

Information about

HUNTER SYNDROME

MUCOPOLYSACCHARIDOSIS II (MPS II): AN OVERVIEW FOR HEALTHCARE PROFESSIONALS



Kyle (13 years old)

Brigham (9 years old)

Hunter syndrome, or mucopolysaccharidosis II (MPS II), is a serious, X-linked recessive disorder caused by a deficiency or absence of the lysosomal enzyme iduronate-2-sulfatase (I2S).¹⁻⁴ This enzyme is required for degradation of the glycosaminoglycans dermatan sulfate and heparan sulfate; thus its absence results in a deleterious accumulation of these substances in cells throughout the body.¹⁻³ Hunter syndrome, which occurs at a calculated estimate of at least 1 in 155,000⁵⁻¹³ live births, is one of a group of hereditary metabolic diseases known collectively as lysosomal storage disorders.⁴

GENETICS

The I2S gene is located at the Xq27–28 boundary, and has been completely isolated, cloned, and sequenced.^{1,2} It is a large gene, spanning approximately 24 kb and containing 9 exons.² The remarkable clinical heterogeneity seen in Hunter syndrome (MPS II) is thought to result from the large variety of I2S gene mutations that have been observed to occur.² Identified mutations include deletions, insertions, major rearrangements, and point mutations (missense, nonsense, frame shifts, altered splice sites).^{2,4,14} In addition, in some cases, complete I2S gene deficiencies have been documented, and may be associated with the loss of adjacent loci, suggestive of a contiguous gene syndrome.²

PRESENTATION/PROGRESSION

Hunter syndrome (MPS II) is associated with a wide spectrum of clinical manifestations, which may be correlated to residual enzyme activity. Current testing methodology, however, does not distinguish between small amounts of enzyme activity.¹⁴

Patients generally present between 2 and 4 years of age with coarse facial features (including thickening of the lips and nostrils and macroglossia), short stature, progressive conductive and sensorineural hearing loss, frequent upper respiratory tract infections, umbilical or inguinal hernias, progressive mental retardation, dysostosis multiplex, and/or stiff joints

(Table 1).^{1,2,4} Atypical retinitis pigmentosa or retinal degradation may also occur, although the corneal clouding seen with Hurler syndrome is absent.² Upper airway difficulties secondary to a narrowed trachea, thickened vocal cords, and redundant tissue in the upper airway are often observed; such obstructions may lead to sleep apnea.¹⁴ Hepatosplenomegaly and cardiac and valvular heart disease are also seen, especially as disease progresses.¹

TABLE 1: SYMPTOMS ASSOCIATED WITH HUNTER SYNDROME (MPS II)^{1-4,14}

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| <ul style="list-style-type: none"> • Large head (macrocephaly); coarse facial features • Short stature; short neck; dental abnormalities • Thick skin; whitish, nodular, pebble-like skin lesions • Atypical retinitis pigmentosa or retinal degradation • Progressive conductive and sensorineural hearing loss • Obstructive airway disease (obstructive sleep apnea and reduced pulmonary capacity) | <ul style="list-style-type: none"> • Upper respiratory tract infections • Frequent pneumonia • Restrictive pulmonary disease • Cardiac/valvular heart disease • Hepatosplenomegaly • Umbilical or inguinal hernias • CNS involvement • Dysostosis multiplex • Joint stiffness/contractures |
|--|---|

Continued on reverse

Patients are hirsute and may have whitish, nodular, pebble-like skin lesions on the posterior thorax and upper arms.² A large head, thick skin, a short neck, and dental abnormalities may also be seen.⁴ In some cases of Hunter syndrome, there is very little or no central nervous system (CNS) involvement, and intelligence and stature may be close to normal.^{1,2} In these cases, progression may occur at a much slower rate. Hearing impairment, cardiac disease, hepatosplenomegaly, joint stiffness, degenerative arthritis of the hips, and carpal tunnel syndrome may also be observed.² Older patients with Hunter syndrome may have rosy cheeks and a hoarse voice.²

Life expectancy is one area of variability in people with Hunter syndrome. Some patients with Hunter syndrome have life expectancies of 15 years or less.¹ Other patients may survive into their 20s or 30s, and beyond.^{1,14} Death usually occurs as a result of respiratory or cardiac failure.

DIAGNOSIS

Diagnosis of Hunter syndrome (MPS II) usually occurs in early childhood, with some people diagnosed later in life. Diagnosis often depends upon the specific features of clinical presentation and familiarity of caregivers with Hunter syndrome. The most commonly employed screening test for Hunter syndrome is quantitative measurement of urinary glycosaminoglycans.¹⁴ A definitive diagnosis is usually made by measuring I2S enzyme activity in serum, white blood cells, or fibroblasts from skin biopsy.¹⁴ Prenatal diagnosis via the measurement of I2S activity in amniotic fluid, amniocytes, or chorionic villus tissue is also available.¹⁴

TABLE 2: DIAGNOSING HUNTER SYNDROME (MPS II)^{1-4,14}

- **Screening: quantitative measurement of urinary glycosaminoglycans**
- **Definitive diagnosis: measurement of I2S activity in serum, white blood cells, or fibroblasts from skin biopsy**
- **Prenatal testing is available**

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