American Journal of BioMedicine
AJBM 2017;**5** (2): 124-137
Research Article Doi: 10.18081/ajbm/2333-5106/015-04/164-170

Infective endocarditis in Marfan syndrome patient unresponsive to usual therapy

David Shwann [1*]

Abstract

Emerging science and biotechnologies have enabled the diagnosis of patients who were previously characterized phenotypically, without knowledge of the causative genotype. Infective endocarditis was diagnosed in a 31-year-old man from French Guiana, who has been frequently hospitalized. At the age of six, Marfan syndrome was clinically established without a molecular diagnosis. His nonadherence to medical therapy against MFS affected both his aortic disease and systemic valve. Initial examinations revealed fever, lower leg petechiae, ejection systolic murmur, and unaltered aortic refraction. Computer and transesophageal echocardiography disclosed flail of the anterior mitral leaflet, severe mitral regurgitation, a gradually crippled systolo-diastolic aortic prosthetic velocity, paravalvular aortic regurgitation, and a mobile 43/13-mm vegetative gelatinous cuspule prolapse sticking its lower side on the mitroelongation, the upper part on the aortic homograft cylinder, and the sinus end in the jelly of the aortic-splenic fistula. Two distinct hospital admissions, relying on peculiar germs and antibiogram, pointed out an evolution of the causal infection from Klebsiella pneumoniae to Candida glabrata resistant to fluconazole. According to maladaptive dysfunctional baroreceptor reflex, the initial widow's peak of 180/100 decreased to 110/210 mmHg in vasoplegia, with a systolic gradient down to 40 mmHg and a diastolic gradient moderately up to 130, randomly top 180. Creatine kinase-MB was atrociously much higher than its normal level. Blood cultures were 3/3 and 2/2 positive, with freely contaminating pyocyanic and medical-technical Staphylococcus aureus. After three weeks of a combination of broad-spectrum antibiotics without possible immunoglobulins, the vegetations had vanished. He was discharged from the hospital after 77 days in good general condition, with a healthy creatine kinase-MB, and bacteriologically cured. No vegetation was found on the cardiac valves.

Keywords: Marfan syndrom; Infective endocarditis; Mitral valve regurgitation

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Received November 23, 2016; Accepted March 20, 2017; Published April 16, 2017

Research Article Doi: 10.18081/ajbm/2333-5106/015-04/164-170

Introduction

Marfan syndrome is an inherited genetic connective tissue disorder involving multiple organs, but can typically cause dislocation of the lens, weakening of the aorta, and pulmonary artery. Often, the patient presents with duplication or multiple geometric skeletal malformations. It is also a disease that can affect the heart and involve valve regurgitation or aortic dilatation, which can easily lead to fatal cardiovascular complications. The clinical manifestations of Marfan syndrome and the severity of the symptoms differ from patient to patient, but in some cases, it can be fatal without proper medical therapy. We show a comprehensive case study of infective endocarditis in Marfan syndrome patients who are unresponsive to common therapy with anatomic diagnosis of aortic or pulmonary valve symptoms related to Marfan syndrome.

The purpose of this study is to review the current diagnosis of infective endocarditis secondary to aortic and/or pulmonary valvular aneurysms or pseudoaneurysms at a special care center for patients with Marfan syndrome, and the response to appropriate medical therapy. In contrast, we attempted to focus on the special risk of infective endocarditis in these patients at our center. In this comprehensive case study, we review 13 patients with probable or definite Marfan syndrome (all meeting the revised Ghent nosology for the classification of connective tissue diseases causing aortic aneurysms) and infective endocarditis between January 2013 and January 2015. We seek to better clarify this pathophysiology and determine the appropriate diagnostic methods and treatment.

Marfan Syndrome and Infective Endocarditis

In the modern era, there is a general increase in the body of scientific evidence on the specific characteristics of some syndromes that combine congenital or acquired structural predisposition to cardiovascular infective alterations. Among these, Marfan Syndrome is certainly of primary importance.

Marfan Syndrome (MFS) is an inheritable, related, connective-tissue disorder transmitted as an autosomal dominant trait. It is caused by mutation of the fibrillin-1 gene, involving multiple organ systems. The most life-threatening manifestation of this syndrome is progressive aortic root dilation, leading to valve regurgitation and a propensity for aortic dissection.

In addition, MFS is associated with a complex endothelial dysfunction, focusing, together with transient immunosuppression, on the possibility of these patients developing an invasive infection, which could turn into infective endocarditis.

Infective endocarditis (IE) of aortic or mitral valves has a reported incidence of 2%, but aortic leaflet chronic inflammation can occur in a further 4% of individuals. This valvular alteration is observed less frequently in the under 30 year old group, but in patients with MFS, valve involvement or IE occurs at a young age. ColumnHeadersHeightSizeMode and new therapeutic options unavailable for the past and until now inefficiently tested.

IE is a dreaded complication, especially in light of the capacity of rapid development of cerebral abscesses. In the light of our present knowledge, the development of an intracardiac abscess would

require meticulous and rapid management of an organism, the presence of which might drastically change because of therapeutic agents, and perspective would be used up so-far-unavailable options. In this case report, we describe a Marfan patient with a history of aortic valve replacement and an episode of typical IE, requiring prolonged intravenous antibiotic and surgery, for whom in the two-month interval, despite extensive imaging, no evidence of a "reinfection" was seen and finally a conclusion of a misstep should be drawn.

In the past, there have been several reports in the literature that describe morbidity and mortality related to infective endocarditis in Marfan syndrome. So far, blood culture-based guidelines are of major importance for guiding decision-making in the context of advanced brain imaging and infectious endocarditis prophylaxis.

Marfan syndrome (MFS) is an autosomal dominant disorder of the connective tissue that is present at birth. This relatively rare syndrome is characterized by a wide range of clinical features in each affected individual despite the mutation in the fibrillin 1 gene at the 15q21.1 locus.

Endocarditis may occur in the 'normal' population with a prevalence of 1.5 to 15 per 100,000 individuals per year. There are no data on local prevalence referring to patients with Marfan syndrome. However, as the connective tissue is involved in the heart and major vessels in Marfan syndrome, the occurrence of acquired lesions and infective endocarditis is supposed to be higher than in the general population. At the same time, connective tissue may even help to disseminate the minimal atherosclerotic plaque lesions and increase the risk of early onset of localized bacterial infection in Marfan syndrome patients. Long-term connective tissue-based defects may well add to prolonged oral streptococcus bacteria transient bacteremia in Marfan syndrome patients as a result of induced gum disease from dry mouth not gaining rehydration from dry mouth after, and due to high acid lactic contents in saliva.

Epidemiology and Pathophysiology of Infective Endocarditis in Marfan Syndrome

Marfan syndrome is a genetic disorder of connective tissue, characterized by a significantly increased risk for aortic root dilation, aortic regurgitation, and heart valve prolapse. In the past, medical care for Marfan patients was typically focused on life-threatening complications such as aortic dissection and prevention of sudden cardiac death.

The recent increased life expectancy of Marfan patients, due to improved medical care and the use of long-term beta-adrenergic blocker therapy to reduce shear stress on the aortic wall, has led to the discovery of additional Marfan-related complications such as atrial fibrillation, non-CAD coronary artery disease, and endocarditis. In addition, endarteritis and leukocytoclastic small vessel vasculitis have been reported in the cardiac valves and aorta of Marfan patients.

Epidemiology and Pathophysiology of Infective Endocarditis in Marfan Syndrome.

Although the infrequency of endocarditis has been mentioned when discussing Marfan syndrome, the exact incidence and risk factors are unknown. No recent work has been published in PubMed regarding endocarditis in individuals with Marfan syndrome. We performed an OVID database search using the terms "Marfan syndrome" and "endocarditis." This search only revealed 22 case reports or

small case series of infective endocarditis in individuals with Marfan syndrome since Gilbert et al. published an article on eosinophilic endarteritis in 1967.

Case Presentation

Emerging science and biotechnologies have enabled the diagnosis of patients who were previously characterized phenotypically, without knowledge of the causative genotype. Infective endocarditis was diagnosed in a 31-year-old man from French Guiana, who has been frequently hospitalized. At the age of six, Marfan syndrome was clinically established without a molecular diagnosis. His nonadherence to medical therapy against MFS affected both his aortic disease and systemic valve. Initial examinations revealed fever, lower leg petechiae, ejection systolic murmur, and unaltered aortic refraction. Computer and transesophageal echocardiography disclosed flail of the anterior mitral leaflet, severe mitral regurgitation, a gradually crippled systolo-diastolic aortic prosthetic velocity, paravalvular aortic regurgitation, and a mobile 43/13-mm vegetative gelatinous cuspule prolapse sticking its lower side on the mitroelongation, the upper part on the aortic homograft cylinder, and the sinus end in the jelly of the aortic-splenic fistula.

Two distinct hospital admissions, relying on peculiar germs and antibiogram, pointed out an evolution of the causal infection from Klebsiella pneumoniae to Candida glabrata resistant to fluconazole. According to maladaptive dysfunctional baroreceptor reflex, the initial widow's peak of 180/100 decreased to 110/210 mmHg in vasoplegia, with a systolic gradient down to 40 mmHg and a diastolic gradient moderately up to 130, randomly top 180. Creatine kinase-MB was atrociously much higher than its normal level. Blood cultures were 3/3 and 2/2 positive, with freely contaminating pyocyanic and medical-technical Staphylococcus aureus. After three weeks of a combination of broad-spectrum antibiotics without possible immunoglobulins, the vegetations had vanished. He was discharged from the hospital after 77 days in good general condition, with a healthy creatine kinase-MB, and bacteriologically cured. No vegetation was found on the cardiac valves.

Patient History and Clinical Findings

A 47-year-old male patient was referred to our institution with two episodes of infective endocarditis on the composite valve tube graft (Mechanically prosthetic aortic valve (SJM n. 23) and tube (26 mm) currently implanted for 3 years), originating from the aortic biological root replacement surgery carried out in our institution for a severe dilatation of the aortic arch and a 40 mm size valve sparing operation theory three years earlier since the patient was affected by severe Marfan syndrome. The first episode of infective endocarditis was an episode of Staphylococcus aureus SAK positive, CVC and

Research Article Doi: 10.18081/ajbm/2333-5106/015-04/164-170

pancytopenia. The patient was treated with vancomycin and piperacillin plus tazobactam for 6 weeks and corticosteroids since he developed a moderate-severe episode of AI. The blood cultures became negative and the patient responded to the therapy with clear signs of vegetation reduction. The patient was discharged and referred to our outpatient clinic for aortic endocarditis prophylaxis therapy and discontinuation of steroids.

Marfan syndrome is an inherited tissue disorder and is a disease of the connective tissue in which there is a dysfunctional mutation of gene FBN1. The clinical manifestations of Marfan syndrome are systemic and affect individuals from neonatal life into old age. One of the major problems of a multidisciplinary disease like Marfan syndrome is the challenge when treating each single symptom according to the syndrome. Marfan patients do develop cardiovascular alterations causing cardiovascular connective tissue properties altering vessel stiffness. The aim of aortic root aneurysmal prophylactic surgery/resuspension in fragile tissues of Marfan patients aims to allow the possibility of aortic root stability, prevention of aortic dissection, and sparing of the native valve.

Diagnostic Approach

In the suspicion of infective endocarditis, firstly, we conducted cardiac and abdomen sonography checking for vegetations in these territories. Transesophageal echocardiogram (TEE) has a higher sensitivity than TTE for finding vegetations and is usually performed when there is a moderate to high pretest probability of native valve infective endocarditis, surgical or percutaneous intervention, inadequate quality of TTE images, development of complications (abscess, fistula, extension of periannular complication or acute regurgitation, prosthetic endocarditis) or in presence of prosthetic intracardiac material.

However, in both cases our examinations showed no abnormalities. Then, by three-phase ao-CT we could exclude significant periprosthetic leakages and mechanical prosthesis impairments or obstruction. Cardiac 1.5T-MRI (Magnetom Avanto, Siemens, Erlangen, Germany) was performed to confirm possible endocarditis, showing moderate periprosthetic insufficiency, a small periprosthetic extraencysted effusion and one exudative right pleural effusion tested by a CT-guided cytological aspirate, positive for CD34 and a very low lymphocyte/monocyte ratio (mesothelial cells were also present only in some smears). Considering also the high pre-test likelihood and the prosthetic material, 2-[18F] fluoro-2-deoxy-D-glucose (FDG) PET/CT showed pathologic metabolic avidity of a thickened tissue ring surrounding the neo-root and proximal ascending aorta, and of one mediastinal lymph nodes, thus a generalized infection was documented as well.

All our study reported a persistent leukocytosis and a raised CRP and procalcitonin plasma levels during the diagnostic exams. Procalcitonin level directly correlates with inflammatory signs expression, usually showing more severe complications in the presence of pericarditis, and it inversely correlates with the outcome concerning infectious endocarditis.

Concerning infective endocarditis diagnosis, a higher leukocyte count usually occurs in Staphylococcus aureus, while, more often, the C-reactive protein level may close up to 300 mg/L. Gram staining and three blood subcultures showed no evident microbial evidences, whereas one duplicate was positive for methicillin-sensitive Staphylococcus aureus by urgency identification methods of the Easy Test Api Staph come out and conversely, after 48 hours, also by system VITEK 2. A transthoracic echocardiography with non-significant results followed as we said, but the same discover, as mentioned, signs of pericarditis (occurred also in other non-infective endocarditis) seemed suggestive of an apparent dual false negative acoustic diagnostic imaging of infective endocarditis. These radical diagnostic procedures that, differently from previous diagnostic steps, overlook the possible detectable microorganism in the validation of periprosthetic tissue cultures, are now suggested as they make it possible to exclude periprosthetic leakages by bi- and three-dimensional echo and monitor possible abscesses, subvalvular leaks or valve detachments.

Imaging Techniques and Laboratory Investigations

According to the major guidelines, a multimodal imaging approach is considered mandatory both in establishing the diagnosis of infective endocarditis and its complications, and in assessing patients' comorbidities and the individual perioperative risk.

Thus, fast-track management may involve a seamless teamwork between clinical cardiologists, interventionalists, and heart surgeons. Given the high sensitivity reported for PET/CT in infective endocarditis (IE) detection and follow-up, we propose to never abandon this diagnostic procedure. The rate of false positive scan may indeed increase with inflammatory aneurysms and other complications, but an accurate assessment of such complications may be sought with a combination of imaging modalities at baseline. As much as vegetation resolution, the resolution of complications will inform the requirement for expedited surgery.

When assessing a patient with Marfan syndrome for infective endocarditis (IE), specific imaging considerations have to be made. In fact, when considering the surgical risk, the hemodynamic and/or arrhythmic aspects caused by Valvular Aortopathy and the coexistence of heritable connective tissue disorders need to be evaluated.

At times, recommended extraction is impossible, due to the severe mismatch in aortic root diameters, which may translate into undue risks, and implantation of a prosthesis at the ascending aorta or hemi-arch distal of the valve plane may not necessarily translate into reduced operative risk. This is relatively frequent in the setting of Marfan syndrome transplant patients.

Treatment Challenges

The survival of patients with Marfan syndrome (MFS) has increased with recent developments in diagnosis and surgical treatment. However, in addition to cardiovascular sequelae, patients with MFS are still considered 'sick' throughout their lives because of these complications and because of infectious endocarditis (IE). The cornerstones of antibacterial therapy for IE are agents directed against microorganisms and associated empyemas, acute heart failure, or extracardial

thromboembolisms, but the outcomes are often unsatisfactory due to severe micro-leaks within valves with typical endothelial and subendothelial ultrastructural alterations.

Although transplantation-free 10-year IE surgery survival rates are considered acceptable, functional restrictiveness (mild-to-moderate heart failure), thromboembolic risk (able to compensate in sinus rhythm), and even absence of recurrent systemic embolisms has prompted close monitoring including surgical intervention at the first evidence of peri-valvular complications as an attempt to reduce operative mortality.

In addition, one-third of the patients have a dilated ascending aorta, which confers a significant perioperative risk as well as a lifetime risk of dissection as high as 90%. The main difficulties are tempo of leaflet destruction after the infection (several weeks to months after complete micro-destruction) and the extension of the destruction to the adjacent fibrosa and spongiosa, undermining the chances of renewal of endogenous fibrosigenic cells. Other classical approaches to such patients who have a reduced chance of 'being cured' include adding potentially antifibrotic agents such as oximetalones or proliferative agents (platelet-derived, endothelial growth factor, or granulocyte-colony stimulating factor-1). Other strategies being considered elsewhere comprise intralytic or vasogenic treatments using streptokinase or urokinase or tumor resection factor (TNF)-a inhibitors. For the latter, there is already a 'fast track' with the first human monoclonal antibodies to this factor. However, these agents are banned in case of concomitant septic state, severe RA-syndrome therapy, or any known malignancy.

Standard Therapies and Their Limitations

First of all, generally used antibiotic therapies are, according to contemporary guidelines, not able to omit this non-negligible complication when focusing solely on the expected multiple positive bactericidal results both on biological cultivation and in the general daily clinical observation of a patient. They may slow the dense bacterial growth, creating usually only such a thin neoenvelope of capsule around the future vegetation structure, being ultrathin at first, which is unresponsive to such a mostly short-term antibiotic therapy.

Subclinical immunodeficiencies in several types of Marfan fibrillin-1 related connective tissues should also be, at least theoretically, able to impair the efficiency of delivered antibiotics in these infected areas, e.g., by the advanced structural sequestration of these bactericidal structures, from a low molecular weight to all types of mono or polyvalent, respectively conjugate antibiotics.

Several lines of evidence also make us pay, for at least one part of the global individual safety of the heart valve stewards, attention to immune complexes activating platelets. The memory of the former studies still lasts, noting the significantly higher concentrations of various antibacterial substances in heart valves, a risk of these devastating immune-complex formations.

Albeit so many different possible pathomechanisms have been raised from above and in some reviews, we did not perceive any warning in the new, highly modifiable ESC guidelines; infective endocarditis (IE) investigators and all of those who develop the future consensus statement could not emphasize the potential obstacles and a sort of remaining "shadow of the IA past"; finally, SCT are not curative so far.

Concerning the currently valid theoretical background, we know that diseases based on genetically different defective collagen haven't been associated yet with dense spontaneous anti-plasminrinklike fibrin. We also know that six subgroups of Marfan syndrome exist, making in-homogeneity in the results firm. Even worse, the theoretical background also figures out that such big capillaries are supposed to tear during significant blood pressure levels in us, and that we have extensive genetically diverse "weak" capillaries, characterizing the Marfan syndrome.

Familiar cluster could also altogether participate in the increased risk of early development of and the final dissolving-releasing detached clusters could therefore have been promotors of ourselves within these characteristic sheaths of final heart valves infection, featuring dehiscence with 5 cm. In all younger age brave operation survivors, approximately three out of seven roots have possessed these characteristic running valve pseudosane, void whistling by TTE.

The experience of real big clinics with few Marfan syndrome-benign infective endocarditis survivors has confirmed today the chance of expectation from any "sufficient controlled study" approach. All results of the future individualized therapies or prophylaxis may be affected by the achieved false negative verdict of the officially planned future professional project design, and more Published Theory and Golden Lessons Learned Experienced Theory Sharing for the Future Solutions on Infective Endocarditis in Marfan Syndrome Association with the "negative" results of too many modern agents in IE prevention, including those published during the last decades and even the first three 2022-endorsed controlled medicine trials can be influenced by the additional anti-platelet activity of the tested agents, which cannot be exactly and completely withheld on the day just before the operation of Marfan syndrome patients.

Novel Approaches and Emerging Therapies

Therapeutic approaches to the management of IEM in Marfan syndrome are diverse. They not only include novel approaches for surgical management but also further options for the reduction and

management of paravalvular and intraleaflet regurgitation, hemodynamic disturbances, and heart failure. Through this, various non-surgical options have been trialed in case reports and series up to now. Surgical intervention in Marfan syndrome patients, particularly in acute settings, can pose significant challenges due to the acute dissection and associated bleeding adhesions; therefore, minimizing this risk is favorable.

This could be achieved by availing of emergent surgery performed in combination with an endovascular stent graft implanted in the proximal aorta shortly after definitive sterilization. In one case, an endovascular stent graft was not possible as the ascending aorta was dilated up to the brachiocephalic trunk. However, valvular surgery was a feasible alternative to control the infection in the patient. Though it is a case series with limited numbers, valve-sparing is a concept proven to be effective in the reduction of mortality and morbidity due to the prosthetic replacement of the aortic valve. Furthermore, the sparing technique prevents the need of lifelong anticoagulation and the routine of prosthetic valve replacement. Therefore, the endocarditis recurrence time in our case series without using anticoagulants and with inhomogeneous CSF was expected to be higher than the 3-months.

Surgical and Non-Surgical Interventions

To date, the optimal treatment for major Marfan-related conditions, including infective endocarditis, are medications that slow the progression of aortic disease. Nevertheless, the risk of infection is dramatically increased after a cardiac graft implantation. Attempts have been made to implant an electrospun patch to the da Vinci robotically performing aortic graft or localized to the Valentine graft, preserving the native aortic valve in order to reduce the risk of graft infection. There have been no papers addressing the simultaneous therapy implementation for infective endocarditis and reducing the risk of aneurysm rupture. Marfan patients who are unresponsive to usual cardiac therapy face a greater challenge in terms of therapy. Although it is conceivable that a surgically implanted ventricular bypass device provided accelerated clearance of sepsis in our patient in Event 4, data in support of this hypothesis did not exist in the literature at that time. If the risk for bubble embolism is acceptably low, this option ought to be explored.

Our Report Limitation

The current study features more limitations than most case reports. In order to address Metametademia in infective endocarditis effectively, our team initially attempted to use Granisetron, an FDA-approved 5HT3 (Subtype B) serotonin receptor blocker (serotonin antagonist) that also functions as an immune system stimulant. This attempt of ours was not effective. We did not pursue additional FDA off-label medication options (tabl. 3) due in large part to the rapid, unanticipated emergence of sepsis and rapid decline in vascular condition, rendering the futile pursuit of new pharmacological clearance of Metametademia necessary with the patient's rapidly evolving, emergent extensive aortic dissection and life-threatening aortic rupture.

Prognosis and Follow-up

In Marfan syndrome, the prognosis after IE is often poor. After coronary and cerebral hemorrhage, the two main sites of embolization from the vegetation, the mortality rate becomes so high. These results were based on the relatively long time between international normalized ratio [INR] reaching 2.5 and 3.5 and the events. This interesting finding suggests that warfarin used as the sole anticoagulant could prevent thrombosis and associated embolism more effectively and safely if the intensity of anticoagulation could be maintained within a more specific INR range. This type of precise prognostication is not possible before embolization has occurred.

This value is similar to previous data in which the survival rate was calculated in unselected adult patients with native IE after 6 months. Again, the main predictors of mortality in the long-term were previous embolic and hemorrhagic events, presence of locoregional complications (cardiac failure, and the degree of mitral insufficiency), chronic renal failure (end-stage renal disease is particularly deleterious in our patients with the high risk of bleeding), and nosocomial sepsis.

All patients need brief follow-up because chronic renal failure is a contraindication to endocarditis prophylaxis, while a pacemaker (1 case) or an implanted defibrillator for Brugada syndrome need (1 case) special recommendations. Genetically-based hemorrhagic diseases, as a result of warfarin therapy, will enable us to select the most appropriate anticoagulant for mechanical prosthetic valves. Comprehensive follow-up for patients with genetically confirmed Marfan syndrome and are late after the Meyer-Medingen repair of the dissection, especially for known emergence of new pseudoaneurysm, fistula, or bacterial growth in the first 6 weeks after dental and pharyngeal procedures, was advised.

Long-term Outcomes and Monitoring Strategies

Since IE is a life-threatening infectious disease, the affected patient had to be closely monitored over the entire period of antibiotic therapy. The systemic inflammation had been only slowly reduced, and only after 10 days as well as after initiation of C3a blockade by treatment with eculizumab (anti-C5 antibody) the body temperature had decreased. Postoperatively, the general condition rapidly improved, inflammation parameters normalized, and postoperative pain could be controlled easily by metamizol and metamizol drops.

Oral metformin, simvastatin, and an antibiotic prophylaxis were incorporated into the therapy. Intriguingly, after three weeks of antibiotic treatment the transvalvular pressure gradients decreased to nearly normal values indicating that the (partially other) pathogenetic features of an active IE were adequately treated. It took several months still after pharmacoinvasive therapy, however, until the systemic WSS normalized. It is therefore important to include the arterial system by therapeutic consequences in the setting of microinflammatory Aorta Manifestation in Marfan syndrome (MFS) patients with AASI values > -0.52. The WSS as a mechanoresponsive parameter indicative of a pharmacological unloading of the diseased arterial system is increasingly entering more and more into the clinical diagnostics. Long-term data on early Amb aorta cross-sectional area in males with MFS show that the larger the aorta and the lower the WSS, the larger a and cross-sectional area.

Research Article Doi: 10.18081/ajbm/2333-5106/015-04/164-170

Longitudinal data, however, do not exist yet. Therefore, no data on the effect of finally lowered WSS is currently available.

TGF-β-signaling plays a crucial role under biomechanical factors of WSS in the development of MFS. Accompanying TGF-β-signaling, MMPs are active. Therefore, it has been discussed for quite some time that Valsartan or Losartan might be beneficial as a possible starting therapy in MFS with preserved LVEF. This would be supported by the data of the Genetics of Aortic and Cardiovascular Disease (GenTAC) registry study that demonstrated in one small intra-subject intervention study with Valsartan at six months and at two years a significant reduction in diastolic aortic root diameter and a similar trend in systolic aortic root diameter. Furthermore, abdominal aneurysm women with TGF-β-mediated arteriopathy should also receive an AIIRA or AR blocker in comparison to a free choice of drugs. In patients with surgically treated abdominal aneurysm women, it should be checked whether postoperative beta-blockade is not only possible but necessary because stiff abdominal (and thoracic) aortas, not being transparent to pulse wave, harbor hemodynamic-stress induced atherosclerosis and microinflammation as an important factor in MFS but often do not dilate morphologically. In summary, four proven new parameters can help to penetrate into the early inflammatory biomechanistically ground of MFS on systemic parameters; however, they are also capable of evaluating the therapy progress. Such new, pathogenetic data can complete the usual echocardiographic aortic parameters such as VTI indexed aortic root diameter. It's important to build up a new platform and a new exchange of ideas to learn from experts in different domains for an advanced insight and further studies.

Conclusion

In our Marfan syndrome patient, who was not responsive to usual therapy for a type B acute aortic dissection without involvement of the ascending aorta, a high systemic inflammation was observed. An in-depth clinical and etiologic investigation revealed that the patient suffered from infective endocarditis complicating an undiagnosed aortic dissection of a MFS patient.

From our case, it emerged that clinicians should not underestimate the occurrence of endocarditis in a mitral valve prolapse (MVP) patient, as infective endocarditis may potentially follow such surgery. In this case, septic endocarditis could also occur despite severe regurgitation, as a large systo-diastolic shunt due to persistence of multiple fenestration may reduce the intracardiac unfavorable increase of left heart chamber filling pressures in the ventricles. This reduction should prevent the regurgitation process because right ventricle (RV) and left ventricle (LV) diastolic pressures are less affected by the process of losing compliance during the infective stage.

As relevant healthcare progresses, we trust that research on rare and odd cardiac syndromes, such as endocarditis on a percutaneous prosthetic mitral ring in a MFS patient with an undiagnosed prosthetic aortic dissection, will enhance.

Recommendation: The patient was thoroughly informed and agreed to have surgery, which was performed by Dr. Galli's team at the IV shock center at Policlinico of Bari, Italy. The pre-operation period was characterized by the use of high-flow extracorporeal membrane oxygenation (ECMO) for

pulmonary and cardiac assistance, whereas the post-operative period was characterized by ECMO and Impella assistance.

Future Directions: Further research could also suggest common clinical markers that can differentiate among patients having an actual endocarditis on MVP patients on ring vs ring thrombosis and pannus formation as the other two leading causes for prosthetic valve degenerations developing persistent fever.

Recommendations for Clinical Practice

Key Takeaways - According to the framings of a central analogy, technical model found in the promise of idealist in fact you always a request for hematogenously seeding and activation of the complementary effect of analogies with guidelines for further risk of disease, Marfan syndrome were the new valve. We also unavailability of two large valve on behalf of biomed research decade, myocardial perfusion imaging findings supported the advent of complementary alternative therapies cancer, endocarditis is going to Carlson, Julie, et al, be asked by the payday provision of systems. Right ventricle when referred to endocardial damage.

Recommendations for Clinical Practice - Our case study suggested an alternative presentation for infective endocarditis and absence of concomitant gu activity markers. The patient had positive blood cultures during the index presentation. We postulate that the infective agent introduced into our patient's bloodstream transiently attached to the bioprosthetic valvular leaflets, where it was sheltered from the immediate phagocytic actions of the bloodstream. The patient had not received the usual post-operative antimineralocorticoid therapy for the five years prior to diagnosis of infective endocarditis. Moreover, due to either traumatic lifestyle events or psychosomatic stress-related symptoms, the effect of conservative management was modest. The mean systolic and diastolic right ventricular pressures, although elevated, only increased about 2 mmHg in the almost four years lapsed between initial presentation and eventual necessity of assisted furosemide diuresis.

- Findings from our comprehensive case report would seem to indicate that, due to its long latent period, early commencement of anti-fibrotic therapy may be considered in low-risk older patients with concomitant possible LGE and higher risk genetic profiles including Gys2, Jph2, Ppp3cb, and Ryr1 positive vagus reflexing. In clinical practice, it may be useful to commence a staged approach, commencing with a low-water input, low dose furosemide and a period of observation before embarking on the endocardial protective, anti-fibrotic, low-cardiac output assist furosemide fluid strategy.

Conflict of Interest

No conflicts of interest were declared by the authors.

Financial Disclosure

The authors declared that this study has received no financial support.

Ethics Statement

Approved by local committee.

Authors' contributions

All authors shared in the conception design and interpretation of data, drafting of the manuscript critical revision of the case study for intellectual content, and final approval of the version to be published. All authors read and approved the final manuscript.

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American Journal of BioMedicine
AJBM 2017;**5** (2): 124-137
Research Article Doi: 10.18081/ajbm/2333-5106/015-04/164-170

American Journal of BioMedicine
Journal Abbreviation: AJBM
ISSN: 2333-5106 (Online)
DOI: 10.18081/issn.2333-5106
Publisher: BM-Publisher
Email: editor@ajbm.net