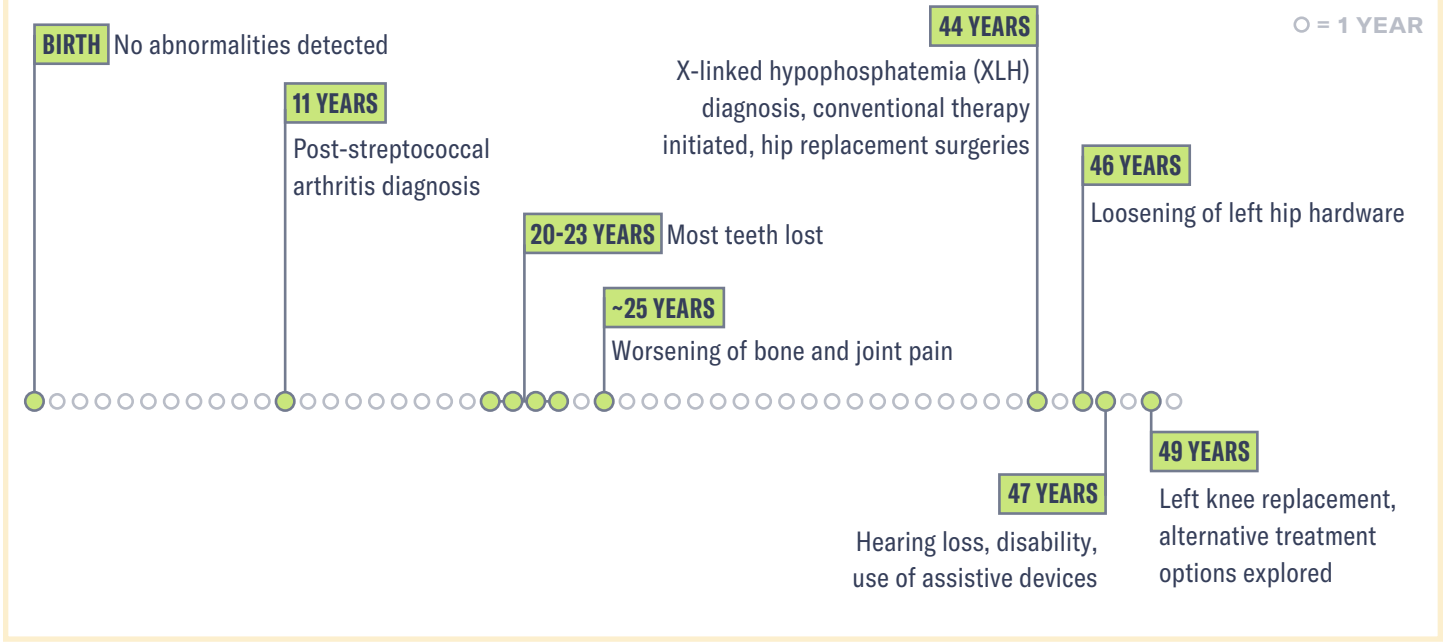
49-year-old male with hereditary XLH*



Case summary

Findings/outcomes

- The patient was not accurately diagnosed with XLH until age 44
  - There is a spectrum of disease for XLH,[1] and the patient's symptoms were not previously attributed to XLH
- Symptoms of XLH progressed throughout adulthood and had long-term impact. The patient:
  - Required surgeries and developed worsening pain
  - Required the use of assistive walking devices
  - Developed hearing loss
  - Needed dentures
- Alternative therapeutic options were explored

It is important to diagnose XLH accurately and early, as the progressive nature of XLH leaves patients susceptible to short stature, fractures, limited function, and pain.[2-4]

*The information for this case study was provided courtesy of Dr. Kathryn McCrystal Dahir, Professor of Medicine, Department of Endocrinology, Vanderbilt University Medical Center, Nashville. This case study represents a real patient and is intended to be illustrative, not a recommendation for treatment or management. Results may vary. This case study does not claim to represent typical results.

Medical history

During childhood

- 6 years of age: humerus fracture from jumping off a moving truck
- Poor dentition of both primary and secondary teeth, with multiple cavities and abscesses
- 11 years of age: reported “bone disease” due to chronic bone and joint pain
  - Pediatrician diagnosed post-streptococcal arthritis
- Mild leg bowing; reported short stature compared to peers

Early to mid-20s

- Lost most teeth by early 20s
- Acute worsening of bone and joint pain
  - Suspected inflammatory arthritis; treated with anti-inflammatory medication

44 years of age

- Presented with acute exacerbation of chronic weakness and right hip pain
  - Required the use of prescription pain medication, including hydrocodone acetaminophen
- Reported no previous diagnosis of rickets or any medical management of low phosphorus

Family history

- Short stature and bowing of the lower legs in mother (height, 4'11"), 3 brothers, and 2 nieces; all had multiple fractures

Physical exam

- Height, 5'3"; weight, 230 lbs
- Ambulating with assistance of a walker; knees in varus alignment
- Pain with internal rotation of hips (left worse than right); 4/5 motor strength in both proximal and distal muscle groups
- Poor dentition and missing most secondary teeth

X-rays

- Pelvis and hips: diffuse increased density of the bones, particularly in the iliac wings and lumbosacral spine; enthesopathic calcifications extending from the superior acetabular walls bilaterally (see X-ray 1 on the right); right subtrochanteric pseudofracture identified, which was incomplete along the medial cortical region (see X-ray 2 on the right)
- Femurs: pseudofractures in the subtrochanteric right femur and mid-left femoral diaphysis; healing stress fracture present in the medial cortex of the left femoral neck; enthesophytes and bilateral hip osteoporosis also noted (see X-ray 3 on the right)
- See Laboratory test results on back

The patient exhibited XLH signs and symptoms throughout childhood and young adulthood, and was not diagnosed until his mid-40s.

Diagnosis and initial treatment

44 years of age

- Hereditary XLH
- Treatment: calcitriol and phosphate supplementation

Disease progression (post-treatment)

44 years of age

After XLH diagnosis, underwent left hip replacement surgery

- Developed worsening right hip pain; underwent right hip replacement surgery 3 months later

46 years of age

Developed worsening left shoulder and knee pain requiring multiple orthopedic visits for steroid injections

- Developed loosening of hardware in left hip due to osteomalacia and continued to require frequent steroid therapy
- Reported being compliant to conventional therapy

47 years of age

Underwent knee replacement therapy evaluation

- Unable to work and required disability benefits
- Dependent on assistive walking devices
- Developed ringing in ears and hearing loss
- Referred to pain management; nerve pain medication added to regimen with little pain improvement
- See Laboratory test results on back

49 years of age

Underwent left knee replacement; advised a right total knee replacement was needed as well

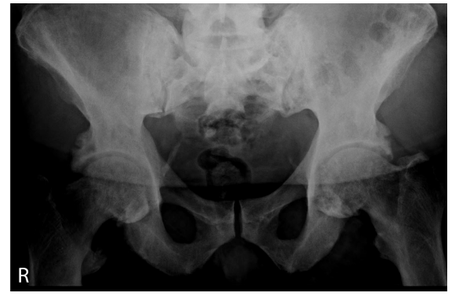
- Insurance started denying coverage for calcitriol and phosphate supplementation on the basis that these medications are supplements/vitamins
- Medication was continued with coverage through a grant

Patient reported compliance with conventional therapy; developed worsening back, neck, and hand pain

Could not afford dentures and had difficulty maintaining adequate nutrition

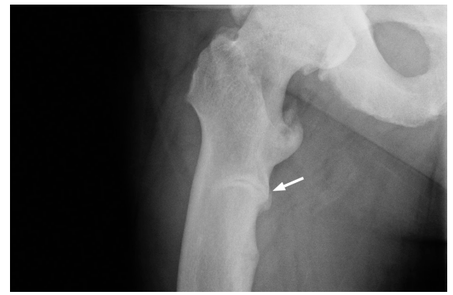
3 months later: Alternate therapeutic options were explored

X-ray 1: **Disease progression in pelvis and hips**



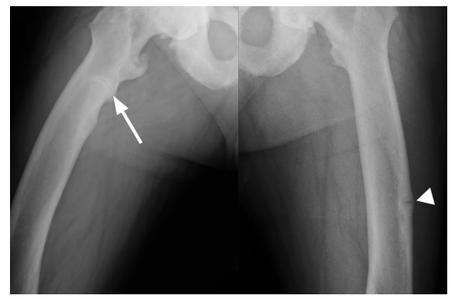
44 years of age: diffuse increased density of iliac wings and lumbosacral spine; bilateral enthesopathic calcifications extending from the superior acetabular walls.

X-ray 2: **Subtrochanteric pseudofracture**



44 years of age: right subtrochanteric pseudofracture (arrow) incomplete along the medial cortical region.

X-ray 3: **Pseudofractures in femurs**



44 years of age: pseudofractures in the subtrochanteric right femur (arrow) and mid-left femoral diaphysis (arrow head); healing stress fracture present in left femoral neck medial cortex; enthesophytes and bilateral hip osteoporosis.

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The patient initiated oral phosphate and active vitamin D and was compliant. Symptoms of XLH continued to progress, leading to a search for alternative treatment options.

Laboratory test results

Test (reference range† unit)	**44 years** (results)	**47 years** (results)
Serum phosphorus (2.4-5.7 mg/dL)	**2.1**	**2.1**
1,25(OH)$_2$D (20-80 ng/mL)	31	25
25(OH)D (25-80 ng/mL)	33	37
BSAP (6.5-20.1 mcg/L)	**39.2**	**32**
PTH (16-77 pg/mL)	**95**	48
Creatinine (0.72-1.25 mg/dL)	0.83	1.12
FGF23 (<180 RU/mL)	73	**383**

†Indicates normal range, age and sex matched. Note that normal range values may vary depending on reference dataset. The ranges in this table were provided by the treating physician. Colored values are outside of the normal range provided by the physician and can raise suspicion of XLH.

1,25(OH)$_2$D=1,25-dihydroxyvitamin D; 25(OH)D=25-hydroxyvitamin D (calcifediol); BSAP=bone-specific alkaline phosphatase, also known as BAP; FGF23=fibroblast growth factor 23; PTH=parathyroid hormone.

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1. Ruppe MD. X-linked hypophosphatemia. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2019. Published February 9, 2012. Updated April 13, 2017. https://www.ncbi.nlm.nih.gov/books/NBK83985/ **2.** Dahir K, Roberts MS, Krolczyk S, Simmons JH. X-linked hypophosphatemia: a new era in management. *J Endocr Soc.* 2020;4(12):bvaa151. doi:10.1210/jendso/bvaa15 **3.** Carpenter TO, Imel EA, Holm IA, Jan de Beur SM, Insogna KL. A clinician's guide to X-linked hypophosphatemia. *J Bone Miner Res.* 2011;26(7):1381-1388. doi:10.1002/jbmr.340 **4.** Hamilton AA, Faitos S, Jones G, Kinsley A, Gupta RN, Lewiecki EM. Whole body, whole life, whole family: patients' perspectives on X-linked hypophosphatemia. *J Endocr Soc.* 2022;6(8):bvac086. doi:10.1210/jendso/bvac086

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COMM-US-RDS-0101 April 2023