Consultation with the Specialist: Tall Stature
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Consultation with
the Specialist

Tall Stature
Bruce S. Alpert, MD*

In 1984, Flo Hyman led the USA women’s volleyball team to the Olympic gold medal. She was a head taller than her teammates and continued to play volleyball after the Olympic Games. In February 1985 she met her untimely death while competing. Her image on the cover of *Sports Illustrated* pointed out to many of us the dangers of sports participation for patients who have Marfan syndrome (previously undiagnosed in Ms. Hyman). Almost annually, a young athlete, usually playing basketball, collapses during competition or practice and dies from aortic rupture. The majority of tall individuals, of course, do not have Marfan syndrome. The purpose of this article is to discuss the differential diagnosis of tall stature and briefly review the restrictions and therapy pertinent to patients who have Marfan syndrome.

An individual is “tall” if he or she is greater than 2.5 standard deviations above the mean for age and gender. In adults this is more than 192 cm in males and more than 179 cm in females. The Table, which shows the major diseases associated with being tall, does not include the largest group of tall people — those who are “normal,” usually associated with tall parents and relatives. Endocrine causes of tall stature include conditions that result from overproduction of growth hormone or thyroid hormone. Three of the diagnoses rely on chromosomal analyses: fragile X syndrome, Klinefelter syndrome (XXY), and XYY syndrome. Homocystinuria may be excluded by amino acid determination, especially among patients who have a negative family history and developmental delay.

Diagnosis of Marfan Syndrome

There is no consistent laboratory test by which Marfan syndrome can be diagnosed. Fibrillin is the affected protein, whose gene maps to chromosome 15q21. Several DNA mutations have been described that confirm the clinical diagnosis and allow for tracking of gene mutations in at-risk family members. Several major manifestations can aid in the diagnosis: ectopic lentis, dilation of the ascending aorta, aortic dissection, and dural ectasia (requires computed tomography or magnetic resonance imaging). If a patient has a family history of Marfan syndrome, it may be diagnosed by noting involvement of at least two of the following systems: skeletal, ocular, cardiovascular, pulmonary, skin, central nervous system, and at least one major manifestation. If the family history is negative, the diagnosis depends on involvement of the following: the skeletal and at least two other systems and at least one major manifestation. Marfan syndrome is transmitted as an autosomal dominant trait with a high degree of expressivity. About 30% of cases result from a new dominant mutation. The body habitus varies substantially, but the classic patient is tall, has arachnodactyly, hypermobile joints, scoliosis, a high arched palate, pectus deformity, and is thin (Figs 1 and 2). Arm span exceeds height, and upper-to-lower body ratio is lower than expected for age. Evaluations by a geneticist, cardiologist, and ophthalmologist may be needed to complete the diagnosis.

Cardiovascular Complications

The cardiac lesions that occur are the result of defective connective tissue that cannot withstand systemic blood pressure. The ascending aorta dilates progressively, thus losing tensile strength. Death usually occurs as a result of either a sudden elevation of blood pressure leading to aortic rupture or a rapid deceleration of the body leading to the severance of the weakened aorta from the heart. In these cases, death is rapid. There may be periods of aneurysmal increases in aortic size with small intimal and/or medial aortic tears; these cause significant chest pain. Aortic dissections may be chronic and subtle in older teenagers and young adults. The ascending aorta usually is replaced surgically when the aorta exceeds 55 to 60 mm. The replacement consists of a prosthetic valve sewn into a tube graft (composite graft), which replaces the dilated aortic segment. When the aortic root dilates significantly, the aortic leaflets no longer may oppose, and aortic regurgitation occurs, resulting in a decrescendo diastolic murmur. This extra volume, which must be ejected with each systole, tends to increase the rate of aortic dilation.

The mitral valve chordae tendineae also may be affected. As these lengthen progressively, the leaflets of the valve may prolapse and lead to mitral regurgitation. The left-sided cardiac chambers dilate, and contractility may be impaired. The physical signs of mitral prolapse and regurgitation are an ejection click at

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the apex followed by a holosystolic
high-pitched murmur. The mitral
valve is affected especially in infants
who have the severe “infantile”
form of Marfan syndrome.

Because tables of aortic root size
for age in tall individuals were not
available, we recruited 192 tall males
and females who had no disease. We
obtained echocardiographic measure-
ments of the aorta and “regressed”
this dimension with respect to height
and body surface area. Independent
of gender, the upper limit of the nor-
mal aortic root size was 1.9 cm/m²
of body surface area.

**Slowing Aortic Dilation**

Virtually all of the mortality and
most of the morbidity associated
with Marfan syndrome results from
the cardiovascular complications. At
least 15 years ago, investigators at
the Johns Hopkins Hospital began to
try to slow the progression of aortic
dilation by using oral beta blockade.

Initially propranolol was used; more
recently, atenolol has been the drug
of choice. Because the initial studies
were encouraging, we undertook a
joint study in which children whose
aortic diameter exceeded the 95th
percentile measurement were treated
with atenolol. The investigators
at Johns Hopkins used a dose of
1.2 ± 0.9 mg/kg per day. We were
somewhat more aggressive, using
1.9 ± 0.6 mg/kg per day (P < .008 vs
Hopkins dose). A control group of
13 who did not receive beta-block-
ers was followed clinically at Hop-
kins. The rate of dilation of the aor-
tic root differed significantly when
controls (2.1 ± 1.6 mm/yr increase)
were compared with patients treated
at Hopkins (1.1 ± 1.1 mm/yr) or at
our institution (0.7 ± 1.8 mm/yr). The
higher dose of medications tended to
lead to a lower rate of aortic dilation
(P > 0.05). More patients are needed
to determine the optimal dosage of
beta blocker for minimal aortic root
growth. During the past decade of
beta-blockade use, the rate of surgi-
cal intervention has declined signifi-
cantly. At our institution, only one
medication “non-complier” required
surgery. A precipitous decline in
emergency surgery has been noted
at Johns Hopkins.

The age at which beta blockade
should be started is debatable.
Several institutions begin therapy
during infancy. Our policy has been
to wait until: 1) the aorta exceeds
the 95th percentile or 2) a rapid
rate of dilation is observed. We
give the atenolol either bid or tid
to reduce side effects from the dose
of 2 mg/kg per day. Some individu-
als who have Marfan syndrome do
not have a significantly abnormal
aortic wall; they are at a low risk
for aneurysm, dissection, or rupture
and may never need treatment.

**Sports Restrictions**

Patients who have Marfan syndrome
with aortic enlargement may not be
able to participate in contact sports
or other activities that put stress on
the aorta.
participate in sports or activities that require isometric (static) exercise. This form of muscle use causes excessive elevations of systolic blood pressure and may lead to sudden death. Similarly, patients must be restricted from contact sports that involve sudden body acceleration or deceleration. In addition, we do not allow competitive sports in which “all-out” effort may be required. Any time a score is kept or a coach or parent is involved, the child or adolescent may want to “sprint to the finish.” This could lead to an excessive systolic blood pressure response and disastrous results. We encourage low-impact aerobic exercise to try to maintain a reasonable level of fitness and long-term “cardiac health.” It often is difficult to prevent the tallest member of a school class from participating in basketball, but parents must understand the risk and encourage alternative activities. The life expectancy of patients who have Marfan syndrome will be lengthened significantly by the use of beta blockade unless the adolescent or young adult patient dies suddenly while participating in prohibited sports.

**SUGGESTED READING**


**PIR QUIZ**

6. The most significant complication of Marfan syndrome is:
   A. Detachment of retina.
   B. Juvenile diabetes mellitus.
   C. Recurrent thromboemboli in cerebral blood vessels.
   D. Rupture of aorta.
   E. Sarcoma associated with undescended testes.

7. In the diagnosis of Marfan syndrome, the most useful information is:
   A. History of consanguinity of parents.
   B. Measurement of fibrillin precursors in peripheral leukocytes.
   C. Chromosomal mapping to detect deletions on chromosome 15.
   D. Width of aortic root exceeding 95th percentile.

8. Each of the following is characteristic of Marfan syndrome except:
   A. Arm length disproportionately long for height.
   B. Dislocated lens.
   C. Height greater than 2.5 standard deviations for age.
   D. Mental retardation.
   E. Scoliosis.

**FIGURE 1.** Young child who has Marfan syndrome. Note scoliosis (A) and pectus excavatum (B). The child was above the 90th percentile for height.

**FIGURE 2.** Older boy demonstrating classic features of Marfan syndrome.