EARLY-ONSET OSTEOPOROSIS DUE TO LRP5

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INTRODUCTION

Primary osteoporosis are frequently linked to syndromic conditions such as osteogenesis imperfecta, wich involves extra esqueletic- tissues. With the advancement of medicine, this group has been reduced, specifying the causal pathogenic variants. Among these, the LRP5 (Low-density lipoprotein receptor-related protein 5) gene are the most frequent cause.

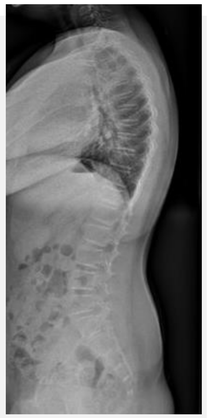
LPR5

LPR5 is a fundamental coreceptor in the wnt/betacatenin signaling pathway, which is the main metabolic pathway of osteoblasts, the mutations with loss function result in decreased bone formation (figure 1). It has been reported as one of the main causes of primary osteoporosis.

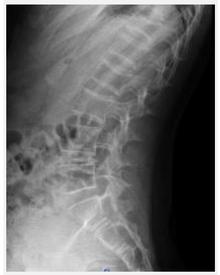
CASE REPORT

Case Nº1: A 12-year-old boy, Previously helthy, he was evaluated for chronic pain located in knees and back pack . Not medical history of bone disease, no familiar history of osteoporosis.
At fisical examen with out blue esclera, not dismorfic features, not enamal tooth alterations or other extraesqueletic findings.
Laboratory in table 1 . A chest X-ray showed diffuse osteopenia, vertebral fracture in T6-T9
Bone mineral densitometry of the lumbar spine: 0.136 gr/cm3, Z score: -5.0
Genetic study shows a variant of uncertain significance in LPR5 gene c.1021G> A; pGlu341Lys. Then is reclassified in varsome, and it could be reclassified as probably pathogenic, if correspond a de novo variant.

Case Nº2: 12-year-old boy, evaluated for a history of 1 year of lumbar pain, x ray of spine showed a fracture in vertebral bodies from D 12 to L3.
No personal or family history of bone mineral disease, not history of bone fractures.
Physical exam: not extraesqueletic findings. Laboratory on table 2.
Lumbar spine volumetric bone density of 0.205 gr/cm3 and Z score -2.7 DS.
Genetic study results in a variant of uncertain significance in LPR5, c.1696C> T; p.Arg566Cys, which is reclassified into varsome as probably pathogenic, However, if parentes do not have the mutation this variant could be reclassificated like patogenic



Case 1

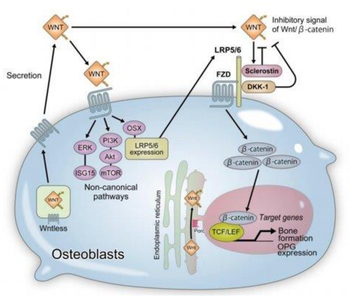


Case 2

Case 1	
Calcium: 2.34 mmol/L	Negative hypercalciuria
Phosphemia: 1.42 mmol/L	Negative anti-transglutaminase ab
albumin 4.5 g/dl	Negative Nugent Test
FA:172 U/L	
PTH: 5.3 pmol/L	
25OH vitamin D 16.7 mg/dl	
TSH 1.98 IU/L, FT4 1.4 ng/dl	

Case 2	
Calcium: 2.15 mmol/L	Negative hypercalciuria
Phosphemia 1.23 mmol/L	Negative anti-transglutaminase ab
Albumin: 4 gr/L	Negative Nugent Test
FA: 246 U/L	
PTH: 2.6 pmol/L	
25OH vitamin D 51 mg/dl	
TSH 1.87 IU/L, T4 9.3 ng/dl	

WNT SIGNALING



CONCLUSIONS

Discussion/Conclusion: It has been reported as one of the main causes of primary osteoporosis. There are 2 phenotypes due to loss of protein function, early-onset osteoporosis autosomal dominant, and the osteoporosis-pseudoglioma syndrome autosomal recessive.

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