SPONDYLOOCULAR SYNDROME: PRESENTATION OF TWO SIBLINGS DIAGNOSED WITH THE RARE DISEASE AND THE RESULTS OF PAMIDRONATE THERAPY

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Spondyloocular syndrome (OMIM 605822) is an autosomal recessive disorder caused by biallelic sequence variants of *XYLT2* gene (OMIM 608125) encoding xylosyltransferase II enzyme which catalyzes the first step of proteoglycan assembly. Significantly involved in cellular homeostasis, proteoglycans impact fundamental biological processes including growth factor function, morphogen gradient formation, and co-receptor activity. Therefore, defective proteoglycan assembly results in skeletal findings (severe osteoporosis, platyspondyly, multiple bone fractures), hearing loss and ocular symptoms (cataracts, retinal detachment). Herein we present the results of bisphosphonate treatment for osteoporosis in two siblings diagnosed with spondyloocular syndrome. This paper is of clinical importance as sufficient data on treatment options and long term treatment results of spondyloocular syndrome are lacking.

CASE REPORT

Sibling 1
11 year-old, girl, admitted for difficulty in walking, lomber pain and inability to run

History:
- Operated for bilateral congenital cataracts – 1.5 years-old
- Retarded growth and development – 2.5 years-old
- Retinal detachment – 10 years-old
- Parents are third degree cousins

Physical examinaton:
- Weight: 33.2 kg (-0.65 SDS), Height: 125.6 cm (-2.6 SDS)
- Disproportionate short stature (Upper/Lower ratio 0.76)
- Pectus excavatum deformity, increased lomber lordosis and scoliosis
- Horizantal nystagmus and mild mental retardation

Laboratory tests:
- Ca, P, ALP were within the normal range
- 25-OH vitamin D: 16.23 mcg/L

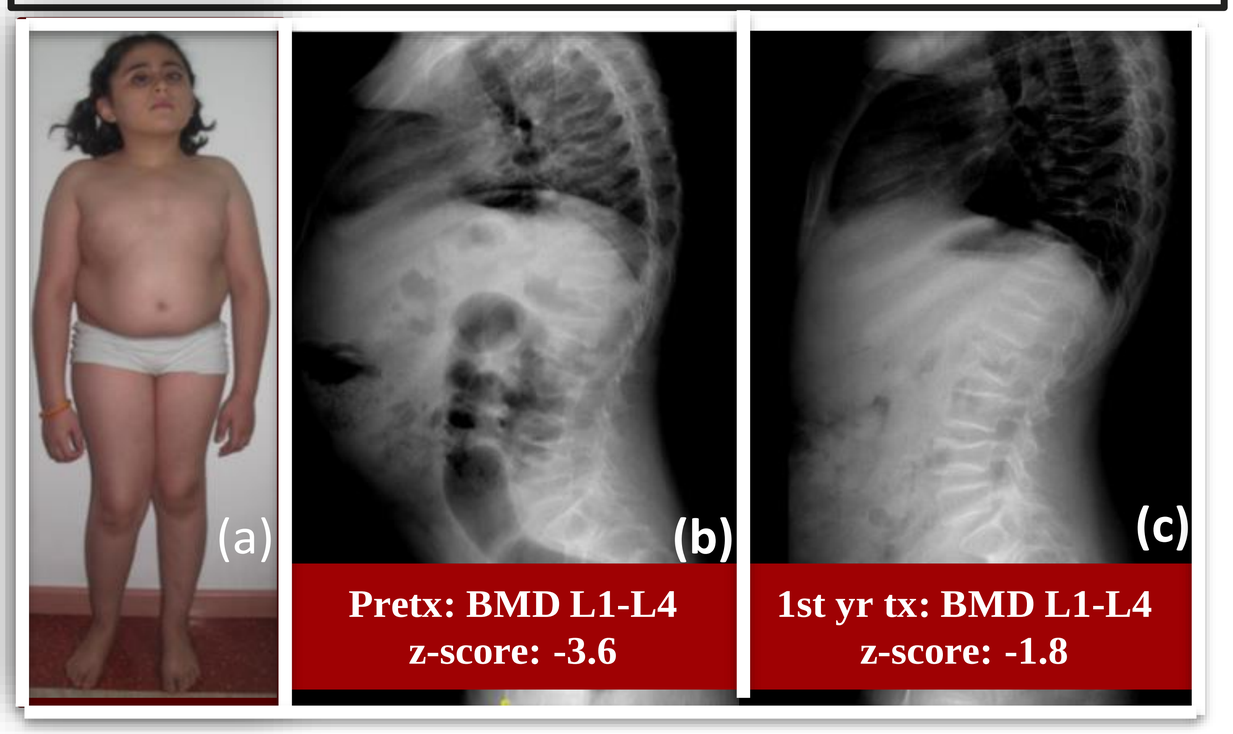

Figure 1: (a) Physical features of the patient at admission, X-rays of the patient at (b) admission and (c) following the first year of bisphosphonate treatment .

Spondyloocular syndrome
XYLT2 sequence analysis →
homozygous mutation on
11. exome c.2548G>A (p.Asp850Asn)

Sibling 2
7 year-old boy was unable to walk.

History:
- Bilateral congenital cataracts
- Severe mental retardation
- Global motor and developmental delay

Physical examinaton:
- Weight: 25 kg (0.49 SDS), Height: 108 cm (-2.63 SDS)
- Proportionate short stature (upper/lower ratio:0.96)
- Kyphosis, increased lumbar lordosis

Laboratory tests:
- Ca, P, ALP were within the normal range
- 25-OH vitamin D: 6.5 mcg/L

The same homozygote mutation was detected in patient's seven year old brother via family screening.

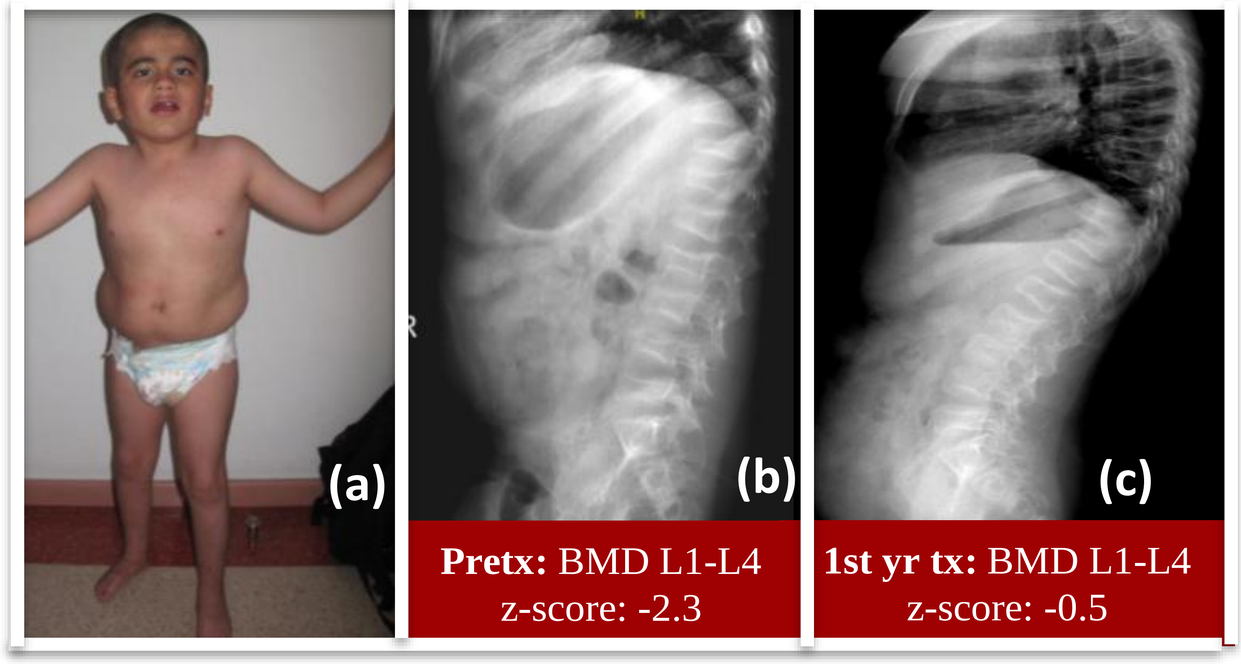

Figure 2: (a) Physical features of the patient's brother at admission, X-rays at (b) admission and (c) following the first year of bisphosphonate treatment.

- 1 mg/kg bisphosphonate (pamidronate) treatment every three months for a year
- Vitamin-D replacement

L1-L4 bone mineral density z-scores improved in both siblings.

CONCLUSION

Treatment options for osteoposis in spondyloocular syndrome are scarce and data on results of bisphosphonate therapy are limited. The increase in BMD z-score suggests that bisphosphonate treatment can be beneficial for osteoporosis in patients with spondyloocular syndrome. More data is required to understand long term effects of bisphosphonate treatment for osteoporosis in this syndrome.

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