

# Investigating XLH: Natalie's case<sup>†</sup>

## Case overview

Natalie is a 34-year-old female patient who presents with the following:

- Short stature (143 cm height)<sup>1,2</sup>
- Mild, bilateral bowing of femurs<sup>1,2</sup>
- Early-onset tibiotalar osteoarthritis<sup>1-3</sup>
- Joint stiffness that makes completing simple daily tasks, like cooking and cleaning, difficult<sup>1,2,4</sup>
- History of root canal surgery<sup>1</sup>
- Joint and bone pain<sup>1,2,4</sup>
  - Notable knee and ankle pain leading to difficulty walking up and down stairs
  - Severe and prolonged bone pain she describes as “her bones ripping”
  - Often finds that she has to take breaks during activities, due to the pain

## Patient history

- Family history (as described by Natalie):<sup>1,2,5</sup>
  - Father passed away in a car accident at the age of 45, but was short in stature (160 cm), suffered multiple fractures throughout his life, required root canal surgeries, and had osteoarthritis
  - Mother and brother are average height and have no history of fractures
  - Younger sister (26 years old) also struggles with joint stiffness and pain, and has a history of fractures and osteophytes
- Recalls experiencing joint stiffness, tiredness, headaches, and pain since early childhood, which have worsened in adulthood<sup>2,6</sup>
- Diagnosed with early-onset bilateral tibiotalar osteoarthritis at age 31<sup>1-3</sup>
- Root canal surgery at age 30<sup>1</sup>

## Laboratory test results

Test (reference range) <sup>5,7‡</sup>	Results <sup>2,5,8</sup>
Serum phosphorus (2.5–4.5 mg/dL)	<b>1.2 mg/dL</b>
TmP/GFR (2.4–4.45 mg/dL)	<b>1.5 mg/dL</b>
1,25(OH) <sub>2</sub> D (18–78 pg/mL)	31 pg/mL
25(OH)D (20–50 ng/mL)	36 ng/mL
ALP (35–104 U/L)	<b>157 U/L</b>
PTH (15–65 pg/mL)	<b>81 pg/mL</b>

1,25(OH)<sub>2</sub>D=1,25-dihydroxyvitamin D; 25(OH)D=25-hydroxyvitamin D; ALP=alkaline phosphatase; PTH=parathyroid hormone; TmP/GFR=tubular maximum reabsorption of phosphate corrected for glomerular filtration rate; XLH=X-linked hypophosphatemia.

<sup>†</sup> Fictitious patient. May not be representative of all patients.

<sup>‡</sup> Reference ranges may vary based on assay and instrument used. Reference ranges provided by the laboratory conducting the test should be used to ensure accuracy.

# Radiographic evaluation

X-ray 1: Knees



Bilateral bowing of femurs and tibiae; diffusely demineralized bones with bilateral narrowing of the knee joint space compartment<sup>1,9</sup>

X-ray 2: Feet



Bilateral tibiotalar osteoarthritis; prominent bilateral calcaneal enthesophytes<sup>1,3,9</sup>

## Recommendation from the XLH Guidelines

“In adults and adolescents with closed growth plates, diagnosis of XLH should be considered in the presence of or if there is a history of lower-limb deformities, clinical, biochemical and/or radiological signs of osteomalacia (including pseudofractures, early osteoarthritis, spinal degeneration and stenosis, dental abscesses and enthesopathies) in the context of serum levels of phosphate below the age-related reference range associated with isolated renal phosphate wasting, especially in the case of a positive family history. We recommend that any at-risk family member of a patient with XLH should be investigated for XLH.” —Haffner *et al.*, 2025<sup>9</sup>



Would you consider genetic testing to confirm a diagnosis of XLH for Natalie?  
Would you consider recommending a medical examination for her sister?



Visit **XLHLinkHCP.ca** for more information  
and resources about XLH!

XLH=X-linked hypophosphatemia.

**References:** 1. Skrinar A, *et al. J Endocr Soc.* 2019;3(7):1321-1334. 2. Dahir K, *et al. J Endocr Soc.* 2020;4(12):bvaa151. 3. Akta C, *et al. Front Endocrinol (Lausanne).* 2023;14:1111104. 4. Theodore-Oklota C, *et al. Value Health.* 2018;21(8):973-983. 5. Ruppe MD. X-linked hypophosphatemia. In: Adam MP, Everman DB, Mirzaa GM, *et al.*, eds. GeneReviews®. Seattle (WA): University of Washington, Seattle; February 9, 2012. Updated April 13, 2017. <https://www.ncbi.nlm.nih.gov/books/NBK83985/>. 6. Lo SH, *et al. Qual Life Res.* 2020;29(7):1883-1893. 7. Dahir K, *et al. J Endocr Soc.* 2021;5(9):bvab099. doi:10.1210/jendso/bvab099. 8. Haffner D, *et al. Nat Rev Nephrol.* 2019;15(7):435-455. 9. Haffner D, *et al. Nat Rev Nephrol.* 2025; Epub ahead of print.