Marfan 101: Understanding the Basics

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Objectives

- Learn about Marfan syndrome including what causes this condition, who is affected, and what are common signs
- Consider related disorders with findings that may overlap with Marfan syndrome
- Discuss how Marfan syndrome is diagnosed and common tests to expect when undergoing evaluation
- Briefly review recommended management
Marfan Syndrome

- **Genetic disorder** that affects the body’s connective tissue

- **What is ”connective tissue”**?
  - A substance made up of proteins that is found throughout our bodies and holds our cells, organs and tissues together

  - *Fibrillin-1* is the protein specifically affected in Marfan syndrome

  - Defects in the gene which makes *fibrillin-1* cause an increase in *transforming growth factor beta* or *TGF-β*, which causes problems with connective tissue throughout the body
Marfan Syndrome

- **Prevalence:** 1 per 5000 individuals
  - Males = females
  - All races and ethnic groups equally affected

- **Inherited condition** with autosomal dominant transmission
  - 50% chance that a person with MFS will pass along the mutation each time they have a child
  - 25% *spontaneous* mutations which occur for the first time in a family
What are the signs of Marfan syndrome?

- Features may be present at birth or may develop and worsen with increasing age.

- **Variable expression** means that every individual is affected differently.

- **Affected systems** may include:
  - Heart and blood vessels
  - Bones and joints
  - Eyes
  - Lungs
  - Skin
  - Spinal cord
Disorders related to Marfan syndrome

- Involve the connective tissue and may have overlapping findings
- May also have progressive enlargement of the aorta
- Some related disorders include:
  - Loeys-Dietz syndrome (LDS)
  - Ehlers-Danlos syndrome (EDS)
  - Familial Thoracic Aortic Aneurysm and Dissection (FTAAD) syndrome
Heart and blood vessels

Progressive aortic enlargement
- Aneurysm
- Aortic valve insufficiency
- Aortic dissection and/or rupture

Mitral valve prolapse
- “Floppy” valve
- Mitral insufficiency
- Abnormal heart rhythm
Aortic dissection

Associated with severe pain in anterior chest, back and/or neck

Potentially life-threatening emergency – immediate medical evaluation should be pursued
Bones and joints

- Flat feet
- Hypermobile joints
- Long fingers

Chest wall abnormalities

- High arched palate
- Dental crowding
Ocular system

Myopia = nearsightedness

Ectopia lentis (Lens dislocation)

Glaucoma

Retinal detachment

Cataracts
Pulmonary

Pneumothorax = sudden lung collapse

Healthy

Emphysema

Emphysema

Sleep apnea

SNORING DIAGRAM
Other systems

Striae = stretch marks

Dural ectasia
Making the diagnosis: Early and accurate is essential!

- Seek a physician experienced in connective tissue disorders

- Exam should include:
  - Detailed medical and family history
  - Complete physical examination
  - Echocardiogram
  - Electrocardiogram
  - Eye exam, include slit lamp exam of lens
  - CT or MR may be necessary to evaluate the spine
  - Genetic testing may help confirm or rule out a diagnosis of Marfan syndrome in family members at risk
Aortic dilation – a key feature of diagnosis

The Revised Ghent Criteria

- In the absence of family history:
  - Aortic dilation AND ectopia lentis
  - Aortic dilation AND FBN-1 mutation
  - Aortic dilation AND systemic findings (≥7)

- In the presence of family history:
  - Ectopia lentis
  - Systemic findings (≥7 pts)
  - Aortic dilation (Z ≥ 2 above 20 yrs old, ≥3 below 20 yrs old)

Cardiovascular surveillance

- Initial echo with f/u echo within 6 mos
  If dimensions are stable, echo annually
- More frequent imaging indicated if:
  - Aortic root > 4.5 cm
  - Rate of aortic root dilation > 0.5 cm/year
  - Progressive aortic regurgitation

- Intermittent CT or MR in young adulthood
- At least annual CT or MR s/p aortic root replacement or dissection
Management

- Exercise restriction
- Medical management is aimed at slowing aortic growth
  - Beta blockers (*propranolol, atenolol, metoprolol*)
  - Angiotensin II receptor blockers (*losartan, irbesartan*)
  - ACE inhibitors (*enalapril, lisinopril*)
- Surgical intervention when needed
- Supportive services
Marfan syndrome is a genetic disorder of the connective tissue, which primarily affects the ocular, musculoskeletal and cardiovascular system.

Cardiovascular complications in Marfan syndrome, as well as in related disorders may be life-threatening, and therefore early and accurate diagnosis is essential.

Regular surveillance, medical therapy and surgical intervention if needed can improve long-term outcomes and save lives.
Sharing health information

Medical alert bracelets

Backpack Health App

Key to improving outcomes when time is of the essence