Pycnodysostosis in a Czech toddler

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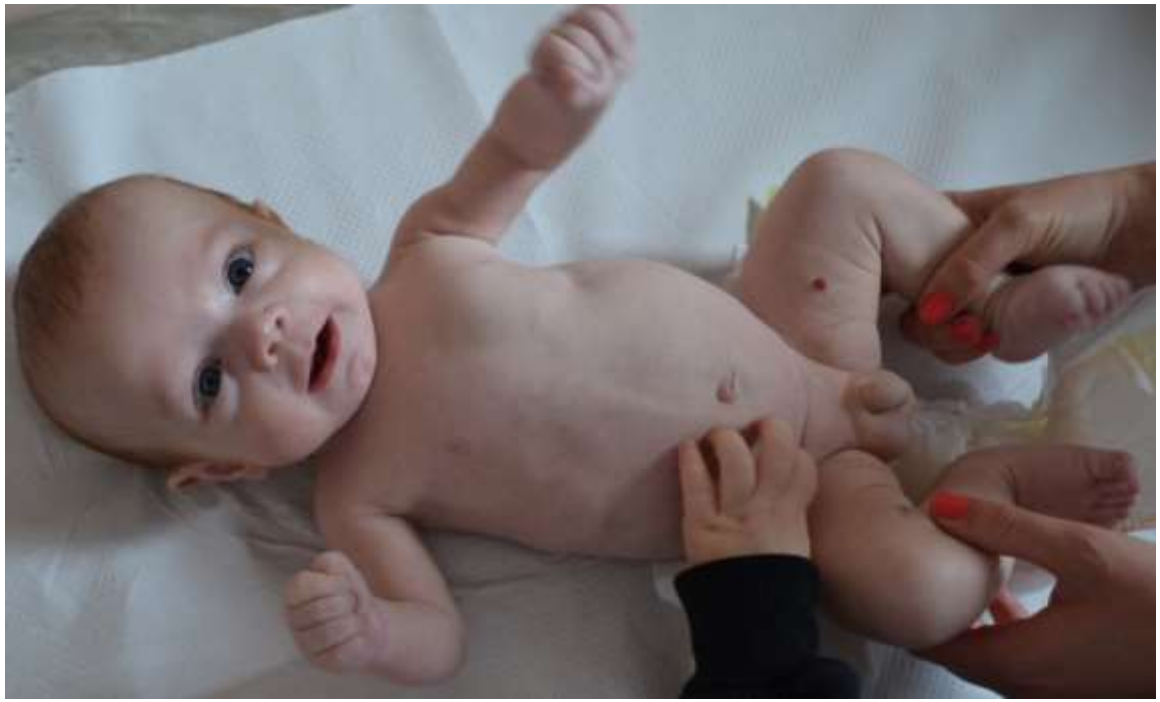
Pycnodysostosis – case report

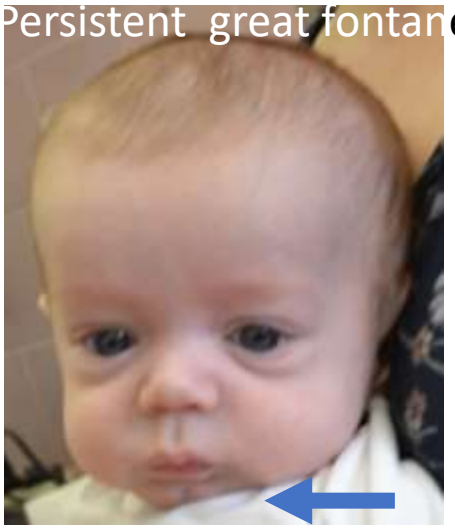
- II/IInd physiological gravidity, boy
- Born in 32nd gestational week, 2060g/45 cm (AGA), APG 9-9-10
- First sign – **Pierre Robin sequence**
- Choanal atresia
- Sleep apnea
- Failure to thrive

6 months (corr. 4)

Genetic examination



6 months (corr.4)



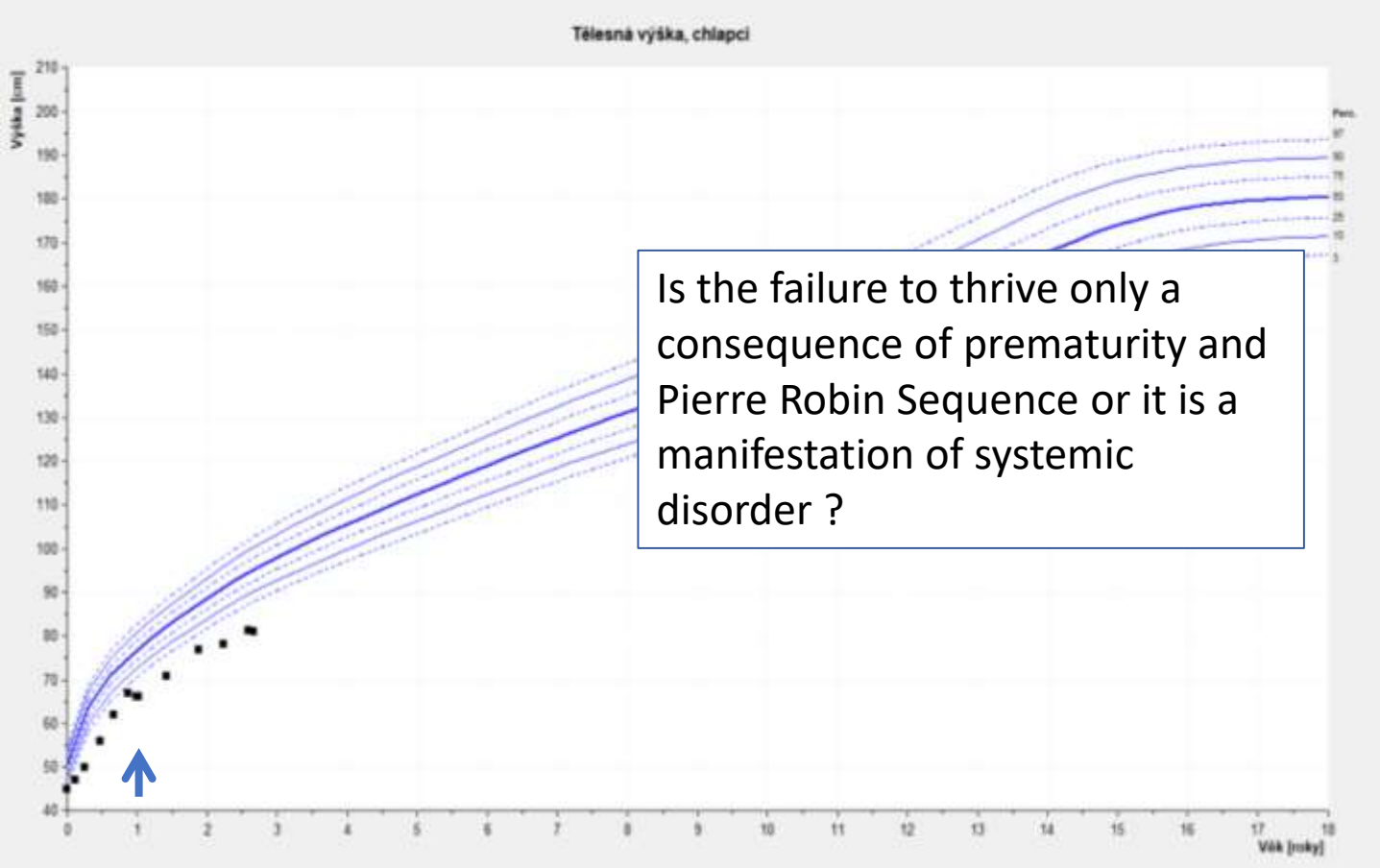
Rethrognatia, gothic palate

46 XY array CGH without pathology

FGFR3 negative

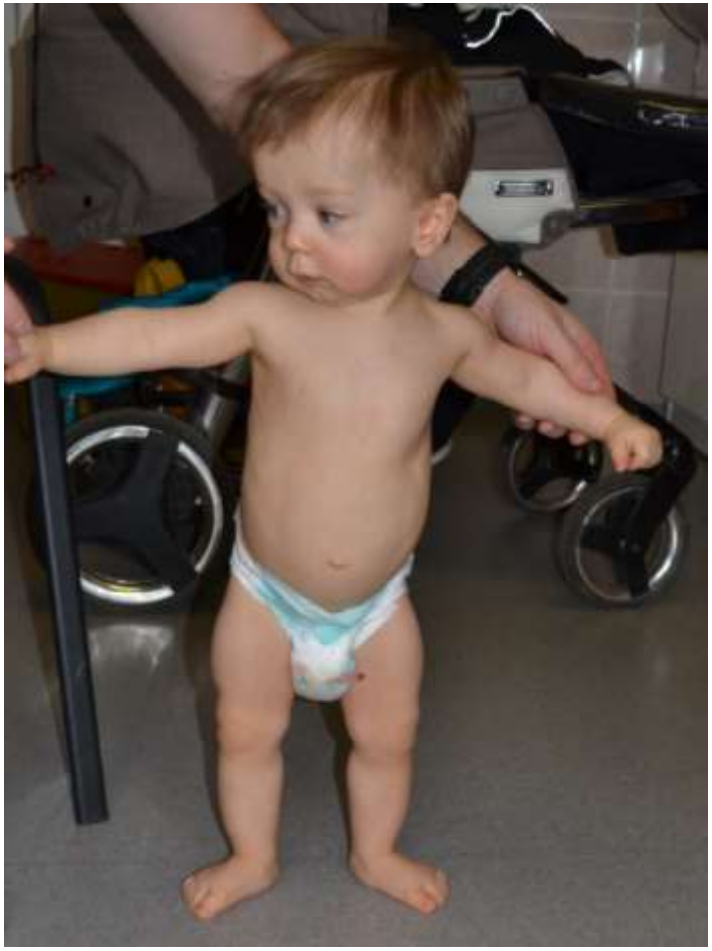
Stickler syndrome excluded

Anthropological examination



- At the age of 1 year he measured 66 cm (-3.3 SD), weighted 7.44 kg (-2.9 SD), weight to height was on the 56th percentile.

Anthropometric examination



- Anthropometric examination proved short stature with short limbs, narrow chest and shoulder, relative macrocephaly, delayed closure of the great fontanelle and mandibular hypoplasia. He has short tips of fingers and onychodystrophy.

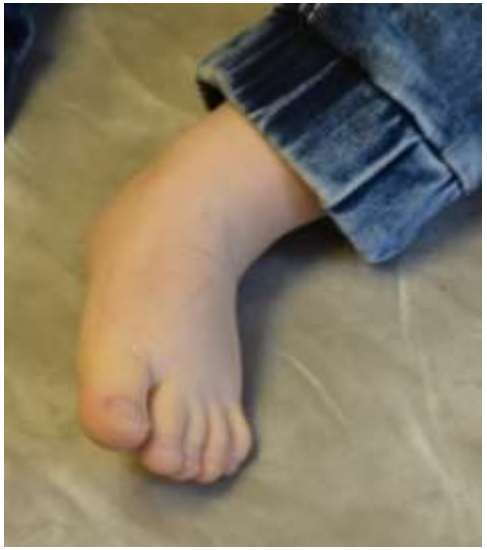
3D facial morphometry

Mandibular hypoplasia
Eye proptosis

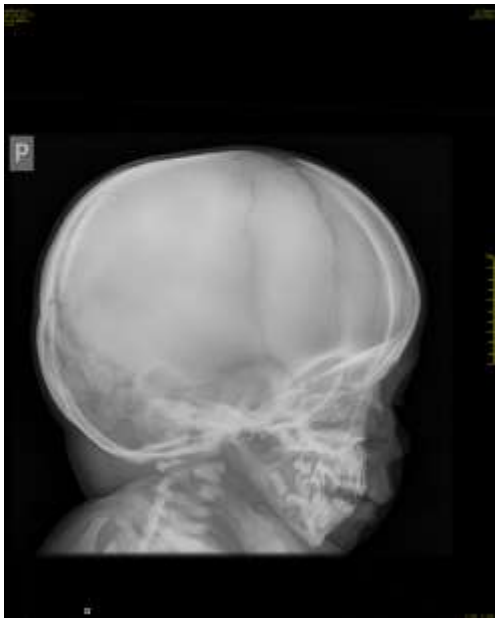
Growth during follow-up

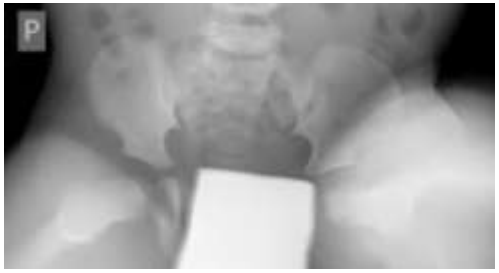
Orthopaedic examination

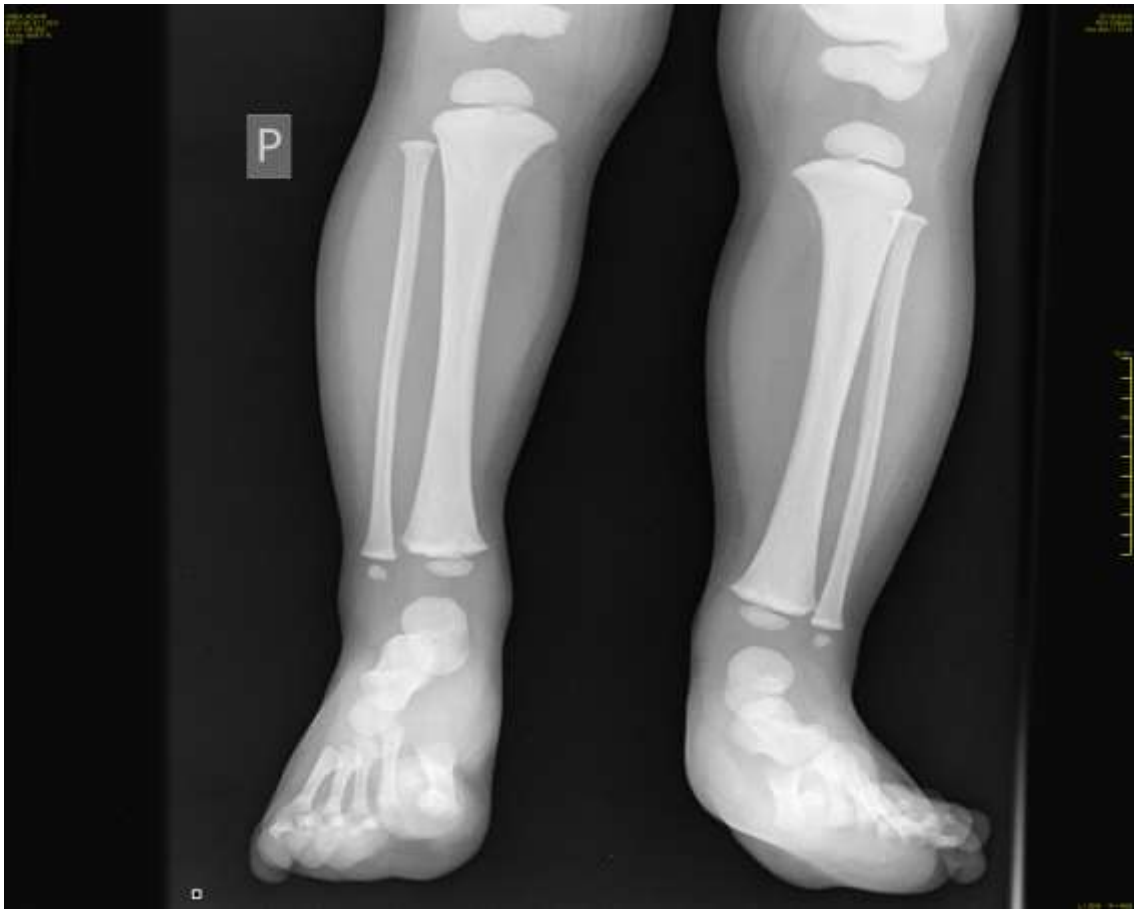
- On the basis of anthropological examination he was at the age of 2 years reffered to the Centre for disorders of locomotor apparatus - suspected **bone dysplasia**



Radiological examination

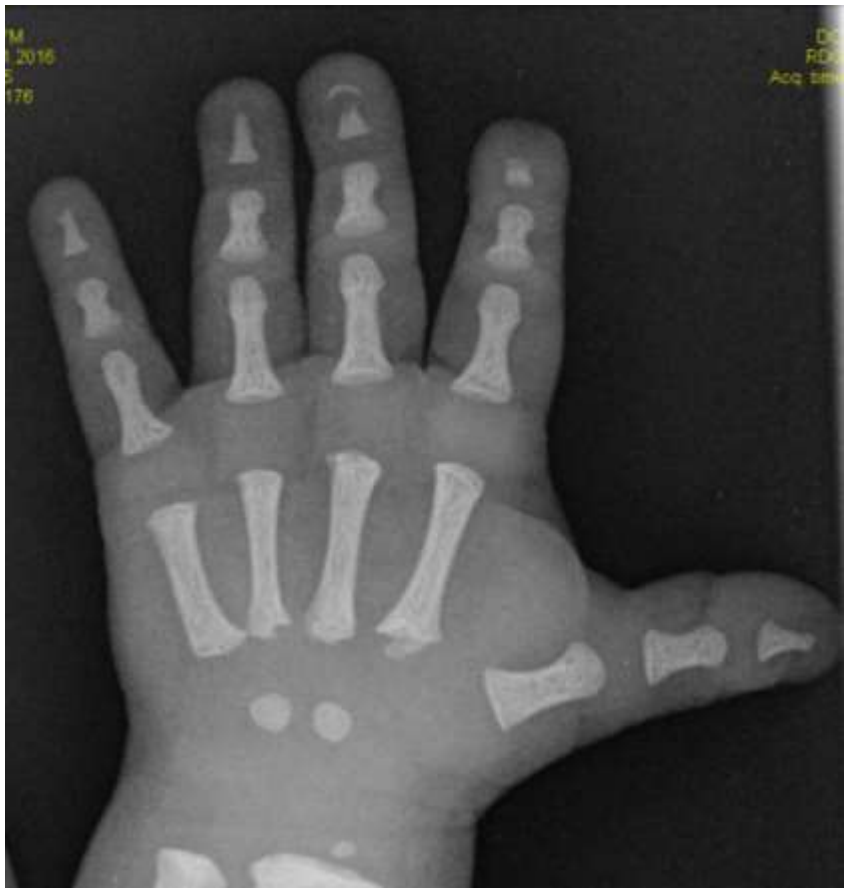






Radiological examination ascertained diffuse osteosclerosis of the skeleton. No fractures.

Radiological examination



diffuse osteosclerosis of the skeleton and acro-osteolysis of the distal phalanges.

On the basis of these findings the suspicion on **pycnodysostosis** was pronounced.

Pycnodysostosis

- **Pycnodysostosis** is a genetic lysosomal disease characterized by
- **short stature**, short **extremities**
- increased density of the bones (**osteosclerosis**/osteopetrosis), and **brittle bones**.
- Other features may include underdevelopment of the **tips of the fingers** with absent or small nails, an abnormal collarbone (clavicle),
- distinctive **facial features** including a large head with a small face and chin, late closure of fontanelles, underdeveloped facial bones, a high forehead, and dental abnormalities

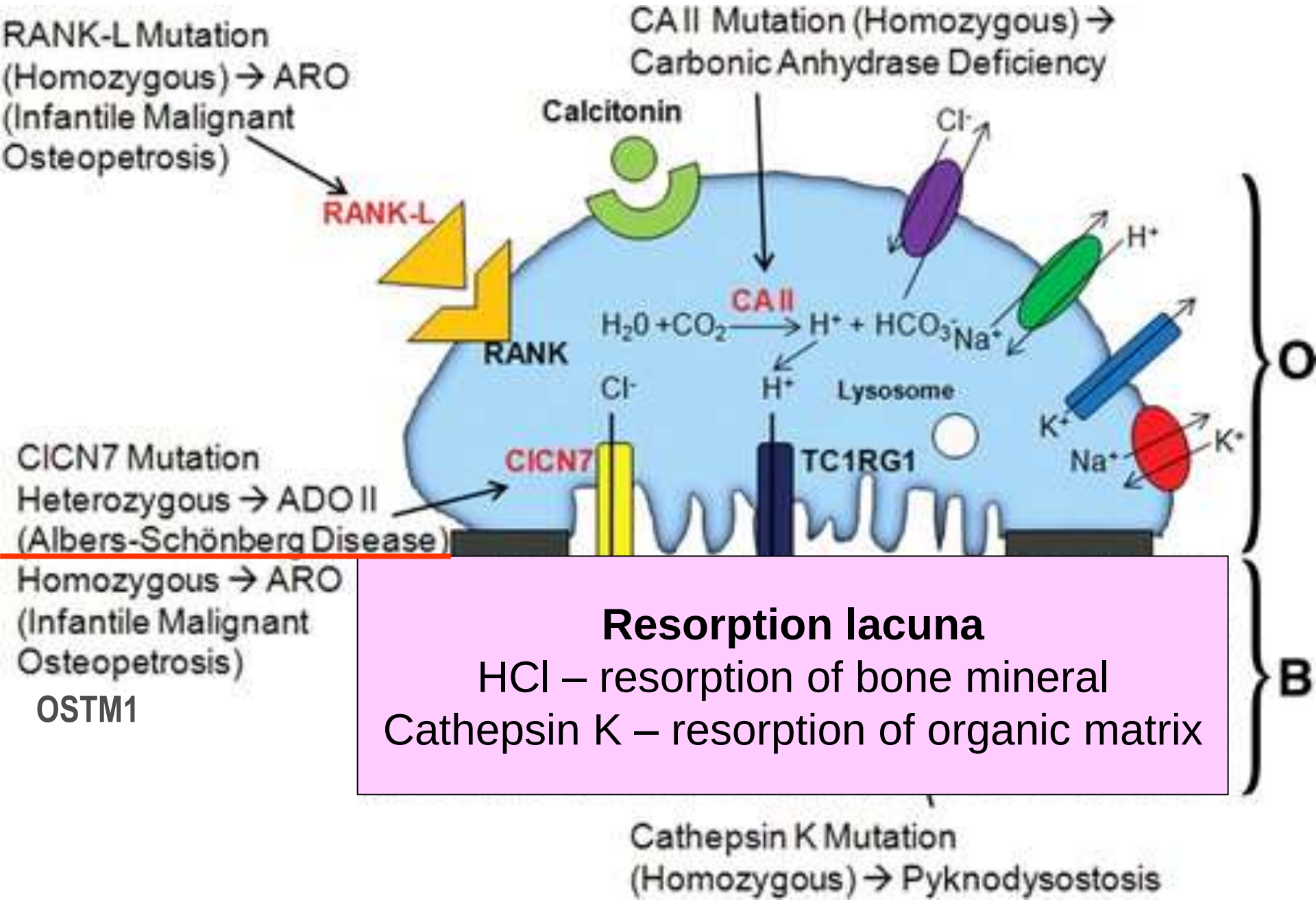
Pycnodysostosis

- **Sleep apnea**
- Lower back pain due to stress fractures of the lower spinal bones (vertebrae)
- Deformities of chest development, respiratory issues.
- Some individuals have growth hormone deficiency and deficiency IGF-1, underdevelopment of the pituitary gland and hepatosplenomegaly

Pycnodysostosis

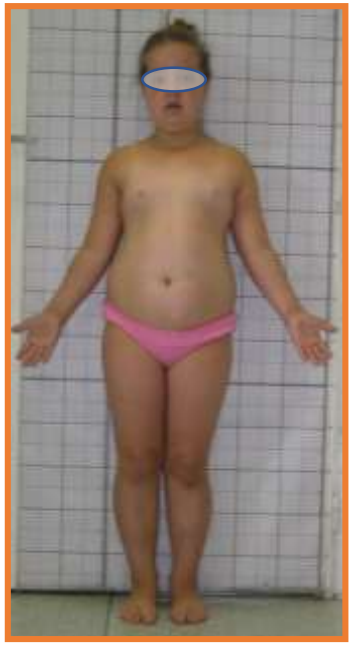
- Pycnodysostosis is extremely rare **autosomal recessive** condition caused by mutations in the gene that codes the enzyme cathepsin K (*CTSK*) on chromosome 1q21.
- **Sclerosing dysplasia** – osteoclasts are not able to break down organic matrix of the bone.

Henri de Toulouse-Lautrec


RANK-L Mutation
(Homozygous) → ARO
(Infantile Malignant
Osteopetrosis)
CA II Mutation (Homozygous) →
Carbonic Anhydrase Deficiency
Calcitonin
RANK-L
RANK
CA II
$H_2O + CO_2 \rightarrow H^+ + HCO_3^-$
Cl^-
H^+
Na^+
K^+
Lysosome
CICN7
TC1RG1
CICN7 Mutation
Heterozygous → ADO II
(Albers-Schönberg Disease)
Homozygous → ARO
(Infantile Malignant
Osteopetrosis)
OSTM1
O
B
Resorption lacuna
HCl – resorption of bone mineral
Cathepsin K – resorption of organic matrix
Cathepsin K Mutation
(Homozygous) → Pyknodysostosis

Pycnodysostosis
Differential diagnostics

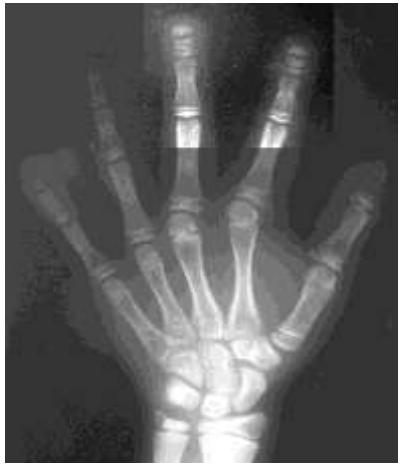
- Osteopetrosis
- Cleidocranial dysplasia
- Osteogenesis imperfecta
- Hajdu-Cheney syndrome (acroosteolysis)



osteopetrosis

Cleidocranial dysplasia

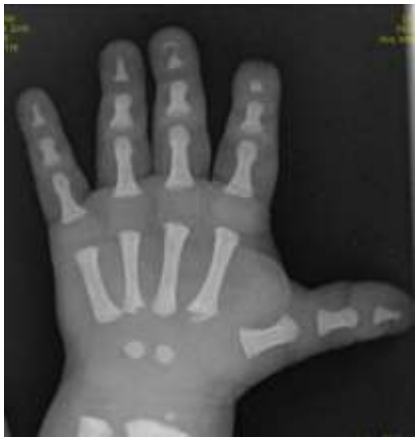
Osteogenesis impf.



Hajdu-Cheney

Molecular genetic testing

- Targeted molecular genetic testing of *CTSK* gene proved the diagnosis of pyknodysostosis.
- pathogenic variant c.(568C>T) and c(830C>T) in trans form - parents are carriers of these variants.



Pycnodysostosis

- Normal mental development
- Coprehensive treatment
- Pediatricians, orthopedists, orthopedic surgeons, endocrinologists, dental specialists, and other healthcare professionals
- Cave anestesia
- Genetic counseling, psychosocial support
- Investigationals therapies: growth hormone, enzyme inhibitors

Conclusion

- Pycnodysostosis is a rare disease characterized by short stature with short extremities, osteosclerosis and brittle bones and distinctive facial features, namely mandibular hypoplasia.
- First manifestation in our patient was atypical: Pierre Robin sequence after birth and sleep apnea.
- Radiological examination led to clinical diagnosis of pyknodysostosis , which was proved by targeted molecular genetic testing.
- Patients with pycnodysostosis should be able to live a full life, with some precautions and the ongoing involvement of a team of healthcare professionals.


Thank you for your attention