PIGN-CDG

PIGN-CDG causes two genetic syndromes: MCAHS1 and Fryns syndrome. It is one of the 17 known defects in the glycosylphosphatidylinositol anchor synthesis.

What is PIGN-CDG?
Maydan and colleagues described the first patients with PIGN-CDG Multiple Congenital Anomalies-Hypotonia Seizures Syndrome 1 (MCAHS1)1. In 2016, McInerney-Leo and collaborators associated PIGN with another disease – Fryns syndrome2. Both disorders are caused by mutations in the PIGN gene, which encodes glycosylphosphatidylinositol (GPI) ethanolamine phosphate transferase 1, a protein involved in GPI-anchor biosynthesis.

What are CDG?
Congenital Disorders of Glycosylation (CDG) are a rapidly growing group of monogenic metabolic diseases, which counts with over 130 different types.

When to suspect PIGN-CDG?
PIGN-CDG should be considered in the presence of development disability, hypotonia, congenital diaphragmatic hernia, epilepsy combined with multiple congenital anomalies. Interestingly, 8 of the 21 reported patients presented with increased birth weight3.

Causes
As with the great majority of CDG, PIGN-CDG is an autosomal recessive disorder.

Diagnosis
Assessment of the surface expression of GPI-anchored proteins in granulocytes has been used as a preliminary diagnostic test4,5. However, mutation analysis through molecular testing is mandatory to make a final diagnosis. Contact us if you wish to connect with a CDG diagnostic laboratory: sindromedcg@gmail.com.

Major signs and symptoms

Neurologic
Developmental Disability  |  Epilepsy  |  Hypotonia  |  Hyporeflexia  |  Cerebellar Atrophy  |  Cognitive Impairment

Cardiac
Patient Foramen Ovale  |  Patent Ductus Arteriosus  |  Various Valvular Defects

Ophthalmological
Nystagmus  |  Abnormal Eye Movements  |  Microphthalmia

Gastrointestinal
Feeding Problems  |  Gastroesophageal Reflux  |  Anal Stenosis

Genitourinary
Hydrocele and Cryptorchidism (males)  |  Renal Dysplasia  |  Cystic and Hydronephrotic Kidneys  |  Hydroureter

Immunological
Recurrent Infections (mainly pulmonary)

Other Symptoms / Signs
Facial Dysmorphism  |  High Birth Weight  |  Congenital Diaphragmatic Hernia  |  Skeletal Anomalies  |  Hypoplastic Lungs

Prevalence
Some 21 patients have been reported since 20111 including 9 new diagnoses made in 20163,4,5. We are aware of 13 other, unreported patients. Similarly to other CDG, PIGN-CDG is most probably underdiagnosed. (8 Israeli-Arab | 3 Japanese | 1 Mexican-American | 2 Northern European | 1 Iraqi | 1 North-African | 4 USA patients | 1 Polish)

Clinical Management
Symptomatic treatment includes anticonvulsive therapy, gastrostomy to overcome feeding and swallowing difficulties, and glasses to promote visual development. In addition, occupational therapy, speech therapy and physiotherapy, including aquatic therapy, can be beneficial. Diaphragmatic hernia requires surgical treatment.

Prognosis
Epilepsy manifests before 1 year of age (although, usually before 6 months of age)1,4,5. Seizures can be therapy-resistant3,6. Cerebellar atrophy is usually progressive. Patients are also infection-prone, particularly with regard to the respiratory tract1. Also, patients usually present severe global developmental disability and hypotonia, with absent speech and no ambulance, thus requiring assistance particularly with regard to the respiratory tract1. Some unreported patients have acquired the capability of walking independently as well as to communicate with the aid of technology devices and/or sign language. One patient died at 2 years and 4 months of age1.

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