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Review

Vascular manifestations of syndromic aortopathies: role of current and emerging imaging techniques

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Patients with connective tissue diseases such as Marfan's syndrome, Loeys–Dietz syndrome, and vascular Ehlers–Danlos syndrome comprise a small but important group of patients who present early with acute aortic syndrome comprising aneurysmal dilation, rupture, or aortic dissection. Cardiovascular pathologies are an important yet treatable cause of morbidity and mortality in these patients. Imaging plays an important role in initial diagnosis, surveillance, and identification of complications. Furthermore, these patients are prone to developing complications in other vascular territories. Effective screening and surveillance will allow early diagnosis and elective treatment thus reducing the morbidity and mortality associated with presentation with acute complications. In this article, we will provide an overview of the role of magnetic resonance and computed tomography angiography in the management of syndromic aortopathies.

Introduction

Connective tissue disorders with a dominant vascular manifestation in the aorta are often referred to as syndromic aortopathies and cover a spectrum of disorders, including Marfan's syndrome, Loeys–Dietz syndrome (LDS), vascular Ehlers–Danlos syndrome (EDS), bicuspid aortic valve (BAV) aortopathy, familial thoracic aortic aneurysm (FTAA), and arterial tortuosity syndromes (ATSs). These are relatively rare conditions but account for a significant proportion of young patients presenting with major vascular complications including aortic dissection, aneurysmal rupture, and intracranial haemorrhage.[1] Major advances in genotyping have resulted in a more detailed understanding of the genetic basic of these diseases and the underlying pathophysiology.[2]

Recent revisions to the criteria used in the diagnostic work-up of these conditions have placed more emphasis on the presence of vascular manifestations.[1,3] Vascular imaging now plays a central role in the diagnosis, surveillance, and detection of complications of these aortopathy syndromes (Table 1).

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Table 1
Summary of clinical and imaging features of syndromes with vascular manifestations.

Syndrome	Genes involved	Inheritance	Clinical features	Vascular manifestations
Marfan's syndrome	Fibrillin 1	Autosomal dominant	Scoliosis, pectus deformity, increased arm span, arachnodactyly, lens dislocation	Aortic root aneurysm and dissection, mitral valve prolapse
Loeys–Dietz syndrome (LDS 1 and 2)	TGFBR1 TGFBR 2	Autosomal dominant	Hypertelorism, bifid uvula, palate deformity, Marfan-like musculoskeletal features, neurocognitive impairment	Ascending aortic dissection and rupture, arterial tortuosity
Aneurysms-osteoarthritis syndrome (LDS 3)	SMAD3	Autosomal dominant	Features similar to LDS, early onset osteoarthritis	Thoracic aortic aneurysm and dissection, arterial tortuosity
TGB2-related Loeys–Dietz syndrome (LDS 4)	TGFB2		Features similar to Marfan's syndrome and LDS	Thoracic aortic aneurysm and dissection, arterial tortuosity
Reinhoff syndrome (LDS 5)	TGFB3	Autosomal dominant	Features similar to LDS with growth retardation, hypotonia due to decreased muscle mass and distal arthrogryposis	Potential risk of vascular disease
Classical Ehlers–Danlos syndrome (type I/II)	COL5A1 COL5A2	Autosomal dominant	Fragile skin, joint hypermobility	Mitral/tricuspid valve prolapse, aortic root dilation, spontaneous large vessel rupture, AV fistulae, intracranial aneuryms
Vascular Ehlers–Danlos syndrome (type IV)	COL3A1	Autosomal dominant	Thin skin, extensive bruising, prominent eyes, pinched nose.	Aneurysm, dissection, rupture and ectasia, affecting thoracic and abdominal aorta, head and neck, abdominal visceral and iliac arteries
Shprintzen–Goldberg syndrome	SKI	Autosomal dominant	Craniosynostosis, characteristic facial features, e.g., hypertelorism, exophthalmos, micrognathia, marfanoid habitus, umbilical and inguinal herniae, neurocognitive impairment	Mitral valve prolapse, MVR, AVR, aortic root dilation
FBN2-related Beal's syndrome (congenital contractural arachnodactyly)	FBN2	Autosomal dominant	Marfan-like appearance, flexion contractures, muscular hypoplasia	Aortic dilation
Arterial tortuosity syndrome	SLC2A10	Autosomal recessive	Hyperextensible skin and joints	Tortuosity of small and large vessels, aortic aneurysm and dissection
Turner's syndrome	45XO	X-linked	Small stature, broad chest, mild pectus excavatum, renal anomalies, ovarian dysgenesis, kyphoscoliosis	Coarctation of the aorta and aortic dilatation
Polycystic kidney disease	PKD1 PKD2	Autosomal dominant	Enlarged, multicystic kidneys, renal stones, increased risk of renal cell carcinoma, hepatic and pancreatic cysts	Intra and extracranial aneurysms, cardiac abnormalities including mitral valve prolapse
Bicuspid aortic valve syndrome	NOTCH1	Autosomal dominant	Cardiovascular manifestations only	BAV results in valve dysfunction, acute coronary syndrome, aortic dilation and acute aortic syndrome
Non syndromic familial thoracic aortic aneurysm	ACTA2 MYLK MYH11 PRKAG1	Autosomal dominant	Mild musculoskeletal features	Aneurysm and dissection of the thoracic aorta

AV, arteriovenous fistula; MVR, mitral valve regurgitation; AVR, aortic valve regurgitation.

Syndromic aortopathy: aetiology, diagnosis and clinical features

Marfan's syndrome

Marfan's syndrome is the commonest connective tissue disorder and has an autosomal dominant mode of inheritance. Marfan's syndrome is usually caused by mutations in the gene fibrillin 1 (*FBN1*), encoding the fibrillin-1 glycoprotein, found in extracellular matrix microfibrils.[4] This results in increased transforming growth factor beta (TGFB) signalling due to failed TGFB inactivation. Loss of elastin and disordered elastic fibres results in loss of aortic wall integrity.[2] Other mutations are also recognised such as TGFB receptor mutations, also present in LDS.

Patients have characteristic cardiovascular, skeletal and ocular manifestations and clinical diagnosis is established