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ACUTE MYOCARDIAL INFARCTION IN A PATIENT WITH MARFAN SYNDROME

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ABSTRACT

Marfan syndrome is an autosomal dominant genetic disorder of the connective tissue which is characterized by a mutation of the fibrillin-1 (FBN1) gene. The disease primarily affects the cardiovascular system, eyes and the skeletal system. Cardiovascular manifestations of the disease, including progressive dilation of the aorta and mitral valve prolapse, can manifest in pediatric patients with Marfan syndrome which require constant monitoring by echocardiography and medical treatment. The aneurysm of the aorta which typically occurs at the sinuses of Valsalva and aortic dissection are considered as serious complications of this disease and can affect on the survival and prognosis of patients. The early diagnosis, drug therapy and prophylactic aortic root surgery are important steps in the management of patients with Marfan syndrome which can improve the quality of life and increase the survival of patients. The main treatment method for young patients with Marfan syndrome is the surgical replacement of the aortic root.

The improvement of the therapeutic and surgical treatment of this disease has increased the survival of patients with Marfan syndrome. The vascular complications which can develop after the aortic surgery generally increase with age. According to literature data new aneurysms in the arterial tree are found in about 70% of adult patients which require surgical intervention. The development of aneurysms and thrombosis of coronary arteries is a rare clinical state which can lead to postoperative complications in this patient population. The continuation of a long-term treatment after surgery is strongly recommended to patients with Marfan syndrome with echocardiographic evaluation of the descending and abdominal aorta.

The disease history, diagnostic procedures and performed treatment are discussed in this article. A 30-year old female patient applied to hospital with progressive acute chest pain. She was diagnosed Marfan syndrome and unerwent an operation for the replacement of ascending aorta in 1998. The indication for operation was the presence of congenital aortic valve insufficiency and aneurysm of A. ascendens. The occlusion and aneurism of coronary arteries were found out during the coronarography which caused the development of acute myocardial infarction.

This clinical case demonstrates the range of cardiovascular complications caused by Marfan syndrome. The main severe complication remains the aneurysm of the ascending aorta, a serious medical condition which requires surgical intervention, monitoring by echocardiography and medical therapy. The early diagnosis and prophylactic treatment of aortic pathology in infants can prevent the further development of life-threatening cardiovascular complications in patients with Marfan syndrome.

KEYWORDS: Marfan syndrome, aortic dissection, coronary aneurism.

Introduction

Marfan syndrome is an inherited connective-tissue disorder with autosomal dominant trait of inheritance. [Kansara B et al., 2013]. It has an estimated prevalence of one in 3000 to 5000 individuals [Keane M, Pyeritz R, 2008]. This syndrome is the result of mutations in the firillin-1 gene on 15th chromosome, which encodes the glycoprotein of fibrillin [Nachum E et al., 2013]. Mutations of these genes lead to defects in multiple organ systems. Among these systemic complications, the cardiovascular system complications are the most critical because most deaths are due to aortic or mitral valve incompetence, aortic dissection, aneurysm rupture, intramural complications of ascending aorta or subacute bacterial endocarditis [Murdoch J et al., 1972; Brooke B et al., 2008].

The characteristics of Marfan syndrome include

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aortic valve regurgitation with progressive dilatation of the aorta, which may cause dissection and rupture of the ascending aorta, mitral valve prolapse, mitral regurgitation, lens dislocation, myopia, thin stature with long extremities, arachnodactilia, chest wall distortion and scoliosis [De Paepe A et al., 1996; Dean J, 2007; Ammash N et al., 2008].

Mitral valve prolapse and mitral regurgitation occur before aortic valve involvement and progress early in children with Marfan syndrome [Ammash N et al., 2008]. This valvular pathology with congestive heart failure is the leading cause of cardiovascular morbidity and mortality in young patients with Marfan syndrome [Sisk H et al., 1983]. The deformation of both mitral leaflets is common and the need for surgical intervention arises earlier than in adult patient' population [De Paepe A et al., 1996; Dean J, 2007; Ammash N et al., 2008].

The aortic dilation in Marfan syndrome tends to progress over time and in most cases becomes evident before 18 years of age [Tinkle B, Saal H, 2013]. The dilation typically occurs at the level of the sinuses of Valsalva but dilation of any part of aorta can be seen in these patients [Tinkle B, Saal H, 2013].

The survival of patients with Marfan syndrome depends on preventing the development of cardiovascular complications from childhood. The life expectancy of these patients is 32 years without therapy and early diagnosis is a key issue in the medical treatment of Marfan syndrome [Murdoch J et al., 1972]. The monitoring of cardiac function, pharmacological treatment and prophylactic aortic root surgery are the main interventions currently used to manage cardiovascular complications in patients with Marfan syndrome [Cook J et al., 2015].

The medical history, physical examination and laboratory findings are discussed in this report. This clinical case presents a medical history of a female patient who was born with Marfan syndrome and has been operated for the implantation of prosthesis of ascending aorta at the age of 15. The development of accompanying thrombosis and aneurysms of coronary arteries are relatively rare in this clinical condition.

Case Presentation

A 30 year-old woman was applied to the cardiology clinic of the Vienna General Hospital complaining of a sudden onset of acute chest pain radiating to the left arm and diaphoresis. She was originally diagnosed with Marfan syndrome and underwent an aortic arch interposition operation in 1998. The indication for operation was the diagnosis of congenital aortic valve insufficiency and aneurysm of the ascending aorta. The surgical intervention included the replacement of the ascending aorta, resuspension of the aortic valve and direct reimplantation of A. coronaria for revascularization of myocardium. The presence of arterial hypertension in family wasn't mentioned in patient's past medical history and was considered as a cardiovascular risk. The patient was on hormonal therapy for conception preparation before her admission to the clinic and a spontaneous pneumothorax was found in 2000.

The physical examination performed after the admission to the hospital revealed stable hemodynamic parameters: arterial pressure - 123/77 mm Hg, SaO_2 - 98%, heart rate - 54 beats/min. The heart sounds were clear, rhythmic. No pathological murmurs were revealed by auscultation. The lungs were clear, no crackles or congestion were revealed. The palpation of abdomen was soft and painless. The liver was not enlarged by palpation. No peripheral edema was revealed.

The instrumental diagnostic procedures and laboratory tests were performed. The electrocardiography performed upon admission to the clinic has revealed sinus rhythm, heart rate - 68 beats/min, ST-segment depression and T-wave inversion in II, III, AVF, V_1-V_3 (+T) waves, rS complexes in V_1-V_2, signs of left ventricular hypertrophy and no repolarization disorders. The echocardiography was performed which revealed a normal size of left ventricle with diameter of 41.0 mm and slight concentric hypertrophy of left ventricular hypertrophy (the thickness of interventricular septum was 12.0 mm) with borderline systolic function (Fig. 1).

The motion disorders in the inferior wall of left ventricle and abnormal septal movement were found. The diastolic left ventricle function was not determined due to poor visualization. The dilation and reduce of right ventricle function were shown during the study. The prosthesis of ascending aorta was visualized. The aortic and mitral valves were morphologically unaffected. The cardiac ultra-

sound revealed no signs of aortic dissection. The diameter of ascending aorta measured from the parasternal long axis view was 28.0 mm (Fig. 1, 2).

The Doppler examination revealed minimal aortic and mitral insufficiency, the peak velocity on the aortic valve (AV Vmax) was 1.12 m/s, the pressure gradient through AV (AV PPG) was 5.05 mm Hg. The Doppler flow analysis of the tricuspid valve revealed light to moderate tricuspid insufficiency and the peak velocity of tricuspid regurgitation (TI Vmax) was 1.70 m/s. The pressure gradient between the right atrium and ventricle (RV/RA Grad) was 11.5 mm Hg The systolic pulmonary artery pressure was measured 16.0 mmHg.

The analysis of laboratory parameters revealed elevated levels of cardiac enzymes as biomarkers of myocardial necrosis, including aspartate aminotransferase, lactate dehydrogenase -1 and creatine kinase. The level of Troponin T upon admission was 157 ng/L. The inflammatory response was manifested by leukocytosis and increased C-reactive protein levels. The patient also had significantly elevated levels of prohormone B-type natriuretic peptide and triglycerides.

The indication for coronarography was acute coronary syndrome and positive levels of troponin. The cardiac catheterization was performed which revealed 20 x 15 mm proximal aneurism of left main stem with wall thrombus. The main stem was normal, the left coronary artery and circumflex artery were without stenoses. The aneurysm of the left coronary artery was also revealed (Fig. 3).

The coronarography revealed a 17 × 10 mm thrombosed aneurysm of ostium of right coronary artery which was completely occluded with partial filling from the left side (Fig. 4). The right coronary artery was dominant, ectatic and its proximal part was closed. An acute inferior subendocardial myocardial infarction was developed as a result of the right coronary artery aneurysm. The hemodynamic parameters during the study were the following: heart rate - 83 b/min, aorta (s/d-m) - 104/61-89 mm Hg, aorta SaO_2 - 95%.

The diagnostic tests performed at the hospital also included thallium scintigraphy for the assessment of vitality of right coronary artery, lung function, chest X-ray and carotid/vertebral sonography. The thallium cardioscintigraphy has revealed a pathological resting scintigram with less storage in posterobasal, diaphragmal, inferoapical and posteroseptal segments. The significant residual vitality was not excluded in these sections. The lung function examination has revealed a borderline restriction from type of shackled lung. The residual volume was borderline increased at the expense of a restricted vital capacity. There was a normoxemia at elevated levels of $AaDO_2$. The chest X-ray has revealed an angular dorsal effusion in left and right pleural sinuses and left convex scoliosis of thoracic part of vertebral column. The Dupplex sonography of supra-aortic arteries has not revealed any inconspicuous findings of extracranial carotid arteries, as well as A. vertebralis on both sides. The patient had a cardiac magnetic resonance imaging test in 2009 which has revealed pectus excavatum and scoliosis of thoracic part of the spinal column.

The patient has received antianginal and antihypertensive therapy with β-blockers, nitrates, angiotensin-converting enzyme inhibitors, antiplate-

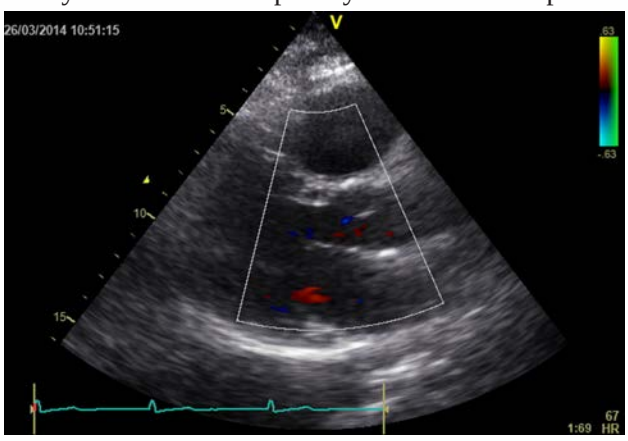

Figure 1. *Transthoracic echocardiogram depicting the prosthesis of A. Ascendens.*

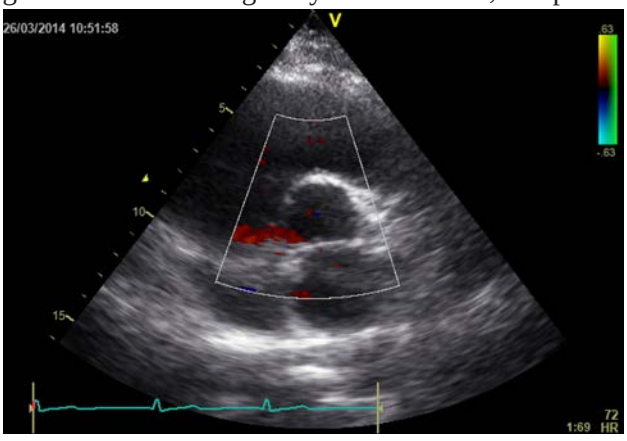

Figure 2. *Transthoracic echocardiogram depicting aortic valve, prosthesis of A. ascendens, atria and right ventricle.*

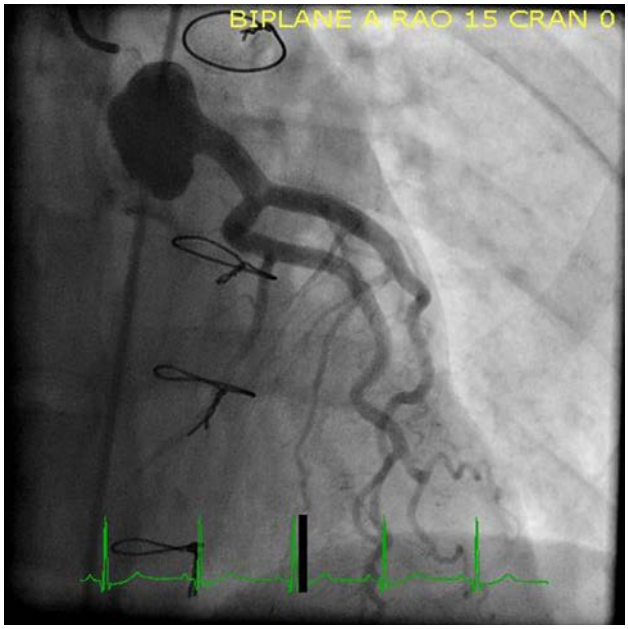

FIGURE 3. Coronary angiogram depicting the aneurysm of A. ascendens and left coronary artery.

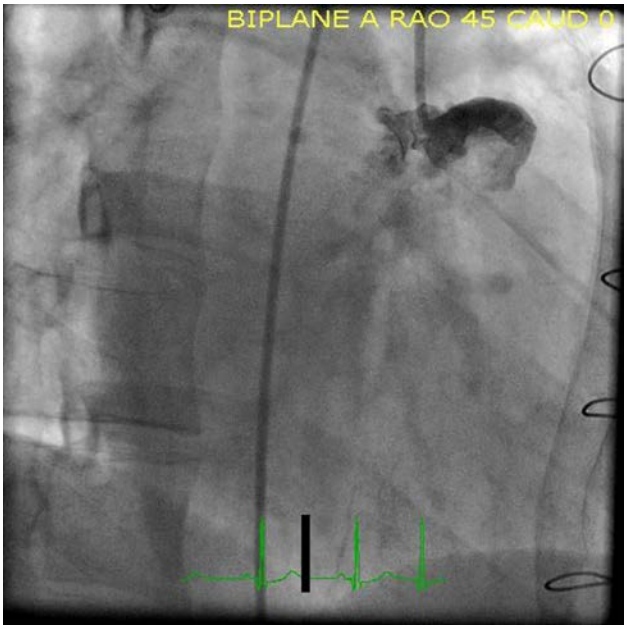

FIGURE 4. Coronary angiogram showing the occlusion and aneurysm of right coronary artery.

let agents, low molecular weight heparin, a proton pump inhibitor, corticosteroids and non-steroidal anti-inflammatory drugs. The coagulation was continuously monitored during the hospital treatment. The levels of cardiac biomarkers have been normalized during one week of hospital treatment. The hemodynamic parameters were stable during the course of therapy. The patient is currently waiting to undergo the coronary artery bypass surgery.

Discussion

Marfan syndrome is an autosomal dominant connective tissue disorder that results from mutations in the FBN1 gene on 15th chromosome which encodes the glycoprotein of fibrillin [Kansara B et al., 2013]. Fibrillin is a major building block of microfibrils which serves as a substrate for elastin in the aorta, aortic leaflet [Fleischer K et al., 1997] and other connective tissues [Frydman M, 2008]. The pathology of mitral valve and dilatation of the aortic root usually develop since childhood. Common mitral valve abnormalities are annular dilatation, fibromyxomatous changes in leaflet and chordae, chordae elongation, rupture of the leaflets and calcium deposition [Ozdemir O et al., 2011]. Aortic root disease, leading to aneurysmal dilatation and often aortic regurgitation, affects about 50% of children and 60–80% of adults with Marfan syndrome [Roman M et al., 1989]. Abnormalities involving microfibrils result the weakening of the aortic wall [Kansara B et al., 2013]. The dilatation of the aortic root also impairs leaflet coaptation and this causes aortic regurgitation [De Paepe A et al., 1996; Dean J, 2007; Ammash N et al., 2008]. Progressive aortic dilatation and eventual aortic dissection occur because of tension caused by left ventricle ejection impulses [Kansara B et al., 2013]. If untreated, this disease can lead to life-threatening aortic dissection, rupture or both conditions [Roman M et al., 1993; Coselli J, LeMaire S, 1996] that are the main causes of morbidity and mortality in patients with Marfan syndrome [Adams J, Trent R, 1998].

The management of patients with Marfan syndrome includes assessment of cardiac function, exercise restriction, administration of drug therapy and elective aortic root replacement [Milewicz D et al., 2005]. The early detection of cardiovascular abnormalities and regular follow up of children with Marfan syndrome is necessary. The clinical evaluation of patients, consisting of medical examination and echocardiography, should be performed. Serial echocardiography is recommended to children at 6-12 month intervals depending on the aortic diameter and the rate of its increase [Dean C, 2007].

Medications that reduce hemodynamic stress on the aortic wall, such as β-blockers, are often prescribed [Cañadas V et al., 2010]. In young pa-

tient subgroups and patients with smaller aortic diameters, β-blockers reduce the risk of sudden death and improve survival rates [De Paepe A et al., 1996; Dean J, 2007; Ammash N et al., 2008]. This therapy should be considered at any age if the aorta is dilated, but prophylactic treatment may be more effective in those with an aortic diameter of less than 4 cm [Dean C, 2007]. If medical treatment fails and the aortic root dilates to 5 cm or more, then prophylactic surgery should be considered [De Paepe A et al., 1996; Groenink M et al., 1999; Meijboom L et al., 2004].

Previously, Bentall and de Bono described the technique of replacing the ascending aorta and aortic valve in patients with Marfan syndrome [Bentall H, de Bono A, 1968]. Techniques for aortic valve-sparing root replacement were subsequently introduced by Yacoub in 1979 (remodeling) and David in 1988 (re-implantation) [Fagan A et al., 1983; David T, Feindel C, 1992]. The surgical correction of aortic aneurysm, however, does not exclude the recurrence of postoperative complications. Previous studies have shown that the formation of coronary artery aneurisms constitutes only a small percentage of cardiovascular complications in this patient population.

The study performed by Finkbohner R et al. (1995) and colleagues has shown that the majority of patients had subsequent aneurysms or dissections after the surgical repair of the aortic aneurysm involving other regions of the aorta (95%) and the arteries directly arising from the aorta, including the iliac, carotid, renal, subclavian, and innominate arteries (5%).

According to Meijboom L et al. (2005) and colleagues, the development of coronary artery aneurism manifested as myocardial infarction constitutes only less than 1% of all cases and is only described in adults. Although the incidence of development of this complication is low, it may cause ischemic damage to the cardiac muscle which may compromise the course of the disease and complicate the treatment of patients with Marfan syndrome. The clinical cases when myocardial infarction develops as a result of the coronary artery aneurisms in patients with Marfan syndrome are rarely described in literature sources. These patients are considered potential candidates for coronary artery bypass surgery to restore the perfusion of the myocardium if left ventricular function is preserved. Further management of these patients requires echocardiographic follow-up of the diameter of the aortic root, left ventricle structural and functional parameters and continuous medical therapy.

Conclusion

Acute myocardial infarction can develop as a result of a coronary artery aneurysm in the postoperative period after the surgical correction of the aortic aneurysm. The vascular complications of the disease can manifest from early childhood which require diagnostic evaluation and treatment of this patient population. The medical therapy, lifestyle modifications and echocardiographic monitoring of aorta should be performed for the assessment of a clinical status and prevention of cardiovascular complications in patients with Marfan syndrome.

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REFERENCES

1. *Adams JN, Trent RJ*. Aortic complications of Marfan's syndrome. Lancet. 1998; 352(9142): 1722-1723.
2. *Ammash NM, Sundt TM, Connolly HM*. Marfan syndrome: diagnosis and management. Curr Probl Cardiol. 2008; 33: 7-39.
3. *Bentall H, de Bono A*. A technique for complete replacement of the ascending aorta. Thorax. 1968; 23(4): 338-339.
4. *Brooke BS, Habashi JP, Judge DP., et al*. Angiotensin II blockade and aortic-root dilation in Marfan's syndrome. N Engl J Med. 2008; 358(26): 2787-2795.
5. *Cañadas V, Vilacosta I, Bruna I, Fuster V*. Marfan syndrome. Part 2: treatment and management of patients. Nat Rev Cardiol. 2010; 7(5): 266-276.

6. *Cook JR, Carta L, Galatioto J, Ramirez F*. Cardiovascular manifestations in Marfan syndrome and related diseases; multiple genes causing similar phenotypes. Clin Genet. 2015; 87(1): 11-20.
7. *Coselli JS, LeMaire SA*. Aortic manifestations and surgery in Marfan syndrome in pediatric patients. Prog Pediatr Cardiol. 1996; 5:189-203.
8. *David TE, Feindel CM*. An aortic valve-sparing operation for patients with aortic incompetence and aneurysm of the ascending aorta. J Thorac Cardiovasc Surg. 1992; 103(4): 617-621.
9. *Dean JCS*. Marfan syndrome: clinical diagnosis and management. Eur J Hum Genet. 2007; 15: 724-733.
10. *De Paepe A, Devereux RB, Dietz HC, Hennekam RC, Pyeritz RE*. Revised diagnostic criteria for the Marfan syndrome. Am J Med Genet. 1996; 62: 417-426.
11. *Fagan A, Pillai R, Radley-Smith R, Yacoub MH*. Results of new valve conserving operation for treatment of aneurysms or acute dissection of the aortic root. Br Heart J. 1983; 49(3): 302.
12. *Finkbohner R, Johnston D, Crawford ES, Coselli J, Milewicz DM*. Marfan syndrome. Long-term survival and complications after aortic aneurysm repair. Cirulation. 1995; 91(3): 728-733.
13. *Fleischer KJ, Nousari HC, Anhalt GJ, Stone CD, Laschinger JC*. Immunohistochemical abnormalities of fibrillin in cardiovascular tissues in Marfan's syndrome. Ann Thorac Surg. 1997; 63(4): 1012-1017.
14. *Frydman M*. The Marfan syndrome. Isr Med Assoc J. 2008; 10(3): 175-178.
15. *Groenink M, Lohuis TAJ, Tijssen JG., et al*. Survival and complication free survival in Marfan's syndrome: implications of current guidelines. Heart. 1999; 82: 499-504.
16. *Kansara B, Singh A, Girotra S, Iyer KS*. Combined Bentall and modified Ravitch procedures in a patient with Marfan syndrome. J Anaesthesiol Clin Pharmacol. 2013; 29(1): 95-98.
17. *Keane MG, Pyeritz RE*. Medical management of Marfan syndrome. Circulation. 2008; 117(21): 2802-2813.
18. *Meijboom LJ, Nollen GJ, Mulder BJM*. Prevention of cardiovascular complications in the Marfan syndrome. Vasc Dis Prev. 2004; 1: 79-86.
19. *Meijboom LJ, Timmermans J, van Tintelen JP., et al*. Evaluation of left ventricular dimensions and function in Marfan's syndrome without significant valvular regurgitation. Am J Cardiol. 2005; 95(6): 795-797.
20. *Milewicz DM, Dietz HC, Miller DC*. Treatment of aortic disease in patients with Marfan syndrome. Circulation. 2005; 111(11): e150-e157.
21. *Murdoch JL, Walker BA, Halpern BL, Kuzma JW, McKusick VA*. Life expectancy and causes of death in the Marfan syndrome. N Engl J Med. 1972; 286(15): 804-808.
22. *Nachum E, Shinfeld A, Kogan A, Preisman S, Levin S, Raanani E*. Aortic valve-sparing surgery in Marfan syndrome. Isr Med Assoc J. 2013; 15(8): 439-442.
23. *Ozdemir O, Olgunturk R, Kula S, Tunaoglu FS*. Echocardiographic findings in children with Marfan syndrome. Cardiovasc J Afr. Oct 2011; 22(5): 245-248.
24. *Roman MJ, Devereux RB, Kramer-Fox R, Spitzer MC*. Comparison of cardiovascular and skeletal features of primary mitral valve prolapse and Marfan syndrome. Am J Cardiol. 1989; 63(5): 317-321.
25. *Roman MJ, Rosen SE, Kramer-Fox R, Devereux RB*. Prognostic significance of the pattern of aortic root dilation in the Marfan syndrome. J Am Coll Cardiol. 1993; 22(5): 1470-1476.
26. *Sisk HE, Zahka KG, Pyeritz RE*. The Marfan syndrome in early childhood: analysis of 15 patients diagnosed at less than 4 years of age. Am J Cardiol. 1983; 52(3): 353-358.
27. *Tinkle BT, Saal HM*. Committee on genetics. Health supervision for children with Marfan syndrome. Pediatrics. Oct 2013; 132(4): e1059-1072.