Somatotropic pituitary insufficiency in Kearns-Sayre syndrome – the clinical picture, genetic diagnosis and efficacy of rhGH therapy.

Alessandra Rojek¹, Marek Niedziela¹,²

¹ Poznan University of Medical Sciences, Department of Pediatric Endocrinology and Rheumatology, Molecular Endocrinology Laboratory, Poznan, Poland, e-mail: alesrojek@gmail.com
² Poznan University of Medical Sciences, Department of Pediatric Endocrinology and Rheumatology, Poznan, Poland, e-mail: mniedzie@ump.edu.pl

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OBJECTIVES

Kearns-Sayre syndrome (KSS, OMIM #530000) is a rare disease belonging to a heterogeneous group of mitochondrial cytopathies. KSS is manifested by many systemic abnormalities:
1. a progressive external ophthalmoplegy,
2. pigmented degeneration of the retina
3. cardiac block,
4. neurological problems
5. several endocrine disorders.

KSS is caused by Mitochondrial DNA (mtDNA) rearrangements (deletions and/or duplications), which lead to the dysfunction of the respiratory chain and to disorders in tissues with a high energy demands (muscle, nervous system).

CASE PRESENTATION

• The girl (now aged 17 5/12) was admitted to the hospital at the age of 13 yrs with the suspicion of KSS (ophthalmological symptoms and GH deficiency)
• The girl from the first pregnancy (41/42 w.), Agar 10/10, body weight 3890g, body length 56 cm,
• Progressive body mass deficiency has been noticeable since the age of 4-5 yrs (celiac disease excluded)
• Beginning of the eye movements disorders were difficult to ascertain
• Retinal pigmented retinopathy, ptosis, external ophthalmoplegia characteristic for KSS were observed
• Neurological examination revealed limitation in both eyes abduction, significantly reduced upward movement, bilateral ptosis, without cerebellar symptoms, and features of myopathy or neuropathy
• Cardiological examination (Holter ECG) was normal

HORMONAL STUDIES

• Growth hormone after sleep test (GH levels in serum)
  GH 0' 30' 60' 90' 120' Units
  0.1 0.1 0.1 0.1 0.1 0.1 0.1 4.3 mg/ml

• Growth hormone stimulating tests:
  Clonidine (150 µg/m2 p.o.)
  GH 0' 15' 30' 45' 60' 90' 120' 180' Units
  0.2 0.2 0.2 0.2 0.2 0.2 0.2 0.2 mg/ml
  Glucagon (0,030 mg/kg i.m.)
  GH 0' 15' 30' 45' 60' 90' 120' 180' Units
  0.2 0.2 0.2 0.2 0.2 0.2 0.2 0.2 mg/ml

CONCLUSIONS

(1) KSS is usually detected after the diagnosis of a variety of endocrine disorders,
(2) clinical course of the disease is variable, but the growth deficiency is dominant in childhood,
(3) Muscle biopsy plus mtDNA analysis diagnosed the true molecular background of the disease as mitochondrial abnormalities,
(4) PCR can be used as a quick, easy and reliable method for the analysis of mtDNA rearrangements
(5) In some children, KSS may be the reason for the weak results of the therapy with the standard dose of rhGH
(6) In our patient the significant improvement of growth velocity was observed.