

# Takayasu's Arteritis Concurrent with Marfan syndrome Associated with Severe Renovascular Hypertension

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## Abstract:

*Marfan syndrome (MS) is a dominantly inherited connective tissue disorder characterized by arachnodactyly, tall stature, the presence of aortic aneurysm, and lens dislocation. Takayasu's arteritis (TA) is an inflammatory disease often affecting the ascending aorta and aortic arch, causing obstruction of the aorta and its major arteries. The disease commonly presents in the 2nd or 3rd decade of life, often with a delayed diagnosis. The disease is progressive and there is no definitive therapy.*

*We report an unusual case of concomitant Takayasu's arteritis and Marfan syndrome manifesting bilateral renal artery stenosis and aortic root dilatation. The patient had severe hypertension. The simultaneous presence of TA and MS could be a coincidence, however; the pathogenesis of TA might be linked with autoimmunity induced by abnormal extracellular matrix protein derived from the genetic mutations in MS.*

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A 18-year-old girl was referred to our hospital in November 2016 due to elevated arterial blood pressure, headache and palpitation since 1 year. Upon admission, the girl was in good general condition. The physical examination revealed tall narrow facies body built was below average. Thumb sign and wrist sign were positive with joint hypermobility. She had multiple nonpalpable purplish rash on abdomen and both thigh. Her B.P was 200/110mmHg on upper limb and 140/90mmHg on lower limbs. Her pulse was 84beat/min, regular, and all peripheral pulses were normal. Lower limb pulses were weak and there was no radiofemoral delay. The femoral pulses were present and equal. Her body weight and height were 36 kg (the 10th percentile) and 164 cm (the 25th percentile) respectively, arm span was 172 cm, lower segment 87cm, high arched palate. She gave history of rash on abdomen and both thigh for 3 months. The neurological examination was unremarkable.

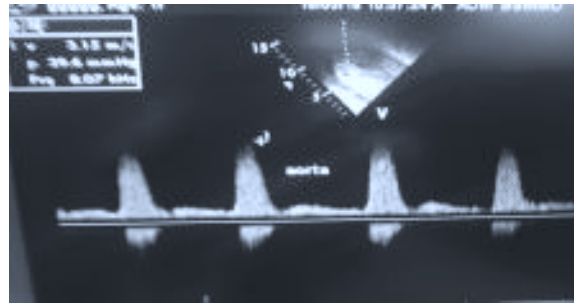
The family history was negative for essential hypertension and cardiovascular diseases.

On examination, there was visible apical impulse, apex beat was on 9cm from midline at 6<sup>th</sup> i.c.s and heaving, loud 1<sup>st</sup> heart sound, 2<sup>nd</sup> heart sound was normal.

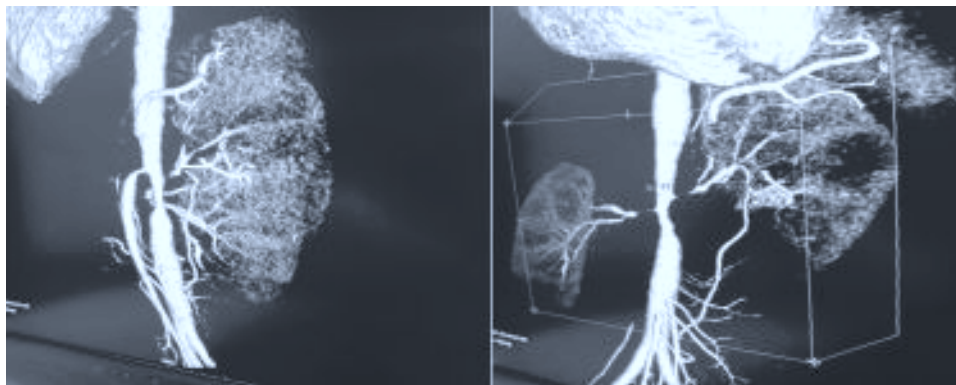
Abdominal bruit was present. Fundoscopic examination was normal.

Laboratory findings showed an elevated erythrocyte sedimentation rate (ESR) of 52 mm/h (normal value <20 mm/1 h) and serum C-reactive protein level of 1.13 mg/dl (normal value <0.5 mg/dl). The rest of the laboratory investigations, including serum creatinine, electrolytes, and urinalysis were normal. Chest X-Ray shows mild cardiomegaly, ECG normal, USG of whole abdomen showed bilateral polycystic ovaries. Color Doppler echo showed turbulent flow and spectral analysis suggested high peak velocity in the left and right renal artery and also in descending aorta at the origin of renal arteries. The gradient was 45mmHg with narrowing of descending aorta (Fig: 1), there was some collaterals arising from upper part of descending aorta. Aortic root was 28mm (Z Score >2STD) mild AR, mild left ventricular dysfunction with LVEF 48%, Mildly dilated LV, Hypoplastic right pulmonary artery.

CT Aorto pulmonary angiogram showed mild about 50% narrowing of mid abdominal aorta and about 3.5cm subtotal occlusion of both proximal renal artery.



**Fig-1:** Color Doppler echo showing gradient in the descending aorta is 45mmHg



**Fig:2 and 3:** CT Aorto pulmonary angiogram showed about 50% narrowing of mid abdominal aorta and about 3.5cm subtotal occlusion of both proximal renal artery with severe ostial disease in Superior Mesenteric artery(SMA), mild infundibular narrowing, moderate narrowing in Right pulmonary artery(RPA), mildly dilated LV and small collateral from upper descending aorta to RPA.

**Discussion:**

The finding of hypertension and arterial bruits in young adults necessitates the examination of pulses and blood pressures in different limbs in order to detect asymmetry. Elevated ESR is a common finding; however, caution is advised, because up to 50% of patients may have active TA disease and a normal ESR.<sup>4,5,6</sup>

On the basis of clinical manifestations and CT angiographic abnormalities, the diagnosis of TA and Marfan syndrome was made. At present, TA is diagnosed on the basis of the criteria proposed by European League Against Rheumatism Pediatric Rheumatology: Table-1

Criterion	Definition
Angiographic abnormality (Mandatory criterion)	Angiography (conventional, computed tomography or magnetic resonance imaging) of the aorta or its main branches and pulmonary arteries showing aneurysm/dilatation, narrowing, occlusion or thickened arterial wall not due to fibromuscular dysplasia or similar cause: changes usually focal or segmental.
Pulse deficit or claudication	Lost/decreased/unequal peripheral artery pulse(s) Claudication: focal muscle pain induced by physical activity
Blood pressure discrepancy	Discrepancy of four limb systolic blood pressure >10 mmHg difference in any limb
Bruits	Audible murmurs or palpable thrills over large arteries
Hypertension	Systolic/diastolic blood pressure greater than 95 <sup>th</sup> percentile for height
Acute phase reactants	Erythrocyte sedimentation rate >20 mm per first hour or C-reactive protein any value above normal (according to local laboratory)

**TA is classified when the mandatory criterion is present plus any other criteria.**

Takayasu arteritis (TA), also known as aortoarteritis and pulseless disease, is a rare condition. It is potentially life threatening. It is a form of granulomatous arteritis, which affects large and medium-sized arteries, primarily the aorta and its large branches as well as proximal portions of pulmonary, coronary, and renal arteries. TA is predominantly a disease of young adults in the second and third decades of life, but it has also been reported in childhood and in adults older than 40 years.<sup>7</sup> The youngest patient described was 6 months old, and the oldest one was 75 years. Females are more likely to be affected than males. However, hypertension is the most common sign in both groups.<sup>8</sup>

Pathogenesis of arterial hypertension due to TA is complex, multifactorial, and not fully understood. At present, it is thought to be the result of three mechanisms: (a) mechanical, in which hypertension proximal to narrowed aorta (atypical coarctation) is due to high resistance to cardiac output imposed by narrowing;<sup>10</sup> (b) neural, in which hypertension proximal to narrowed aorta results from aortic arch baroreceptors readjustment and this allows to ensure adequate blood supply to organs distal to narrowed aorta;<sup>12</sup> and (c) hormonal, in which hypertension is caused by renal hypoperfusion due to stenotic lesions of one or both renal arteries or aorta alone.<sup>19</sup>

Clinical manifestations of TA are nonspecific. The clinical course of the disease is divided into an early active inflammatory phase and late chronic phase. The active phase lasts for weeks to months and may have a remitting and relapsing course. It is characterized by systemic disease with symptoms of fever, general malaise, night sweats, loss of appetite, weight loss, headaches, dizziness, arthralgia, skin rashes, etc. In our patient there is history of rash for three months.

In our patient, systolic arterial hypertension seemed to result from narrowing of abdominal aorta and bilateral renal artery stenosis.

Cardiac complications related to TA are due more to poorly controlled hypertension from aorto-renal arterial disease than to disease of the aorto-ostia of the coronary arteries. Aortic regurgitation that is secondary to aortic root dilation can occur in up to 20% of patients<sup>[7]</sup>. Hypertension occurs in one third of patients and is usually caused by renal artery stenosis<sup>[7,8]</sup>. Left ventricular dysfunction caused by myocarditis has been reported in up to 18% of cases.<sup>10</sup>

Treatment of TA is based on the use of immunosuppressants such as prednisone and/or methotrexate to decrease or eliminate inflammatory activity. About 60% of patients with TA respond to glucocorticoids. However, as many as 40% relapse on tapering steroids. Alternative therapies such as azathioprine, cyclophosphamide, mycophenolate mofetil, and tacrolimus hydrate are also used in TA, especially for corticosteroid-resistant disease.<sup>8,20,21</sup> Hypertension should be treated aggressively often with multidrug regimen, but pediatricians should be warned against ACE inhibitors until renal artery stenosis has been excluded.

In our patient, hypertension was treated using three medications namely: amlodipine (5 mg/day), Bisoprolol Fumerate 2.5mg/day, Bisoprolol 2.5mg+hydrochlorothiazide 6.25mg/day. Initially the hypertension was not well controlled, so the option of stenting of the descending thoracic aorta and renal arteries had also been considered. But due to the fact that nonspecific markers of inflammation were elevated and this girl had never been treated before, she was qualified for continued medical treatment. The patient is currently under a long-term clinical surveillance by a cardiologist, rheumatologist and nephrologist.

**Table-II**

*Clinical features of Takayasu arteritis related to ischemia*

<b>The vessels involved</b>	<b>Clinical features</b>
1. Aortic branches	Malaise, decreased or absent pulse of upper extremities, dysfunction of upper extremities, headaches, dizziness, vision and orientation disturbances, syncope
2. Aortic arch	Congestive heart failure, aortic valve insufficiency, arterial hypertension
3. Coronary arteries	Ischemic heart disease, myocardial infarction
4. Pulmonary arteries	Chest pain, dyspnea, coughing, hemoptysis, congestive heart failure
5. Abdominal aorta or celiac trunk	Ischemia of the stomach and intestines, abdominal pain, nausea, vomiting
6. Renal arteries	Arterial hypertension, chronic renal failure

In the presence of symptomatic stenotic or occlusive lesions, endovascular revascularization procedures like bypass grafts, patch angioplasty, endarterectomy, percutaneous transluminal angioplasty, or stent placement should be taken into consideration.<sup>15</sup>

### Conclusion:

Marfan syndrome is an autosomal dominant disorder of connective tissue involving the skeletal, ocular, and cardiovascular systems.<sup>5</sup> In our case, the patient had concomitant Takayasu's arteritis and Marfan syndrome, the former involving the bilateral renal arteries and abdominal aorta and causing obstruction, the latter causing aortic root dilatation with aortic regurgitation. To our knowledge, this is the first case in which a patient with concomitant Takayasu's arteritis and Marfan syndrome.

### References:

- Acar B, Yalcinkaya F, Ozturk B, Yuksel S, Ozcarkar ZB, Fitoz S, Büyükcelik M, Noyan A, Sanlidilek U, Ekim M. Seronegative spondyloarthropathy associated with Takayasu arteritis in a child. *Clin Exp Rheumatol*. 2005;23:278–79. [PubMed]
- Al Abarawi S, Fouillet-Desjonqueres M, David L, Barral X, Cochat P, Cimaz R. Takayasu arteritis in children. *Pediatr Rheumatol Online J*. 2008;6:17. doi: 10.1186/1546-0096-6-17. [PMC free article] [PubMed] [Cross Ref]
- Aluquin V, Albano S, Chan F, Sandborg C, Pitlick PT. Magnetic resonance imaging in the diagnosis and follow up of Takayasu arteritis in children. *Ann Rheum Dis*. 2002;61:538–46. doi: 10.1136/ard.61.6.526. [PMC free article] [PubMed] [Cross Ref]
- Amano J, Suzuki A. Coronary artery involvement in Takayasu's arteritis. Collective review and guideline for surgical treatment. *J Thorac Cardiovasc Surg*. 1991;102(4):554–60. [PubMed]
- Arora P, Kher V, Singhal MK, Kumar P, Gulati S, Baijal SS, Jain S, Kumar A. Renal artery stenosis in aortoarteritis: spectrum of disease in children and adults. *Kidney Blood Press Res*. 1997;20(5):285–89. doi: 10.1159/000174160. [PubMed] [Cross Ref]
- Balamtekin N, Gurakan F, Ozen S. Ulcerative colitis associated with Takayasu's arteritis in a child. *Acta Paediatr*. 2009;98:1368–71. doi: 10.1111/j.1651-2227.2009.01330.x. [PubMed] [Cross Ref]
- Borazan A, Sevindik OG, Solmaz D, Gulcu A, Cavdar C, Sifil A, Celik A, Akar S, Goktay Y, Camsari A rare cause of renovascular hypertension: Takayasu arteritis with only renal artery involvement. *Ren Fail*. 2009;31(4):327–31. doi: 10.1080/08860220902780093. [PubMed] [Cross Ref]
- Brunner J, Feldman BM, Tyrrell PN, Kuemmerle-Deschner JB, Zimmehackl LB, Gassner I, Benseler SM. Takayasu arteritis in children and adolescents. *Rheumatology (Oxford)* 2010;49:1806–14. doi: 10.1093/rheumatology/keq167. [PubMed] [Cross Ref]
- Campos LMA, Castellanos ALZ, Afiune JY, Kiss MHB, Silva CAA. Takayasu arteritis with aortic aneurysm associated with Sweet's syndrome in childhood. *Ann Rheum Dis*. 2005;64:168–69. doi: 10.1136/ard.2003.006353. [PMC free article] [PubMed] [Cross Ref]
- Dabague J, Reyes PA. Takayasu's arteritis in Mexico: a 38 year clinical perspective through literature review. *Int J Cardiol*. 1996;54(Suppl):103–09. doi: 10.1016/S0167-5273(96)88779-1. [PubMed] [Cross Ref]
- Dudina AL, Moore DP, Keogh B, Foley D, Graham IM. Chest pain and hypertension in an 18 year old girl. *Ir Med J*. 2008;101(9):285–86. [PubMed]
- Fadouach S, Abid-Allah, Mehadji BA, Tahiri A, Chraïbi N. Hypertension and Takayasu disease. Report of 8 cases. *Ann Cardiol Angeiol (Paris)* 1998;47(3):155–59. [PubMed]
- Gerhardt RT, Lorenzo LA. Takayasu arteritis presenting as a recurrent respiratory tract infection: a diagnosis facilitated by bedside echocardiography and increased erythrocyte sedimentation rate. *Mil Med*. 2002;167(2):170–71. [PubMed]
- Goodman D, Shulman S, Fenik J, Rowley A, Lane J, Rozenfeld R, Donaldson J, Miller M, Wyers M, Stevens K. A 19-month-old girl with congestive heart failure, hypertension, and coronary artery dilatations. Interview by Robert Listernick. *Pediatr Ann*. 2005;34(1):14. [PubMed]
- Gumus B, Cevik H, Vuran C, Omay O, Kocyigit OI, Turkoz R. Cutting balloon angioplasty of bilateral renal artery stenosis due to Takayasu arteritis in a 5-year-old child with midterm follow-up. *Cardiovasc Intervent Radiol*. 2010;33:394–97. doi: 10.1007/s00270-009-9623-6. [PubMed] [Cross Ref]
- Hahn D, Thomson PD, Kala U, Beale PG, Levin SE. A review of Takayasu's arteritis in children in Guateng, South Africa. *Pediatr Nephrol*. 1998;12:668–75. doi: 10.1007/s004670050526. [PubMed] [Cross Ref]
- Hall S, Barr W, Lie JT. Takayasu arteritis. A study of 32 North American Patients. *Medicine (Baltimore)* 1985;64:89–99. [PubMed]
- Hall S, Nelson AM. Takayasu arteritis and juvenile rheumatoid arthritis. *J Rheumatol*. 1986;13:431–32. [PubMed]
- Hamida BM, Maazoun F, Marzouk S, Frigui M, Bouattour F, Chaabouni Y, Salah BR, Kacem H, Kaddour N, Bahloul Z. Hypertension in Takayasu disease. *J Hypertens*. 2010;28:15–72. doi: 10.1097/HJH.0b013e328331b7ff. [Cross Ref]
- Hom C (2010) Pediatric Takayasu arteritis. <http://emedicine.medscape.com/article/1007566-overview>. Accessed 25 Aug 2010
- Hotchi M. Pathological studies on Takayasu arteritis. *Heart Vessels Suppl*. 1992;7:11–17. doi: 10.1007/BF01744538. [PubMed] [Cross Ref]