WNT1 Osteoporosis in a Child: A Case Report

[1]N. Tran, OMS-3, [2]J. Steelman, MD

[1]Texas College of Osteopathic Medicine, University of North Texas Health Center, Texas, USA
noratran@my.unthsc.edu
[2]Endocrinology Department, Cook Children's Medical Center, Texas, USA,
joel.steelman@cookchildrens.org

The authors declare no conflicts of interest.

INTRODUCTION

Pediatric osteoporosis remains an elusive condition with diagnosis requiring both densitometry and fracture history.

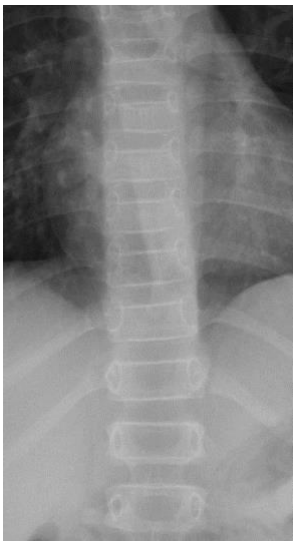
Osteoporosis can be considered either primary related to underlying genetics or more commonly secondary related to multiple factors including medication, impaired mobility, and underlying illness.

We report a case of pediatric osteoporosis secondary to heterozygous pathogenic variant in WNT1 gene

CASE PRESENTATION

A 7-year-old male presented to the emergency room with fever and complaints of abdominal and leg pains. Medical history was insignificant for routine medications and medical problems.

A KUB incidentally showed flattening of the lumbar vertebrae and a mild wedge deformity in T12 and L1.



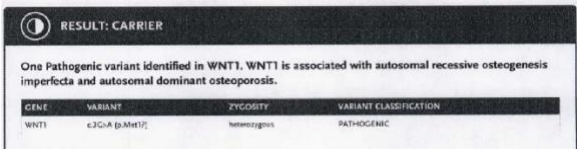
He was initially evaluated for concerns of leukemia with negative findings. He was then sent to pediatric endocrinology for further investigation. No pain or limitations in mobility were reported. He was well appearing on exam with stature (z-score -0.79) in range for family and an otherwise normal examination.

Laboratory investigation showed only mild vitamin D deficiency (vitamin D25OH 23.7 ng/ml)

Bone age and bone density studies were ordered. Bone age was equal to chronologic age. Bone mineral densities were below mean w with a total hip z score of -3.0 and lumbar spine -4.1.

Ergocalciferol 4000 units was started daily for inadequate Vitamin D levels and additional genetic work-up was ordered for assessment of underlying genetic basis for findings.

Genetic testing revealed a heterozygous pathogenic variant in WNT1 gene.


RESULT: CARRIER

One Pathogenic variant identified in WNT1. WNT1 is associated with autosomal recessive osteogenesis imperfecta and autosomal dominant osteoporosis.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
WNT1	c.3G>A (p.Met1?)	heterozygous	PATHOGENIC

DISCUSSION

WNT signaling is important in the bone and effects all aspects including accrual, osteoblast differentiation, and maintenance of bone mass.

The effects of impaired WNT1 expression leads to lowered bone formation with normal bone turnover and no reduction in activity of WNT1 inhibitors such as sclerostin.

Inheriting two pathogenic copies of WNT1 leads to a rare autosomal recessive form of

osteogenesis imperfect (XV) whereas a single pathogenic variant leads to early onset osteoporosis and vertebral deformities as seen in this case.

Response to bisphosphonate treatment in children and adults has been modest making treatment of WNT1 associated osteoporosis challenging.

CONCLUSION

The patient presented is currently asymptomatic without physical complaints due to low bone mass. Close follow-up is required. The case is challenging as there are no reported definite treatments for this particular condition.

Sclerostin antibody has been suggested to be effective in increasing bone mass density and decreasing peripheral fractures in animals with WNT1 mutations. Sclerostin is a known inhibitor of WNT signaling in bones, a signal for favoring bone formation.

However, further study and ideally clinical trials are needed to further explore sclerostin antibody treatment or other therapies in WNT1 associated osteoporosis.

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