What is GMPPA-CDG?

The first patients were described in 2013 by Koehler and collaborators. Several clinical features overlap with the manifestations observed in triple A syndrome patients. However, GMPPA-CDG patients do not exhibit adrenal insufficiency. GMPPA (MMM 615945) encodes a GM3PBP homologous protein, the mannos-1-phosphate guanylytransferase alpha. This protein has been suggested to act as a regulatory subunit of GMPPB, allowing allosteric feedback inhibition of GMPPB by GDP-mannose. Interestingly, only homoygous mutations were observed in all reported patients.

What are CDG?

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

When to suspect GMPPA-CDG?

GMPPA-CDG should be considered in the presence of clinical manifestations with a great resemblance to triple A syndrome, characterised by gastrointestinal defects (including achalasia), intellectual disability, alacrima and different degrees of involvement of other organs. However, none of the reported GMPPA-CDG patients have adrenal gland insufficiency. Alacrima, which is a very noticeable clinical sign, and feeding difficulties have been mentioned as the first clinical manifestations prompting further medical evaluation. Increased GDP-mannose levels are a distinctive feature.

Causes

As the wide majority of CDG, GMPPA-CDG is an autosomal recessive disorder.

Diagnosis

Biochemical diagnosis of this condition is complicated as both serum transferrin, apocIII glycosylation profiles and enzymatic activity are normal in these patients. Thus, the presence of normal glycosylation patterns, high GDP-mannose levels and clinical manifestations resembling triple A syndrome without adrenal failure should prompt mutation analysis to confirm the diagnosis. Contact us if you wish to connect with a CDG diagnosis laboratory: sindromecdg@gmail.com.

Major signs and symptoms

**Clinical Management**

Achalasia and strabismus have both been corrected through surgery. Tube feeding, namely by gastrotomy for CDG patients who can feed orally, pureed foods may be a good approach. Additional gastrointestinal manifestations have been successfully treated, including a duodenal perforation by laparotomy. Inflammatory bowel disease has been treated with prednisolone, azathioprine, and salazopyrine.

Osteopenia has been treated with Zoledronate, whilst seizures seem to respond to therapy with anticonvulsants. Recurrent upper respiratory tract infections have improved in a patient after tonsillectomy and adenoidectomy. Osteopenia has been treated with Zoledronate, whilst seizures seem to respond to therapy with anticonvulsants. Recurrent upper respiratory tract infections have improved in a patient after tonsillectomy and adenoidectomy. Inflammatory bowel disease has been treated with prednisolone, azathioprine, and salazopyrine. Osteopenia has been treated with Zoledronate, whilst seizures seem to respond to therapy with anticonvulsants. Recurrent upper respiratory tract infections have improved in a patient after tonsillectomy and adenoidectomy.

**Prognosis**

Both feeding difficulties and neurologic manifestations are usually progressive. Alacrima is most frequently present since birth, whilst achalasia usually develops during the first 2 years of life. Microcephaly also appears to be progressive in these patients. Seizures have been described to have their onset in late childhood. Patients reaching adulthood have been reported.

**Prevalence**

Seventeen patients, from 11 unrelated families have been reported in the literature. Additionally, 3 USA patients (not reported in literature) have also been diagnosed with GMPPA-CDG. (4 Pakistani | 3 Arabic | 2 Lebanese | 2 Palestinian | 2 Mexican | 1 Turkish, Kosovan, Dominican and Morocan).

**References**


GMPPA mutations cause an alacrima, achalasia and mental retardation syndrome. It’s one of the 5 CDG caused by defects in nucleotide-sugar synthesis.