NBAS gene mutation causes Insulin-dependent Diabetes Mellitus in a patient with a multisystem disorder consisting immunodeficiency and extremely short stature

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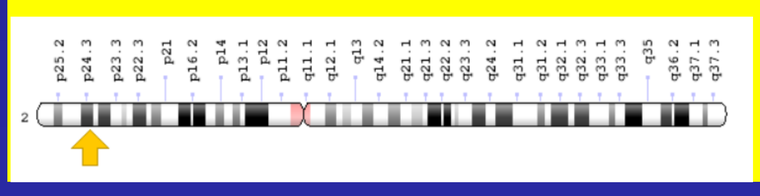
Introduction

We report the case of a 19 years old male patient suffering from a multisystematic disease involving the skeleton, connective tissue, immune system, brain and endocrine system due to compound-heterozygote mutations in the *NBAS* gene, who has also developed an insulin-dependent Diabetes Mellitus at the age of 11 years.

He has an immunodeficiency including decreased CD4+ T-cells, B-cells and NK-cells with expanded early CD8+ effector and activated T-cells, and absence of immunoglobulins

NBAS Gene (Neuroblastoma amplified sequence gene)

This gene encodes a protein with two leucine zipper domains, a ribosomal protein S14 signature domain and a Sec39 like domain. The protein is thought to be involved in Golgi-to-ER retrograde transport of vesicles, allowing the distribution of proteins from the ER to the Golgi compartments.



Gene location:2p.24.3

Whole –exome DNA sequencing by our patient:

Compound heterozygote mutation (c.5741G>A [p.(Arg1914His)]; c.6565_6566insT [p.(Glu2189Valfs*7)])

Clinical features associated with NBAS mutation

Red: clinical features of our patient

Short stature
Optic nerve atrophy
Retinal dystrophy
Pelger-Huet anomaly of the granolocytes
Normal intelligence
Akute infantile liver failure
Senile face
Reduced skin turgor and elasticity
Osteoporosis
Skeletal dyspasia
Hypogammaglobulinemia
Elevated transaminases
Hepatomegaly
Cervical instability
Cerebellum hypoplasia
Inflammatory bowel disease
Celiac disease

Appearance of Diabetes Mellitus

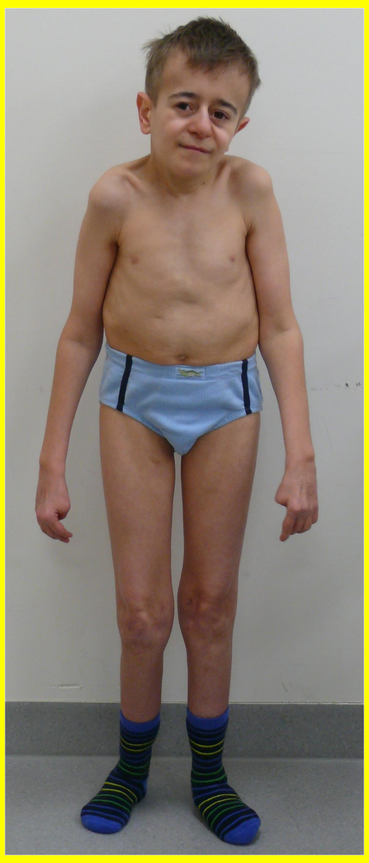
At the age of 11 our patient developed an insulin-depended diabetes mellitus with a decreased c-peptid.

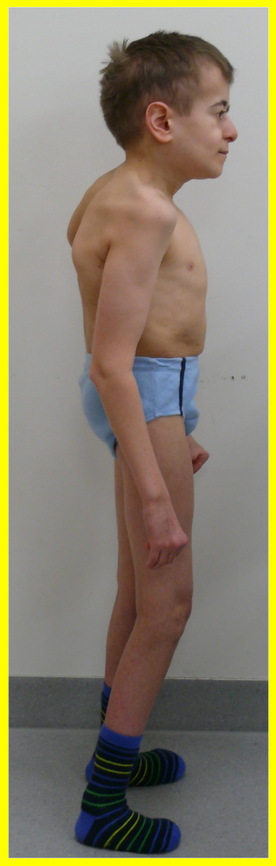
Conclusions

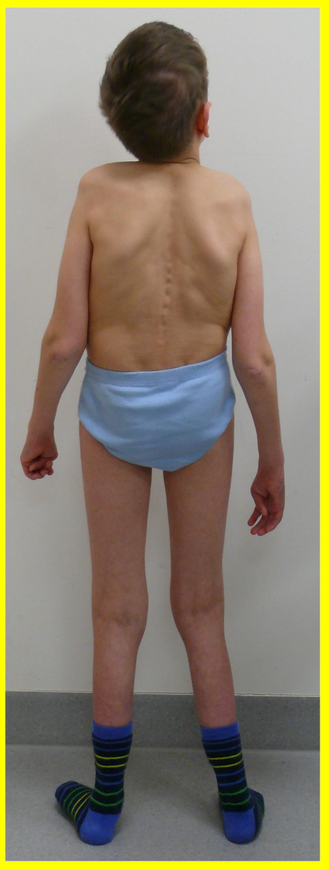
Our patient is the first patient with a mutation of the *NBAS* gene who has developed a diabetes mellitus.

We suggest that the immune dysregulation associated with the NBAS gene mutation promoted the development of the diabetes.

Phenotype of our Patient





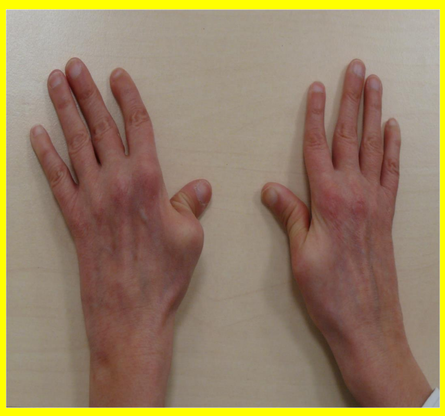


<u>Extremely short stature:</u> 125 cm; height–SDS: -10.7
<u>Dystrophia:</u> weight 27 kg, BMI 17,3 mg/m^2, BMI–SDS: -2,1

Short neck
Dorsal Kyphosis
Prominent scalpula

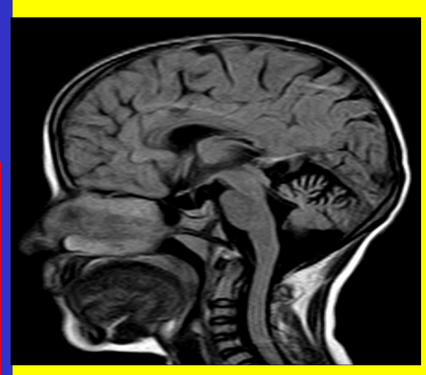
Reduced subcutaneous fat, progeroid appearance

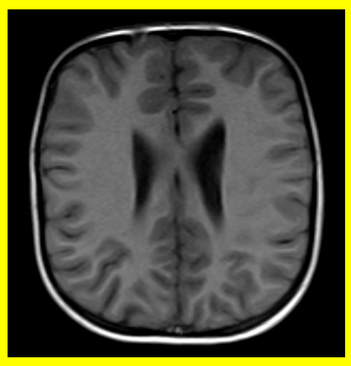
-Triangular face
-Pointed chin
-Prominent eyes
-Narrow forehead
-Brachycephaly
-Progeroid appereance

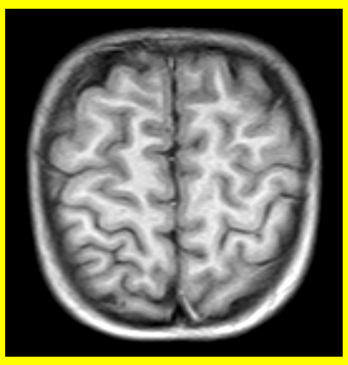


Skeletal dysformities of the hands, brachydaktyly

MRI of our patient : cerebellum hypoplasia







The authors have nothing to disclose.