

# Arterial tortuosity syndrome

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## DESCRIPTION

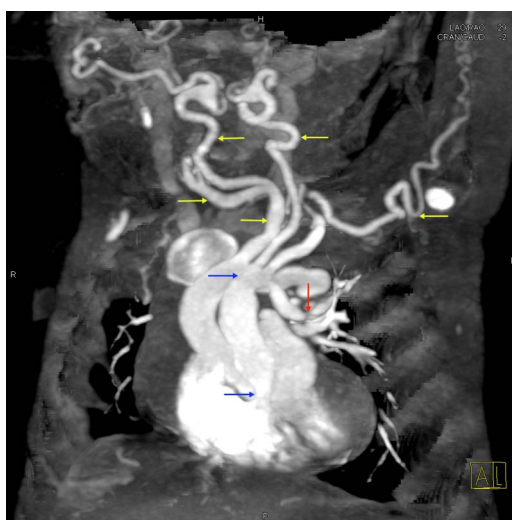
An infant exhibited weight faltering and failure to thrive after birth. She was born full term via an uncomplicated vaginal delivery to healthy, non-consanguineous parents. The mother received prenatal care and standard screening tests were reportedly normal throughout pregnancy. There was no family history of disease. Birth weight was 6 pounds, head circumference was 36 cm and length was 51 cm. On examination, there was a significant blood pressure discrepancy of 90–95 mm Hg systolic in the upper extremities and 60 mm Hg systolic in the lower extremities. The patient was noted to have micrognathia, prune skin and down slanting palpebral fissures. Laboratory analysis was within normal limits. CT angiography with 3D reconstruction revealed tortuosity throughout the arterial tree (figure 1). There was a right-sided kink of the descending aorta (figure 2) and mild stenosis of the distal edge of the aortic arch (at and before the ligamentum arteriosum), proximal descending aorta, right and left pulmonary arteries. Electrophoresis and DNA sequencing subsequently confirmed the diagnosis of arterial tortuosity syndrome (ATS). The patient underwent multiple percutaneous balloon dilatations and stent placement for vessel stenosis. She underwent correctional surgery, including multiple patch augmentation, to correct the anatomic abnormalities. She is currently

asymptomatic and is being monitored for disease progression.

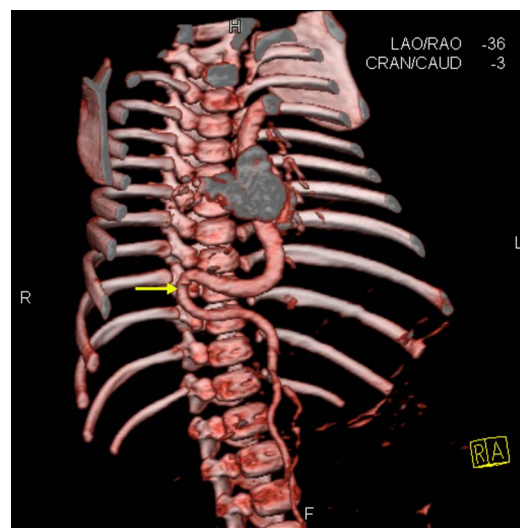
ATS is a rare autosomal recessive connective tissue disease characterised by elongation and tortuosity of the large-sized and medium-sized arteries. This was first described in 1967 by Ertugrul.<sup>1</sup> The aetiology of the disease involves alterations in the vascular elastic fibres of the tunica media, leading to aneurysms, dissections and stenosis of these vessels.<sup>2</sup> A loss-of-function mutation of the *SLC2A10* gene leads to a decreased transcription of decorin, the inhibitor of the transforming growth factor beta (TGFB) signalling pathway.<sup>3</sup> This ultimately leads to disinhibition of the TGFB signalling pathway and inhibition of proper extracellular matrix formation, causing tortuosity of arterial vessels.<sup>3</sup>

Patients present with connective tissue manifestations, including characteristic facial features, hernias, cutis laxa and hyper-extensible skin. Characteristic facial features include micrognathia, elongated face, high palate, beaked nose and down slanting palpebral fissures.<sup>3</sup> Owing to these manifestations, ATS is often misdiagnosed as other connective tissue diseases, including Loeys Dietz syndrome, Marfan syndrome and Ehlers-Danlos syndrome.

Neonates and infants presenting with features of pulmonary artery stenosis, with or without characteristic craniofacial features, should be screened for ATS. Cardiac catheterisation and CT angiography are useful diagnostic considerations.



**Figure 1** CT angiography: at the aortic arch, from right (R) to left (L), there is tortuosity of the brachiocephalic, right subclavian, right common carotid, left common carotid and left subclavian arteries (yellow arrows). There is mild stenosis of the distal edge of the aortic arch and significant stenosis of the proximal descending aorta (blue arrows). A mild degree of left peripheral pulmonary artery stenosis is also seen (red arrow).



**Figure 2** CT 3D reconstruction reveals a right-sided kink of the descending aorta as it approaches the diaphragm (yellow arrow).



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## Learning points

- ▶ A loss-of-function mutation of the *SLC2A10* gene leads to a decreased transcription of decorin, the inhibitor of the TGFB signalling pathway.<sup>3</sup> This ultimately leads to disinhibition of the TGFB signalling pathway and inhibition of proper extracellular matrix formation, causing tortuosity of arterial vessels.<sup>3</sup>
- ▶ A review of 71 cases of ATS described in the literature revealed that consanguinity was present 46% of the time, further corroborating the autosomal recessive inheritance pattern. Additionally, 58% of the diagnosed cases were male.
- ▶ Neonates and infants presenting with features of pulmonary artery stenosis, with or without characteristic craniofacial features, should be screened for ATS. Cardiac catheterisation and CT angiography are useful diagnostic considerations.

**Contributors** EM, KK and SAM were equally involved in planning and writing the manuscript. All authors contributed equally.

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**Patient consent** Obtained.

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