# HYPOPHOSPHATEMIC RICKETS: COULD IT BE ENPP1 DEFICIENCY?

Differential diagnosis of ENPP1 Deficiency can be challenging as patients share similar skeletal complications and biochemical findings to X-linked hypophosphatemia (XLH).[1-4]

## Skeletal Symptoms Common in Hypophosphatemic Rickets

**Patients with ENPP1 Deficiency and XLH can present with similar skeletal manifestations[1-4]**

- Fatigue
- Gait abnormalities
- Short stature
- Hearing loss
- Rickets/osteomalacia
- Enthesopathies
- Bone/joint pain and/or joint stiffness

## Biochemical Findings Are Identical in ENPP1 Deficiency and XLH[5]

| | ENPP1 Deficiency | XLH |
|---|---|---|
| FGF23 | Normal or ↑[a] | ↑ |
| Serum phosphorus | ↓ | ↓ |
| $1,25(OH)_2D$ | Normal | Normal |
| 25(OH)D | Normal | Normal |
| TmP/GFR | ↓ | ↓ |
| ALP | ↑ | ↑ |
| Serum calcium | Normal | Normal |
| Urinary phosphate | ↑ | ↑ |
| PTH | Normal/moderately ↑ | Normal/moderately ↑ |

[a]Although only some of the affected individuals show FGF23 levels above the normal range, the levels are inappropriately high in the context of low phosphate serum levels.

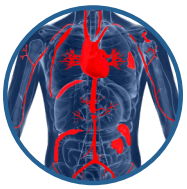


inozyme pharma

# HOW CAN ENPP1 DEFICIENCY BE DIFFERENTIATED?

## Differentiating Findings in ENPP1 Deficiency

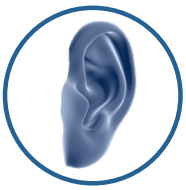
### Clinical Findings[1,2]



**Mineralization of arteries, organs, and joints**

**Fused cervical vertebrae**

**Unexplained cardiac complications**
***(Prominent in infancy and childhood)***
Cardiomyopathy, hypertension, aortic narrowing, right ventricular hypertrophy, pulmonary hypertension, calcific valve disease, diminished peripheral pulses



**Hearing loss in children**

**Neurological complications**
Seizures, ischemic stroke

**Delayed shedding of primary teeth**

### Family History

A family history of early fetal death or ECHO brightness prenatally or postnatally warrants genetic testing for ENPP1 Deficiency[1,2]

**For free genetic testing to confirm ENPP1 Deficiency, please visit https://www.inozyme.com/patients-hcps/genetic-testing-program/**

**Abbreviations:** ALP, alkaline phosphatase; ECHO, echocardiogram; ENPP1, ectonucleotide pyrophosphatase/phosphodiesterase 1; FGF23, fibroblast growth factor 23; PTH, parathyroid hormone; TIO, tumor-induced osteomalacia; TmP/GFR, tubular maximum reabsorption of phosphate per glomerular filtration rate.

**References: 1.** Rutsch F, et al. *Circ Cardiovasc Genet.* 2008;1(2):133-140. **2.** Ferreira C, et al. Ectopic calcification and hypophosphatemic rickets: natural history of ENPP1 and ABCC6 deficiencies. Forthcoming 2021. **3.** Ferreira CR, et al. *Genet Med.* 2021;23(2):396-407. **4.** Chesher D, et al. *J Inherit Metab Dis.* 2018;41(5):865-876. **5.** Haffner D, et al. *Nat Rev Nephrol.* 2019;15(7):435-455.



inozyme pharma