Marfan, a 'look-alike' disorder, or neither?

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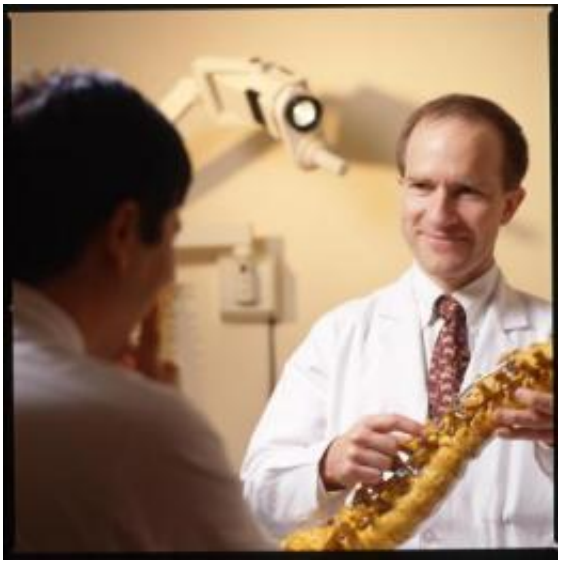

This is Paul Sponseller, M.D., of Johns Hopkins Children's Center. Credit: Johns Hopkins Children's Center

Johns Hopkins researchers have compiled what they believe are reliable lists of tell-tale physical signs to help doctors recognize children with Marfan and Loeys-Dietz syndromes. Timely and early diagnosis of both genetic disorders can mean the difference between life and death, but some of the most common physical features are also found in people with neither of the syndromes, which can cause confusion.

Published as two separate studies in the August issue of the Journal of Bone and Joint Surgery, the two lists enumerate physical features that in certain combinations are highly suggestive of either Marfan or Loeys-

Dietz syndromes, connective tissue disorders similar in presentation but caused by different genetic glitches. Many of the signal features of these disorders involve the face, skull, joints and spine, making them easy to spot during a physical exam, but not always easy to sort out.

"The beauty of our lists is that they require no fancy imaging tests and most of the signs are right there for the pediatricians and the orthopedic surgeons to see," says co-investigator Paul Sponseller, M.D., M.B. A., director of Orthopaedics at Johns Hopkins Children's Center. "All they have to do is see the forest for the trees. The lists will help them do so."

If diagnosed in childhood, both disorders can be managed with drugs or surgery to head off the most life-threatening complications — arterial aneurysms or enlargement and rupture of the aorta — according the investigators.

"We miss that prevention opportunity in people diagnosed as adults," Sponseller says.

Both Marfan and Loeys-Dietz syndromes affect the connective tissue of the heart, spine, joints and eyes, but Loeys-Dietz is also marked by twisted arteries that are prone to aneurysms, a feature absent in Marfan. And because people who have Loeys-Dietz tend to experience tearing of the aorta earlier than Marfan patients, they often need earlier and more aggressive treatment, including surgery.

Marfan

Starting out with a comprehensive list of 20 or so classic Marfan features, including long tapering fingers, a spinal curvature and a long narrow face, the researchers examined how often they occurred in 183 Marfan and 1,250 non-Marfan patients seen at Hopkins. The researchers calculated the diagnostic potential of each feature based on two factors:

how common it was among Marfan patients and how well it could help differentiate between patients with the disorder and those without it. The strongest diagnostic predictor of Marfan in the study was the combination of certain facial features with a very long thumb. With a diagnostic accuracy index of 0.97, this combination correctly predicted Marfan in 97 out of 100 every patients.

A patient with any two of the following signs with high diagnostic potential should be sent to a Marfan specialist:

- One or more cranial or facial signs including a long lean skull, downward slanted eyes, a receding jaw (diagnostic accuracy 0.93)
- An extra long thumb: when folded inside the clenched fist of the hand, the thumb reaches the outer rim, past the pinkie (diagnostic accuracy 0.87)
- Wrist test: A thumb that covers the entire nail of the same-hand pinky finger when encircling the wrist of the opposite hand (diagnostic accuracy 0.83)

A patient with three or four of the following should be sent to a specialist:

- Cranial and facial features described above
- High-arched palate
- Hollow chest

- Severely flat feet, with or without deformity
- Arm span more than 1.5 times longer than the total height

Another potent combination was the pairing of scoliosis (a curvature of the spine) with either facial features or an extra long thumb. Commonly seen in people without Marfan, scoliosis by itself is not a reliable predictor of the disorder, the researchers say.

The researchers warn their tool is not perfect — no screening test is — and may miss some Marfan patients with "silent" syndrome, while raising suspicion about some who don't have the disorder. Indeed, one in five Marfan patients in the study had none or only one physical feature, while 13 percent of the non-Marfan patients had two skeletal features suggestive of the syndrome.

Loeys-Dietz

Researchers reviewed the charts of 65 Loeys-Dietz patients sent to Johns Hopkins after a diagnosis elsewhere. Investigators say primary-care pediatricians and orthopedic surgeons should be on the lookout for Marfan-like features in all patients, but consider Loeys-Dietz syndrome if they also notice any of the following signs that are not found in Marfan:

- Widely spaced eyes
- Club foot
- Translucent skin that bruises easily
- Bi-forked or split uvula, the dangling protrusion seen in the back

of the throat • Cleft palate • Scoliosis with isolated deformities of the upper spine

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