Long term effects of bisphosphonate treatment in a case with infantile onset severe form of juvenile Paget's disease

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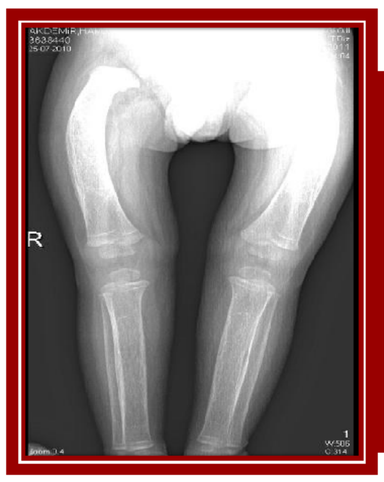
BACKGROUND

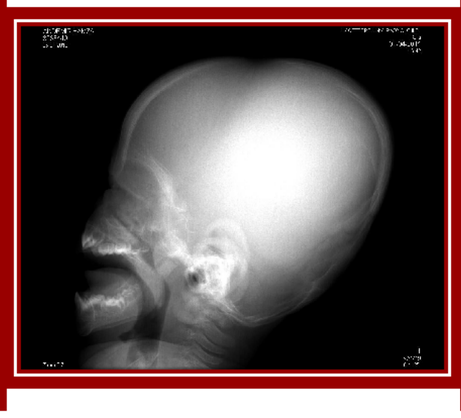
Juvenile Paget's disease is a rare autosomal recessive osteopathy and characterized by rapidly remodeling woven bone, osteopenia, fractures and progressive skeletal deformity. Patients presenting in infancy develop severe bone deformities and may never walk. The accelerated bone turnover caused by increased osteoclastic activity is the underlying feature of this disorder. Bisphosphonate therapy is used to decrease bone turnover and it has generally good responses in milder forms of the disease. However there is no long-term experience of bisphosphonates in severe infantile forms. Here we report a 4.5 year-experience of bisphosphonate therapy in a 5 year old male patient with juvenile Paget's disease.

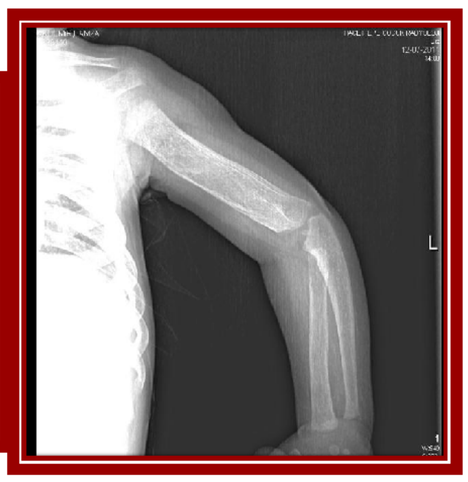
CASE REPORT

A 9 month-old boy was referred to our clinic for bone deformities.

- Severe bone pain
- Delayed developmental milestones
- Sensorineural hearing loss
- Consanguineous parents
- Height: 67 cm (<3p)
- Weight: 7.3 kg (<3p)
- Head circumference: 44 cm (50-75 p)







Laboratory results

- Calcium:9.4 mg/dL (9-11)
- Phosphate: 5.9 mg/dL (3.5-6.6)
- Alkaline phosphatase: 1692 U/L (133-347)
- PTH:37.4 pg/mL (12-95)
- Bone ALP >140 µg/L

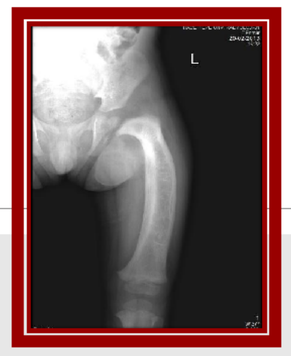
Radiographic findings

- Generalized demineralization
- Expansion of long bones with coarse trabeculation
- Widened skull bones
- Cortical thickening and periosteal reaction

Genetic analysis showed a large homozygous deletion started from intron 1, including exon 2,3,4,5 and ligand binding domain in *TNFRSF11B* gene (novel mutation)

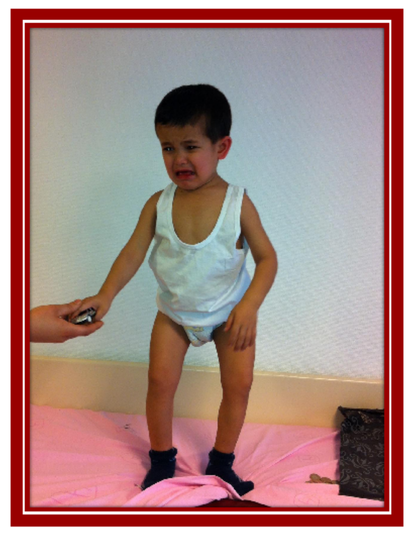
Pamidronate treatment
1 mg/kg / every 3 months

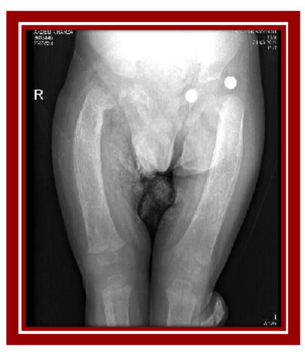
- Bone pain alleviated
- Motor development improved
- Periosteal reaction in long bones decreased
- ALP decreased

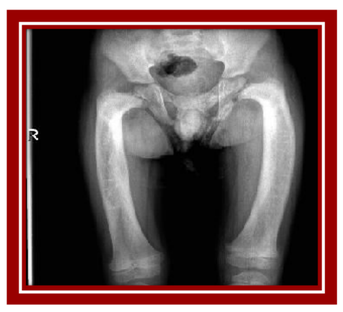


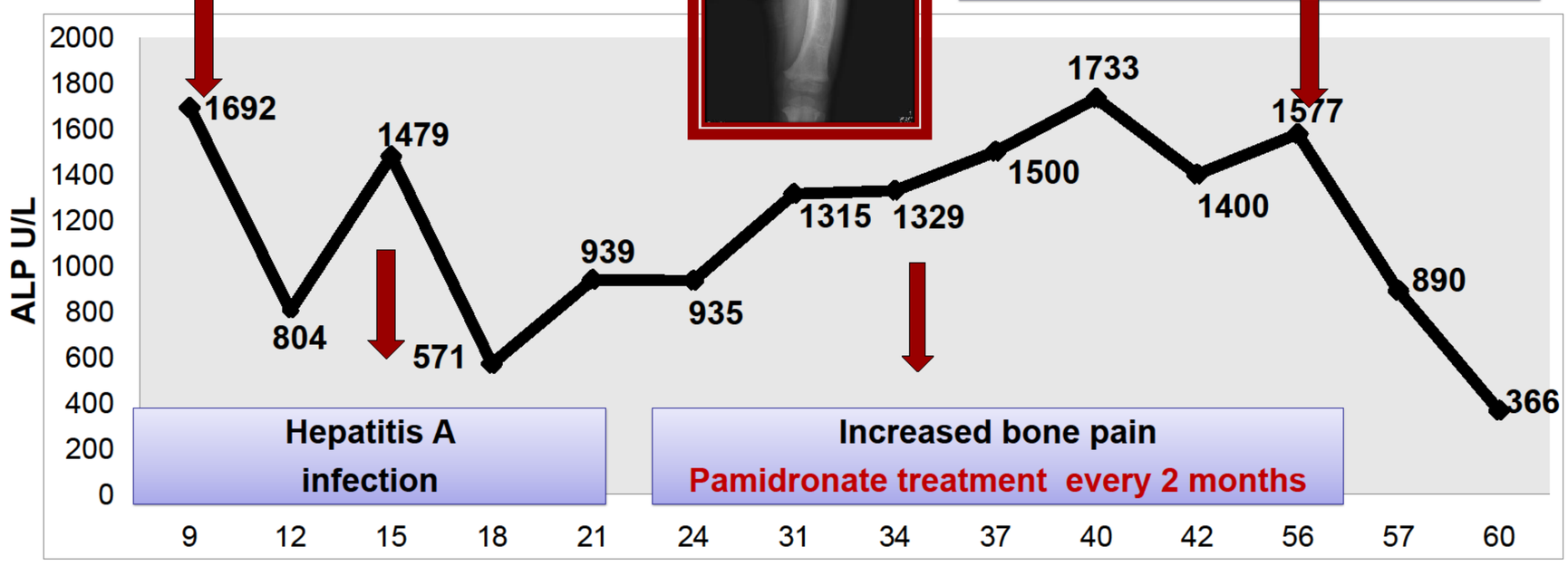
- Bilateral humeral fractures
- Bone pain restricting movements
- Cervical CT: Atlanto-axial subluxation

Zoledronic acid treatment
0.05 mg/kg/day
2 days every 6 months









CONCLUSIONS

Intravenous pamidronate therapy is very effective in reducing bone pain, improving the bone deformities and motor development in infantile onset severe form of juvenile Paget's disease. However this effect is transient. Changing to another bisphosphonate is an alternative treatment in case of resistance to pamidronate therapy.
Zoledronic acid can be considered as a first line treatment in severe form of juvenile Paget's disease.

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