A rare cause of growth delay- Jacobsen syndrome

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Introduction

❑ Jacobsen syndrome is a rare genetic condition caused by partial deletion of the long arm of chromosome 11.
❑ The 11q24.1 subband deletion is crucial for the full clinical expression of the syndrome.

Characteristic clinical features that include:

❑ skull deformities (macrocrania, high prominent forehead, facial asimmetry, trigonocephaly)
❑ hypertelorism, ptosis, coloboma, epicanthal folds
❑ broad nasal bridge, short nose, anteverted nares
❑ V shaped mouth, long, flat philtrum, thin upper lip
❑ small, low set posteriorly ears
❑ thin fingers, syndactyly, hypoplastic hypotenar regions, abnormal palmar creases
❑ flat feet with large and long first toe, brachydactyly, syndactyly of the 2nd and 3rd toes, crowded toes

Patients may associate:

❑ pre- and postnatal growth retardation
❑ IGF1 and TSH deficiency
❑ abnormal platelet function: thrombocytopenia or pancytopenia
❑ multiple malformations: cardiac, renal, gastrointestinal, genital, central nervous and skeletal
❑ immunological, ocular and hearing problems
❑ mild to severe mental retardation (97%)
❑ conduct problems, most frequently attention deficit/hyperactive disorder
❑ there is strong correlation between the neurocognitive deficiency and the size of deletion

Case report

4 year old boy addressed for short stature
- born at term (36W)
- low birth weight (1780g)
- delayed development
- height 86 cm (-3.95 SD)
- weight 9kg (-6SD)

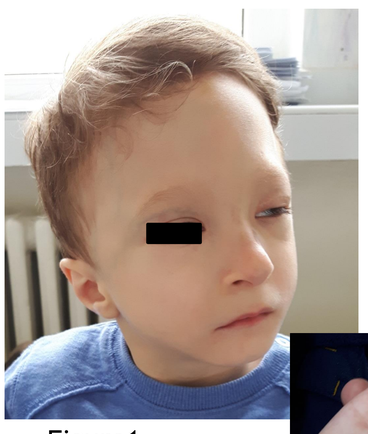

Figure1

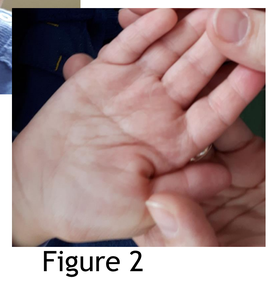

Figure 2

Typical syndromic features:

Facial dysmorphism (figure 1)
- trigonocephaly
- craniostenosis
- ocular hypertelorism
- left palpebral ptosis
- strabismus
- bilateral epicantus
- short nose
- micrognathia
- small, low set ears

- pectus excavatum
- lumbar scoliosis
- unique palmar crease (figure 2)
- multiple toe malformations
- cardiac malformations (ventricular septal defect)
- normal genitalia
- delayed bone age (figure3)
- small pituitary (figure 4)

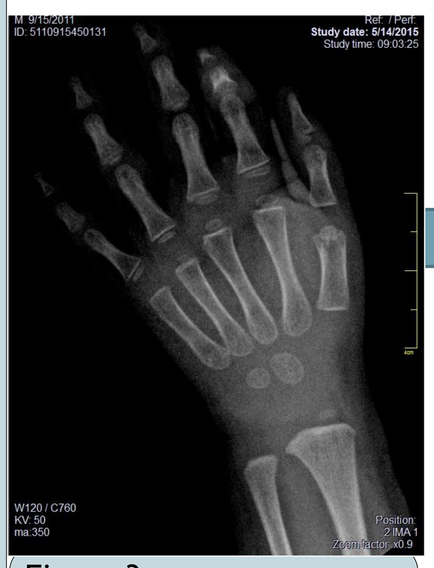

Figure 3
hand radiograph: delayed bone age (3 years)

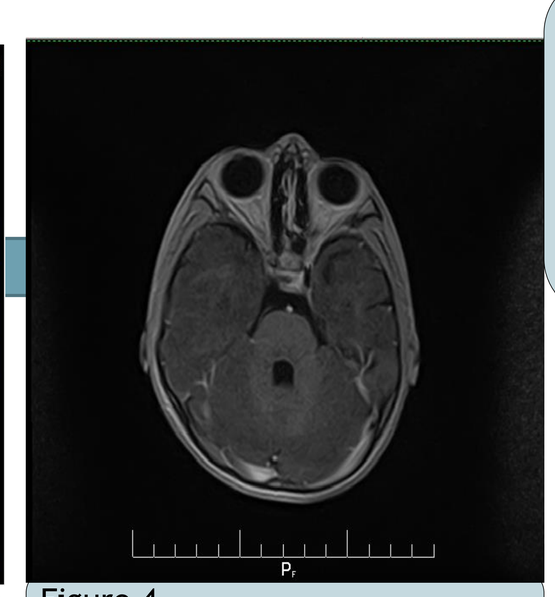

Figure 4
Cerebral MRI revealed small pituitary (7/6/2.5mm)

The low height and weight were explored.
Metabolic causes such as :

- malabsorption syndromes
- chronic disease
- poor nutrition excluded

Biological findings:
- normal thyrotropic and corticotropic axes (table 1)
- low IGF1 levels
- slight polyglobulia (table 2)
- normal platelet count

Table 1

Hormone	Value	Normal Values
TSH	3.30 uUI/ml	0.33- 6.7 uUI/ml
fT4	1.48 ng/dl	0.89-1.76 ng/dl
Cortisol	13.6 ug/dl	5-25 ug/dl
IGF	50.4 ng/ml	49-289ng/ml

Table 2

Parameter	Value	Normal Values
White globules	10000/mm3	6000-10000/mm3
Erythrocytes	5.170.000/mm3	4.000.000-4.900.00/mm3
Hb	12.9g/dl	11-14g/dl
Platelets	251.000	150-400.000

Genetic exploration revealed 46 XY kariotype with **deletion (11) (q23,1qter)**

treatment with rGh introduced

Evolution (6 months later)
- height 93cm (-3.5 SD)
- weight 11.5 kg (+2.5 kg)
- growth rate 1 cm/month

Discussions

❑ Genetic testing diagnosed Jacobsen syndrome and the deletion situs might explain patient's particularities such as:

❑ Haematologically, he did not present pancytopenia or thrombocytopenia but a slight polyglobulia.

❑ His intellectual capacity was not severely affected with mild neuro cognitive deficiency and delayed language development.

❑ Low IGF1 levels reported in children with Jacobsen syndrome was also present in our patient, however in lower normal limit. Nevertheless, this prompted rGH treatment with good outcome.

Conclusion

❑ Jacobsen syndrome is a genetic disorder associated with dysmorphic features, multiple malformations and short stature.

❑ Having into consideration the rarity of the syndrome, there is a sparse number of cases treated with rGH with Jacobsen syndrome with good evolution.

❑ In our case, our patient's evolution was marked by rapid growth and weight gain under treatment.

❑ Therefore, growth hormone treatment should be made individually, directed at understanding the risks and benefits unique to this polymorphic condition.

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Growth
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