection, vegetations and embolic risk, perivalvar infection, valvar obstruction, unstable prosthesis, prosthetic infective endocarditis, fungal infective endocarditis, difficult-to-treat microorganisms and neurological complications. Lactococcus lactis is a mesophilic and microaerophilic fermenting bacteria, used for fermented food products production. It can be isolated even if rarely from oropharinx, intestines, or vagina as a part of normal flora. For a long time it was considered as nonvirulent with low pathogenity in humans.[3]

Case Report

Thirty four year old male patient, previously healthy, sometimes presented with a high fever, cold and chills problems last one mounth. He had first applied to a health care center and oral antibiotherapic mediaction was started but his problems had continued to exist. And than patient was applied to a hospital and though there was a suspicious aspect in transthorasic echocardiography, he was referred to university hospital for transesophageal echocardiography. He was hospitalized in infectious diseases service and there was no signicant pathology in his physical examination. Four blood cultures were taken from patient and lactococcus lactis was seen in one of them. 1,5*2,1 cm sized vegetations on the aortic valve were determined in transesophageal echocardiography. Ejection fraction was 60%. Aortic regurgatition was 2-3rd degree. Intravenous antibiotherapy included gentamicin and vancomycin started to the patient.

The patient was referred to us and because of the risk of embolisation due to vegetation, emergency operation was decided for him. He was interned to cardiovascular intensive care unit and aortic valve replacement was made with 25 no SJ prosthetic valve.Aortic valve wall was fibrocalcific and approximately 1,6 * 2,2 cm sized vegetations was seen on the valve. There was no microorganism produced in valve culture.

Discussion

The incidence of IE continues to rise, with a yearly incidence of ≈15 000 to 20 000 new cases. Although advances in antimicrobial therapy and the development of better diagnostic and surgical techniques have reduced the morbidity and mortality of infective endocarditis, it remains a potentially life-threatening disease.[4] The most common cause of the endocarditis is the infection and endocarditis due to lactococcus lactis is a rare clinical situation that most frequently occurs in immunocompromised patients or in those with impaired local defense mechanism in which this usually non-pathogen microorganism may be cause of severe infection.[5]

Diagnostic work-up, including a complete transthoracic and transesophageal study, must be performed immediately in every patient admitted to an intensive care unit with embolism, heart failure, cardiogenic or septic shock of unknown cause, as the data presented here suggest that prompt surgical intervention can be life-saving in patients with infective endocarditis despite the presence of severe shock and the occurrence of multiorgan failure.[6] Infective endocarditis caused by lactococcus lactis is a rare clinical situation,so it must be considered as one of the factors of infective endocarditis. Early surgical intervention in lactococcus lactis endocarditis can save lives.

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