

Non-Coronary Aortic Sinus Dilatation with Aortic Regurgitation in a Marfan's Syndrome Patient – A Case Report

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Summary:

Aneurysm of the coronary sinus is an uncommon clinical condition. It is rare to come across an uncomplicated aneurysm as it remains silent and most of the available literature describe treatment plan after a rupture has taken place. Our case a 41 year old female also had aortic regurgitation and was a Marfan Syndrome patient. We

carried out a modified Bentall's procedure on an elective basis for this patient. It may be noted this is the first time such a surgical procedure has been carried out successfully in Bangladesh. Here we describe the rationale in deciding our treatment plan.

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Introduction:

Marfan's syndrome is a disease of the connective tissue. In the human body connective tissue holds and provides support to many structures throughout the body. In Marfan's syndrome as the connective tissue is abnormal, many systems are affected particularly the heart, blood vessels, bones, tendons, cartilage, eyes, nervous system, skin and lungs. Marfan's syndrome is caused by a defect in the gene that encodes the structure of fibrillin and the elastic fibers. These are the major components of connective tissue.

In most cases, Marfan's syndrome is inherited. The pattern is called "autosomal dominant," meaning it occurs equally in men and women and can be inherited from just one parent with Marfan's syndrome. People with Marfan's syndrome, have a 50 % chance of passing along the disorder to their children. In 27% of cases a new genetic mutation defect occurs due to an unknown cause¹. Marfan's syndrome is also referred to as a "variable expression" genetic disorder, in that everyone with Marfan's syndrome has the same defective gene,

but not everyone experiences the same symptoms to the same degree.

Marfan's syndrome is present at birth. However, it may not be diagnosed until adolescence or young adulthood. Marfan's syndrome is fairly common, the estimated incidence ranges from 1 in 5,000 to 1 in 10,000 persons². It has been found in people of all races and ethnic backgrounds, but is more common in China.

Sometimes Marfan's syndrome is so mild, few if any, symptoms occur. In most cases, the disease progresses with age and symptoms of Marfan's syndrome become noticeable as the changes in connective tissue occur. Marfan's syndrome patients are usually tall and thin. Their arms, legs, fingers and toes may seem out of proportion, too long for the rest of their body. Their spine may have scoliosis and the sternum may either protrude or be indented inward. Their joints may be weak and easily become dislocated. Often, people with Marfan's syndrome have a long, narrow face and the roof of the mouth may be higher than normal, causing the teeth to be crowded. More than half of all people with Marfan syndrome have eye problems.

Marfan's syndrome cannot be diagnosed by a single molecular test but requires a scoring system that combines various diagnostic items. The so-called Ghent nosology subdivides diagnostic features into "major criteria", "minor criteria", "organ involvement" and manifestations that only in combination with other

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manifestations constitute a “major” or “minor” criterion. Individuals without a family history of Marfan’s syndrome require major criteria in at least two different organ systems and involvement of a third organ system. Individuals carrying an *FBNI* mutation known to cause Marfan’s syndrome or cases with a positive family history require one major criterion and involvement of an additional organ to establish Marfan syndrome³.

A thorough physical examination of the eyes, heart and blood vessels, and muscle and skeletal system; a history of symptoms; and information about family members that may have had the disorder usually leads to a diagnosis. Other tests, such as Chest X-Ray, ECG, Echocardiography, Trans Esophageal Echocardiography, CT scan, MRI and CT Angiography are useful tools in the diagnosis. Nowadays CT Angio is proving itself to be a very valuable tool in showing the vascular system changes.

Case Report:

Ours was a 41 year old female patient born on the 6th of January 1968. She is the youngest among four brothers and three sisters. She grew much taller in comparison to her siblings. The physical height of her parents were in proportion to her siblings. Her first symptom was about the age of 14 years in 1982. She describes her symptoms as “palpitation” for which she consulted a village doctor. The symptoms however continued intermittently and were not severe enough to be a cause of undue concern to her or to the family. She got married in 1991 at the age of 23 years. She gave birth to a daughter in 1993 and a son in 1997. Both the pregnancies had a normal course resulting in normal vaginal deliveries. Around the beginning of 2005 her “palpitation” as she described it increased. She consulted an herbal practitioner who prescribed her a “Hamdard” preparation. This did give her a good response and she was alright till the end of 2005. Now the “palpitation” reoccurred. This time she consulted a cardiologist in early 2007 who arranged for an Echo Doppler study of the heart and a coronary angiogram. The reports showed a normal coronary tree, dilated non-coronary sinus and a grade III aortic regurgitation. With this report she contacted the surgeon at our hospital in December 2007. A repeat Trans thoracic echo study of the heart and a CT Angio was done. The Echo showed a hugely dilated aortic root with aneurismal non-coronary sinus, also

severe aortic regurgitation. CT Angio very beautifully demonstrated the anatomy. The details are given below. Her daughter now 14 years old has also grown much taller than her brother and has a thin skeletal frame. All these findings warranted a surgical intervention. Rationale and logic behind choosing a particular type of surgical procedure is given in the discussion part. The patient was electively admitted on the 3rd of January 2008.

Physical examination revealed she was normotensive with a blood pressure of 130/60 mmHg, heart rate was 60 per minute and regular, heart murmur of aortic regurgitation and a clear chest on auscultation. She was 168cm in height (much taller than her siblings and parents) and weighed 65Kg. All blood investigations were within normal limits, ECG and Chest X-ray were normal. Echocardiography report stated hugely dilated aortic root with aneurismal non-coronary sinus, normal chamber dimensions and wall thickness, intact IAS and IVS, no thrombus or vegetation, severe aortic and mild tricuspid regurgitation, mild pulmonary hypertension. CT Angiogram clearly showed the abnormal anatomy. Root of the aorta measured 55.0X46.6 mm, non-coronary sinus 34.7X36.7 mm in size, ascending, arch and descending aorta appeared normal

After due explanation consent was taken and the patient was taken to the operating room on the 6th of January 08. General anaesthesia was induced taking into account problems specific to the underlying pathology of Marfan’s Syndrome. Systolic blood pressure was maintained between 85 – 110 mmHg throughout the peri-operative period. This is necessary to avoid suture line dehiscence, aortic dissection distal to the prosthesis. Furthermore the patient was unduly sensitive to narcotics and muscle relaxants. This was managed using short/intermediate acting drugs namely Fentanyl and Propofol. The procedure was carried out via median sternotomy. The patient was connected to the heart lung machine using an aortic and two stage venous cannulation. The patient was cooled down to 26 degree Celsius. Heart was arrested after aortic cross clamp using antegrade cold blood cardioplegia directly into the coronary ostia. Operative findings confirmed the preoperative investigations. The wall of the aneurismal non-coronary sinus was extremely stretched and thinned out suggesting a possible rupture in the near future. A modified Bentall’s procedure was carried out with reimplantation of the

coronary buttons. An ATS size 27 composite graft prosthesis was used. After removal of the cross-clamp there was significant bleeding from the left coronary button. We were unable to control it satisfactorily. Also remembering that bleeding and arrhythmias are a common cause of post Bentall mortality. We decided to redo the left coronary button. The heart was again cooled down, cross clamp applied and arrested with antegrade root cardioplegia. The graft to aorta suture line was taken down. The left coronary button was oversewn and the procedure was completed as before. There was good haemostasis this time. The patient came off bypass with moderate inotropic support. The patient was closed and was shifted to the ICU in a stable condition. The Bypass time was 322 minutes and the total cross clamp time was 148 minutes. External pacing was started at 120 per minute as the desired heart rate was not present.

In the ICU patient started getting isolated ventricular ectopics which steadily got worse despite correction of all possible causes and doing the recommended medical management. Arrhythmia following Bentall's procedure is a common complication and sometimes is due to kinking of the coronaries just distal to the buttons. In order to improve coronary perfusion an Intra Aortic Balloon Pump (IABP) was inserted electively. Though this improved the haemodynamics but the arrhythmia did not improve. Soon after, the patient started getting runs of ventricular tachycardia and ventricular fibrillation needing DC shocks. As the situation got worse the patient was reopened in the ICU. There was very little collection, heart behaved normally as long as the sinus rhythm was maintained. But the bouts of VT and VF continued needing defibrillation by internal pedals. Just when we had nearly given up hope we decided to stop the external pacing to carry out a certain maneuver. But this had a completely unexpected response. The heart momentarily went into asystole then reverted back into sinus rhythm with a heart rate of 80 – 82 per minute. There were no further episodes of arrhythmias of any type and haemodynamics improved to the extent that we had to reduce inotropic support rapidly. It seems all this time the arrhythmia was due to "R on T" phenomenon resulting from the external pacing. This was a lucky find in a desperate situation. From this point of time onwards the patient made a smooth and steady recovery. The patient was moved to the surgical ward on the 3rd post operative day. She was

discharged on the 8th post operative day after the INR had come up to the desired level.

On discharge the patient was prescribed Warfarin to keep the INR between 3.00 and 3.5, Metoprolol to reduce the heart rate and blood pressure, Digoxin partly to reduce the heart rate and also to act as an inotropic agent and NSAIDs for pain relief.

Discussion:

The treatment approach depends on the structures affected and the severity. Medications are not used to treat Marfan's syndrome, however they may be used to prevent or control complications. Beta-blockers and calcium channel blockers are used to prevent or to slow down the enlargement of the aorta⁴. Surgery for Marfan's syndrome is aimed at preventing aortic dissection or rupture and treating valve problems. It is also the only way to deal with the same complications when they actually happen. Composite valve graft replacement or valve sparing procedures can be done. With valve-sparing operations, there is risk of possible re-operation in future, because the long-term durability of this type of repair is not yet established⁵.

Advances in the use of medication and surgery have dramatically increased the lifespan of people with Marfan's syndrome. An average life expectancy in 1972 was about 45 years. The average life expectancy now is approaching that of the general population⁶. Providing great hope and optimism to people with Marfan's syndrome and their families. This change has occurred primarily because of the quality of surgical intervention, although drug therapy may also have played a role. But, only through increased awareness about the disorder, earlier diagnosis and proper treatment can a person with Marfan's syndrome have realistic hope to live a normal life span.

Immediate surgical intervention is the single, life-saving measure to rescue patients with acute dissection or intramural haemorrhage of the ascending aorta (Stanford type A). However, it may only be 20% of individuals with acute aortic syndromes who make it into the operating room, and of those who get operated upon more than 10% do not survive acute intervention. Moreover, survivors of emergency surgery frequently experience complications from the dissected aortic flap that persists downstream from the ascending aorta. Conversely, when the aortic root is replaced before

complications occur, both early and late survival improves dramatically. A classical study with retrospective review of outcomes from 10 centers has set the standard for elective prophylactic aortic root replacement in Marfan's syndrome. The vast majority of patients were treated with a composite-graft replacement according to Bentall and De Bono or a modification of that technique. The study documented an early mortality of 1.5% and an actuarial survival rate of 84% at 5 years, 75% at 10 years and 59% at 20 years⁷.

Sinuses of Valsalva are three localized bulgings in the aortic root opposite the cusps of the aortic root. Aneurysm of the sinus is a rare condition which may be a congenital or acquired cardiac anomaly, having an incidence of 1.09% in the oriental population and 0.2% in the western population⁸. Aneurysms of the sinus of valsalva are not usually clinically apparent unless perforation occurs which simulates aortic regurgitation⁹. The two anterior sinuses are named after their respective coronary ostia. That is right coronary sinus and left coronary sinus and posterior coronary sinus is called the non-coronary sinus.

The unruptured aneurysm is usually silent and it often remains undiagnosed but may cause symptoms by right ventricular outflow obstruction¹⁰. The rupture may occur into any cardiac chamber, predominantly the right ventricle¹¹, the intraventricular septum¹², and the pericardial space¹³.

Surgery of the aortic root removes the weakest spot in the cardiovascular system of Marfan patients. However, with increasing life expectancy weaknesses of the heart valves, the myocardium and distal aorta get time to evolve. Currently, about one quarter of Marfan patients requiring surgery undergo mitral valve surgery, another quarter undergo reintervention at distal sites of the aorta, 6% have tricuspid valve surgery, and 3% require heart transplantation for dilated cardiomyopathy¹⁴. Moreover, 21% of adult Marfan patients develop ventricular arrhythmia with lethal outcome in 3% of cases¹⁵. We believe that future strategies need to consider these potential complications¹⁶.

Patients with aneurysm of sinus of valsalva remain asymptomatic clinically unless the aneurysm ruptures. The onset may be sudden or insidious. In our case patient presented with palpitation the investigation of which resulted in the diagnosis.

The decision to operate in these cases is frequently not simple: there is a substantial gray area that changes with time.

Recommending surgery at a diameter of 6 cm may have been appropriate in an era when the surgical mortality for elective replacement of the ascending aorta was relatively high. Today, in light of a markedly reduced risk of elective surgery, it seems excessively conservative. Strict adherence to this guideline from another era undoubtedly leads to missing the opportunity to prevent lethal complications in a substantial number of patients with a dilated ascending aorta¹⁷. There are no large follow-up studies to give a guideline for such a situation¹⁷⁻²⁰. To make matters worse there are hardly any recommendations available for an unruptured coronary aneurysm with aortic regurgitation in a Marfan's Syndrome patient.

Currently, elective root replacement with an appropriately chosen technique should not carry an operative risk much higher than that of routine aortic valve replacement. Composite replacement of the aortic valve and the ascending aorta, as originally described by Bentall, DeBono and Edwards (classic Bentall), or modified by Kouchoukos (button Bentall), remains the most versatile and widely applied method.

In our case we were faced with a clinical situation which by itself is a rare occurrence²¹. Furthermore this clinical entity is usually silent prior to rupture. There are publications in relation to sinus aneurysm but most of them deal with the measures taken after rupture. Publications dealing with an unruptured sinus aneurysm are very difficult to come by. One such paper describes a non-coronary sinus aneurysm²¹ accidentally discovered after a road traffic accident in a 38 year old male. As we already know such aneurysms can be caused by clinical conditions other than Marfan's syndrome²²⁻²⁴. Investigations also showed a moderate to severe aortic regurgitation. The patient underwent elective surgery when a metallic prosthetic valve was used to replace the aortic valve and the non-coronary sinus was repaired by direct suturing. The clinical scenario was very much similar to ours except the fact the patient was a Non-Marfan. This was a prime consideration in deciding our direction of treatment. Marfan syndrome is a progressive disease where the problems usually starts as a sinus dilatation and slowly progresses to full

blown aortic dilatation. Replacing the aortic valve and repairing the aneurysm would have been a simpler approach. But literature exists stating such case have returned years later with aneurysm of the remaining sinuses with or without aortic dilatation. A redo surgery in such situations carries a very high risk.

How do deal with an uncomplicated coronary sinus aneurysm generates much controversy with some advocating a conservative approach whilst others favoring aggressive surgery. We took the following strategy in deciding our surgical treatment.

We established the diagnosis of Marfan's Syndrome based on the following :

Cardio-vascular – regurgitant aortic valve, aneurysmal non-coronary sinus

Skeletal - Increased arm span-to-height ratio , reduced upper-to-lower segment ratio ,positive wrist sign , positive thumb (Steinberg) sign , joint hypermobility, high arched palate with dental crowding

Skin and integument - Striae atrophicae not associated with pregnancy or repetitive stress

Family history – Both her daughter and son exhibited the same skeletal and skin criteria of Marfan's syndrome. But for social reasons the family declined the daughter to be examined. She was approaching marriageable age.

Next we took note of the fact that emergency or urgent surgery after a complication has occurred carries a very high mortality. Even post operative mortality and morbidity is high. Therefore we decided on an elective surgical intervention. We also have to remember all the studies published are in the western countries where the home to hospital time is very short. The complete opposite is true for our country.

Next on deciding upon the type of surgical intervention the underlying Marfan's condition had a very important bearing.. Changes in the vessel walls are the commonest complication of Marfan's Syndrome and these changes manifest themselves with time. An aortic valve replacement with aneurysm repair ran the risk of the patient returning with additional changes in the future. So we went ahead and did a Modified Buttonhole Bentall's Procedure. This procedure also took care of the aneurysmal non-coronary sinus thereby eliminating the possibility of any future rupture.

There are no guidelines how to deal with an aneurysmal coronary sinus. We sifted through existing surgical experience as available. We decided on what we thought was best for the patient taking into consideration the underlying Marfan's Syndrome and aortic regurgitation. We decided to surgically address not only the aneurysmal coronary sinus and the aortic regurgitation , but also the potential problem of aortic root dilatation in the future. Till the write up of this paper the patient was keeping a very good health.

The purpose of writing this paper is to contribute some ideas about a clinical situation, on which very little has been published. We hope our opinion will be shared by others so that a guideline may be established in the future.

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