Autosomal Recessive Weill-Marchesani Syndrome

Alternative Names
WM Syndrome
WMS
Spherophakia-Brachymorphia Syndrome
Mesodermal Dysmorphodystrophy, Congenital

WHO International Classification of Diseases
Congenital malformations, deformations and chromosomal abnormalities

OMIM Number
277600

Mode of Inheritance
Autosomal recessive

Gene Map Locus
19p13.3-p13.2

Description
Weill-Marchesani syndrome (WMS) is a rare genetic disorder that is characterized by short stature, unusually short fingers (brachydactyly), joint stiffness, facial abnormalities, and eye abnormalities. Short stature and brachydactyly are found to be associated with 98% of patients. Eye abnormalities include small round lenses (microspherophakia), ectopia of the lens, severe myopia, and glaucoma. Eye abnormalities have variant frequencies and myopia is the most prevalent with the frequency of 94%. Other eye abnormalities are found as the following frequencies: microspherophakia in 84%, glaucoma in 80%, ectopia lentis in 73%, and cataract in 23%. Many other abnormalities have been reported in WMS cases like; joint limitations, thickened skin, and cardiac abnormalities.

Molecular Genetics
Weill-Marchesani syndrome (WMS) is inherited in autosomal recessive (AR) or autosomal dominant (AD) modes. However, the AR mode of inheritance is more frequent. Homozygous mutations within the ADAMST10 gene (a disintegrin-like and metalloproteinase with thrombospondin type 1 motif, 10 gene) are found to be the cause of AR-WMS. ADAMTS10 plays a major role in human growth and the development of skin, lens, and heart. This is because this gene is a member of the extracellular matrix protease family which is expressed in skin, fetal chondrocytes, and fetal and adult hearts. Thus, impairment of the extracellular matrix will cause the disease. Some carriers of AR-WMS present some mild clinical features of the disease.

Epidemiology in the Arab World
Lebanon
Megarbane et al. (2000) studied three cases with Weill-Marchesani Syndrome (WMS) and their pedigrees to evaluate the association of the 15q21.1 region (FBN1 gene) with the autosomal recessive form of the disease. The studied patients were male and female sibs and their male cousin. They were the product of consanguineous marriages and all parents had short stature. The common physical features of the three patients included short stature, brachydactyly, limitation of joints movements, microspherophakia with luxated lenses, myopia, glaucoma, and heart malformations. The first patient was examined at 20 years and his radiological examination of the skeleton showed diffuse aftermath of Scheuermann’s disease in the dorso-lumbar region. His sister had a severe fever episode around age three that led to hearing loss. She was seen at age 14 with noticeable speech articulation problem. Both sibs had mild pulmonary stenosis. Their other three sibs were normal. The cousin of the affected sibs was seven and a half years old. He had cooked teeth and inguineal hernia. His sibs were normal and his father had a carpal tunnel syndrome of the right hand. Genotyping of the affected individuals and their parents was performed using five markers covering the
15q15-21 region. Haplotype reconstruction with the five markers showed no homozygosity in the affected subjects at that locus. Therefore, FBN1 gene was excluded by Megarbane et al. (2000) in autosomal recessive WMS. Also, it is suggested that other proteins, components of fibrillin-containing associated microfibrils, or molecules associated with fibrillin could be potentially considered at the origin of WMS as this disease is the result of a microfibrillopathy.

Dagoneau et al. (2004) studied three cases of consanguineous parents with autosomal recessive Weill-Marchesani syndrome (AR-WMS). The patients were double first cousins related to two sibships. All patients presented with short stature, brachydactyly, limitation of joint movement, microspherophakia, dislocated lenses, severe myopia, and glaucoma. A nonsense mutation of the ADAMTS10 gene was detected in WMS patients. Accordingly, Dagoneau et al. (2004) provided the first evidence of the involvement of a member of ADAMTS family in brachydactyly and microspherophakia. The fibroblasts were examined by confocal microscopy. Distribution of actin in the patients’ fibroblasts showed large cytoplasmic extensions and a stronger fluorescent signal compared with controls. Also, thick and straight bundles of actin filaments were presented in patients’ fibroblasts which indicated the cytoskeleton anomalies in WMS. A splice-site mutation of the ADAMTS10 gene was detected in those patients. The fibroblasts were examined by confocal microscopy. Distribution of actin in the patients’ fibroblasts showed large cytoplasmic extensions and a stronger fluorescent signal compared with controls. Also, thick and straight bundles of actin filaments were presented in patients’ fibroblasts which indicated the cytoskeleton anomalies in WMS. [See also: Lebanon > Dagoneau et al., 2004].

Riad et al. (2006) reported five cases with classical features of WMS who were subjected to different ophthalmic procedures. Riad et al. (2006) indicated that patients with WMS can present for cataract, glaucoma as well as retinal surgery and that special consideration should be given to difficult intubation, cardiac abnormalities, and patient positioning.

References

Contributors
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