PS34 Obiteljski hipofosfatemijski rahitis: genetska osnova, prikaz slučaja te novi pristupi u liječenju

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Ključne riječi: alkalna fosfataza; faktor rasta fibroblasta 23; fosfati, kalcitriol; obiteljski hipofosfatemijski rahitis

UVOD: Obiteljski hipofosfatemijski rahitis (X-vezani hipofosfatemijski rahitis) je metabolička bolest kostiju karakterizirana povišenom koncentracijom faktora rasta fibroblasta 23 zbog inaktivirajuće mutacije gena PHEX, urinarnim gubitkom fosfata i kliničkom slikom rahitisa.
PRIKAZ SLUČAJA: 15-mjesečna djevojčica, heterozigotna za patogenu mutaciju gena PHEX. Trudnoća je bila uredno kontrolirana, nije bilo komplikacija te je dijete rođeno vaginalno u 39. tjednu trudnoće, Apgar ocjene 10/10. Postnatalni pregled bio je bez osobitosti. Pacijentica je bila prepoznata kao obligatna nositeljica mutacije gena PHEX još tijekom trudnoće budući da otac i njegova majka (baka pacijentice) oboje boluju od X-vezanog hiposfosfatemijskog rahitisa. Otac je testiran tijekom trudnoće te je potvrđeno da nosi hemizigotnu mutaciju gena PHEX, c.1699C>T (pArg567*). Konvencionalno liječenje fosfatnim praškima i aktivnim oblikom vitamina D (kalcitriolom) započelo je u dobi od 3 mjeseca. Aktivnost alkalne fosfataze koja je bila povišena prije započinjanja liječenja se normalizirala uz kontinuirano niže koncentracije serumskih fosfata. Doza lijekova je titrirana prema aktivnosti alkalne fosfataze i PTH. U biokemijskim nalazima urina uočena je povišena ekskrecija fosfatne frakcije uz urednu kalciuriju. Radiološki nalazi u dobi od 15 mjeseci bili su karakteristični za rahitis unatoč ranoj dijagnozi i rano započetom liječenju. Naša pacijentica kandidat je za terapiju burosumabom – FGF23 neutralizirajućim protutijelom.
ZAKLJUČAK: Slučaj prikazuje tipičnu sliku rahitisa otpornog na vitamin D s kliničkom indikacijom za primjenu nove terapije.

Familial Hypophosphatemic Rickets: Genetic Basis, case study and novel therapy

Keywords: Alkaline Phosphatase; Calcitriol; Familial Hypophosphatemic Rickets; Fibroblast Growth Factor-23; Phosphates

INTRODUCTION: Familial hypophosphatemic rickets (X-linked hypophosphatemic rickets) is a metabolic bone disease characterized by an increase in systemic circulating fibroblast growth factor-23 due to an inactivating mutation in the PHEX gene and consequential phosphate wasting leading to rickets.
CASE REPORT: A 15-month-old female child, heterozygous for the pathogenic mutation in the PHEX gene. The pregnancy was well controlled, there were no complications and the child was born vaginally at 39 weeks of gestation with an Apgar score of 10/10. The postnatal screening was unremarkable. The patient was recognized as an obligate PHEX mutation carrier during pregnancy as both the father and his mother (grandmother of our patient) had X-linked hypophosphatemic rickets. The father was tested during pregnancy where he was found to be hemizygous for the pathogenic mutation, c.1699C>T (pArg567*), in the PHEX gene. At the age of 3 months, she started conventional therapy with phosphate and activated vitamin D3 (calcitriol) supplementation. Alkaline phosphatase (AF) activity that was increased before treatment normalized, but with constantly decreased levels of blood phosphate, what is expected. Therapy was titrated due to AF and PTH concentration. Urine samples showed increased fractional excretion of phosphate and normal calciuria. Radiological findings at the age of 15 months were characteristic for diagnosis despite early and adequate previous treatment. This patient is a candidate for burosumab therapy – the FGF23 neutralizing antibody.
CONCLUSION: This case demonstrates typical signs of vitamin D-resistant rickets with a clinical indication for novel treatment.