

Rare case of Arterial Tortuosity Syndrome- Preoperative and Post Operative Imaging Findings

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Abstract: Arterial tortuosity syndrome (ATS) is a rare hereditary, autosomal recessive disorder causing severe and widespread tortuosity of aorta and middle sized arteries, craniofacial and generalized connective tissue involvement. Due to increased vascular fragility imaging modality like sonography, MDCT (Multidetector computed tomography), MRA (Magnetic resonance angiography) are more useful than invasive diagnostic procedure. Definitive diagnosis is by molecular analysis of SLC2A10 gene.

Keywords: Arterial tortuosity syndrome, connective tissue manifestation, CT aortography, MR angiography, SLC2A10 gene

1. Introduction

Arterial tortuosity syndrome (ATS) is a rare hereditary, autosomal recessive connective tissue disorder characterized by dysmorphic facial features, skin and joint laxity, tortuosity, elongation of the major arteries, vascular dilatation, stenosis, formation of aneurysm, pulmonary artery stenosis, and bowel hernia and rupture. Large and medium-sized arteries are mostly affected. Bony changes like scoliosis, arachnodactyly, and chest wall deformity are also well-known associations. ATS is an autosomal recessive disorder attributed to mutations in the SLC2A10 gene. Occasionally close relatives of patients with established ATS are referred for detailed investigation to demonstrate subtle imaging signs.

Many entities with inherited defects of connective tissue like Marfan syndrome (fibrillin-1), Ehlers Danlos syndrome (Type III collagen), Williams Beuren syndrome (elastin), and hereditary cutis laxa syndromes (elastin and fibulin-4 and -5) are known to present with very similar vascular and connective tissue changes.

Due to intrinsic defect in the vascular collagen, blood vessel tends to show increased fragility and tendency for rupture. Hence, in the evaluation of the patients, invasive diagnostic procedures have been replaced by more non-invasive modalities like sonography, magnetic resonance imaging (MRI), and multidetector computed tomography (MDCT). Patients present clinically in different contexts varying from asymptomatic presentation to specific system-related symptoms, like, a patient may present with cardiac failure and cardiovascular involvement or with gastroesophageal reflux/obstruction with hiatus hernia.

2. Case Report

5 year male child came to our department as a referral from cardiology department at U. N. Mehta institute of cardiology and research center, Ahmedabad, Gujarat for CT angiography. Initially patient presented with complains of failure to gain weight, fatigability, feeding difficulty, and vomiting. On clinical evaluation, facial dysmorphic features (micrognathia, elongated face, and epicanthal folds) along with chest wall deformity and cardiac murmurs were noted,

leading to echocardiography and chest radiography which demonstrated enlarged cardiac and mediastinal shadow. Patient showed joint hypermobility, arachnodactyly and skin hyperextensibility. In our department patient underwent MDCT angiography of aortic arch, arch vessel and descending thoracic aorta through intravenous injection of non ionic contrast.

In our patient, following imaging findings were obtained.

Dilated aortic root and ascending aorta without evidence of dissection. Tortuous left sided aortic arch. Markedly tortuous left subclavian, bilateral common carotid and right subclavian arteries. Marked tortuosity of descending thoracic and abdominal aorta.

Diameter of --

- [1] Aortic root – 35.6 x 31.4 x 30.1 mm
- [2] Ascending aorta measures – 40.8 x 35.4 mm
- [3] Arch of aorta – 25.6 x 23.3 mm.

Celiac trunk, bilateral renal, superior and inferior mesenteric arteries appear normal. Additional associated non vascular findings in our case were: Right anterior diaphragmatic hernia with herniating bowel loops in thorax. Malrotated left kidney with anteriorly facing pelvi-calyceal system. Wedging involving multiple lumbar vertebrae.

After CT angio imaging, patient also underwent MRI brain angiography in which involvement of neck and intracranial arteries are seen. There are dilated tortuous intracranial arteries including ACA, MCA, PCA and basilar and vertebral arteries noted on MR angiography.

After all thorough clinical assessment patient underwent cardiothoracic surgery for repair of grossly dilated ascending aorta and arch aneurysm with open book technique graft anastomosis. Patient's parents and close relative were also screened to rule out subtle imaging findings, however no any abnormalities are seen.

3. Discussion

Characteristics of arterial tortuosity syndrome:

- [1] severe and widespread tortuosity of aorta and middle sized arteries.

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[2] craniofacial involvement.

[3] generalised connective tissue manifestation.

Clinical features:- Most affected individuals are identified in early childhood, because of cardiac murmur or cyanosis. Rarely, pulsatile carotid arteries or sudden arterial dissections are the initial presenting symptoms. Few present with cardiorespiratory failure. Rarely, identified in adulthood initially with joint aches and premature ageing.

Diagnosis:- established in a proband with generalised arterial tortuosity and biallelic pathogenic variants in SLC2A10, appropriate to perform molecular analysis SLC2A10 in an individual with the following:- [1] an elongated aortic arch or arterial tortuosity on vascular imaging.[2] a variable combination of craniofacial characteristics. [3]family history consistent with autosomal recessive inheritance. Sequence analysis of SLC2A10 is performed first. If only one or no pathogenic variant is found, deletion/duplication analysis should be performed.

Surveillance:Regular MRI or CT(3d reconstruction) from head to pelvis.Cardiovascular system is a major source of morbidity or mortality. Severe and widespread tortuosity of aorta and middle sized arteries, aortic arterial aneurysms, arterial dissections, ischemic vascular accidents, non hemorrhagic stroke and infarction of abdominal organs, focal stenosis of aorta, stenosis of main and peripheral pulmonary arteries causing pulmonary hypertension, large vein dilatation, valvular regurgitation or mitral valve prolapse may occur.

Craniofacial involvement may lead to blepharophimosis or periorbital fullness, downslanted palpebral fissures, convex nasal ridge, midface retrusion, micrognathia, large ears, long face, high palate and dental crowding.

Skin involvement is characterised by soft and doughy and often hyperextensible loose skin folds and redundancy, scarring is usually normal but may be delayed resulting in atrophic scars.

Skeletal manifestations appear in form of scoliosis, pectus carinatum/excavatum, arachnodactyly, camptodactyly, pes planus with hindfoot valgus, rarely osteopenia, growth of the long bones may be excessive(dolichostenomelia).

Generalised connective tissue manifestation appear in form of joint laxity, knee/elbow contractures, prolapse of bladder, uterus and rectum, hernias, keratoconus, myopia(unclear association).

4. Differential Diagnosis

[1] **EFEMP 2- related cutis laxa-** autosomal recessive cutis laxa type 1 bcharacterised by cutis laxa and systemic involvement, most commonly arterial tortuosity, aneurysms and stenosis, retrognathia, joint laxity and arachnodactyly. Difficult to distinguish from ats as both arterial and skin findings overlap, however:focal stenosis at the aortic isthmus is more common in efep2- related cutis laxa, EFEMP 2 related cutis laxa presents with a more aggressive arterial phenotype with fast progression to aneurysms,

typical facial characteristics found in ATS are often absent in efemp2 related cutis laxa.

[2]**loeys-dietz syndrome-** autosomal dominant, characterised by vascular findings(cerebral, thoracic and abdominal arterial aneurysms and /or dissections) and skeletal manifestations(pectus excavatum, scoliosis, joint laxity, arachnodactyly, talipes equinovarus). 75% have craniofacial manifestations(widely spaced eyes, cleft uvula/palate, craniosynostosis, findings not usually seen in individuals with ATS). Arterial tortuosity is present, lesser degree than in ATS. Individuals with IDS present more frequently with an aneurysm of the aortic root than individuals with ATS.

[3]**Occipital horn syndrome-** ATP7A related cutis laxa x linked characterised by occipital horns- wedge shaped calcifications at the site of attachment of trapezius muscle and sternocleidomastoid to the occipital bone. Also have lax joints, bladder diverticula, inguinal hernias, vascular tortuosity, mainly of cerebral vasculature.

[4]**EhlerDanlos syndrome-** type III autosomal dominant characterised by generalised joint hypermobility, variable skin and internal organ manifestations. In type III hypermobility leads to repeated joint luxation and musculoskeletal pain. Soft hyperextensible skin and autonomic dysfunction do not have arterial tortuosity.

[5]**EhlerDanlos syndrome-** vascular type type IV- autosomal dominant characterised by thin, translucent skin, trophic scars, easy bruising, characteristic facial appearance, arterial, intestinal and/or uterine fragility. Vascular dissection or rupture may occur but arterial tortuosity is absent.

5. Management

Evaluation following diagnosis

- 1) Echo- aortic root measurements based on normal considerations for age and body size.
- 2) MRA or CT Scan with 3D reconstruction from head to pelvis
- 3) Lung function test and imaging when emphysema is suspected.
- 4) Skeletal radiographs, Bone densitometry
- 5) Evaluation of palate to identify patients with highly arched palate, bifid uvula or cleft palate.
- 6) Eye examination for assessment of keratoconus, keratoglobus and corneal thinning.
- 7) Medical genetics consultation.

6. Treatment

Multidisciplinary approach.

7. Conclusion

A spectrum of imaging features seen in a patient with ATS is illustrated in this report. Awareness of early sign of arterial tortuosity and recognition of the described findings lead to early diagnosis of clinically asymptomatic cases of

ATS which may prevent life threatening devastating complication like aortic rupture and can be helped by early operative intervention. MDCT evaluation appears to be the best choice in the investigation of ATS patients. However, keeping the radiation dose to a minimum in the group of patients who may need multiple follow-up examinations, MR angiography would be off help. Use of volumetric images from MDCT studies allows improved image interpretation and provides additional information, as exemplified in our case.

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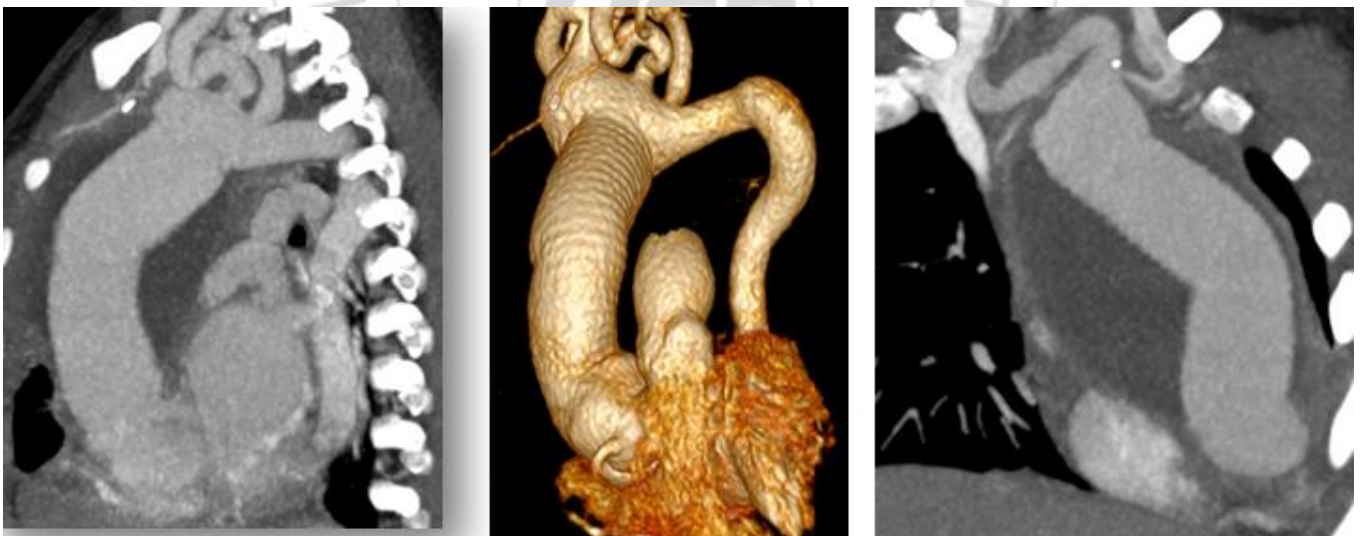
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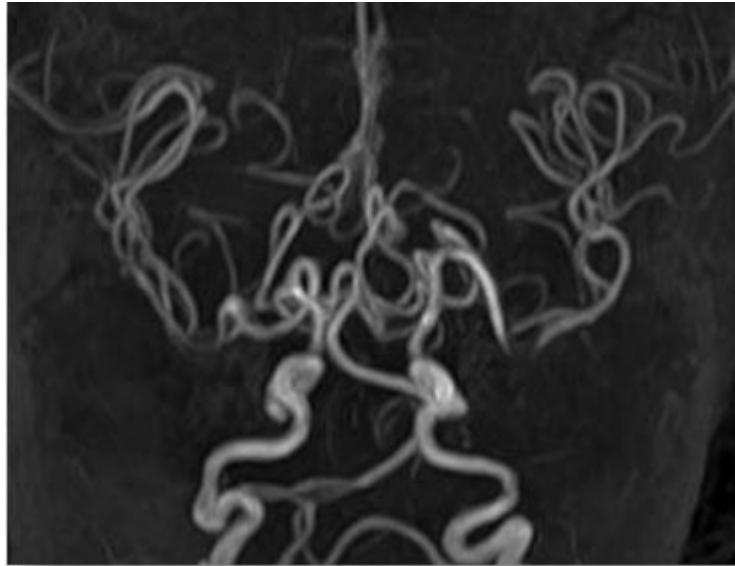
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Tortuous ascending aorta, arch and arch vessels along with marked tortuosity of descending thoracic aorta.



Post operative images showing repair of ascending aorta and arch repair with anastomotic graft by an open book technique



MR angiography of same patient showed marked tortuosity of intracranial vessels

