Growth characteristics of a girl with multicentric carpo-tarsal osteolysis caused by novel mutation in the *MAFB* gene

Lenka Dusatkova[1], Kristyna Potuznikova[1], Daniela Zemkova[1], Ivo Marik[2], Klara Rozenkova[1], Jan Lebl[1], Stepanka Pruhova[1], Zdenek Sumnik[1]

[1]Department of Paediatrics, 2nd Faculty of Medicine, Charles University in Prague and University Hospital Motol, Prague, Czech Republic, [2]Ambulant Centre for Defects of Locomotor Apparatus, Prague, Czech Republic

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Introduction

Multicentric carpo-tarsal osteolysis (MCTO) is a rare skeletal disorder characterised by extensive bone resorption predominantly of the carpal and tarsal bones and frequently accompanied by progressive renal impairment. Recently, causative mutations in the highly conserved region of *MAFB* gene (v-maf musculoaponeurotic fibrosarcoma oncogene ortholog B) have been identified by exome sequencing. The MafB, a basic leucine zipper transcription factor is involved in the regulation of osteoclastogenesis and renal development via RANK (receptor activator of nuclear factor κB) signaling pathway. Clinical presentation in *MAFB* mutation carriers is rather heterogeneous.

Objectives

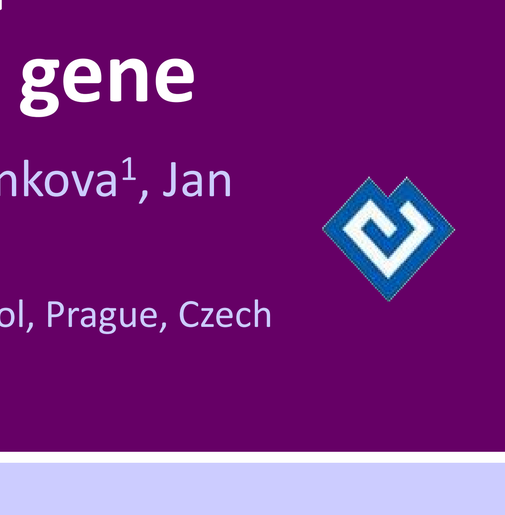
To describe genetic background and growth characteristics in a child with clinical suspicion of MCTO.

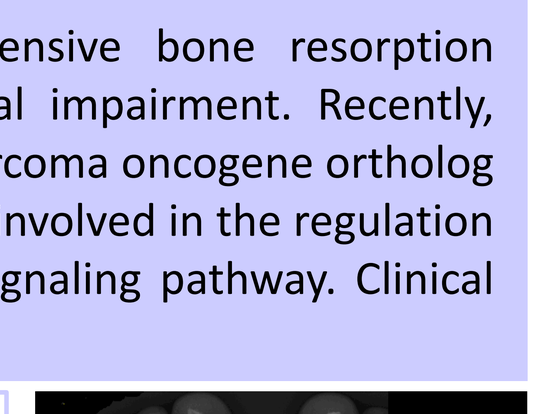
Methods

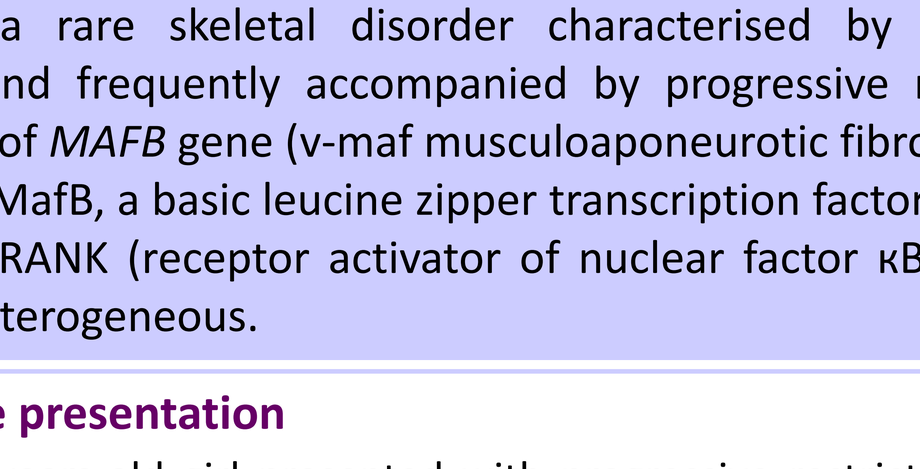
A single exon of the *MAFB* gene (NM_005461.4) was analysed by direct sequencing.

Case presentation

A 6-years-old girl presented with progressive restricted mobility, pain and edema of the wrists. Radiographs revealed osteolysis of proximal phalangs of thumbs, cuneiform and scafoid bones on both ankles. The carpal bones had atypical configuration. Markers of inflammation and juvenile idiopathic arthritis associated antibodies were negative. She has mild proteinuria (297 mg/l) and normal blood pressure.





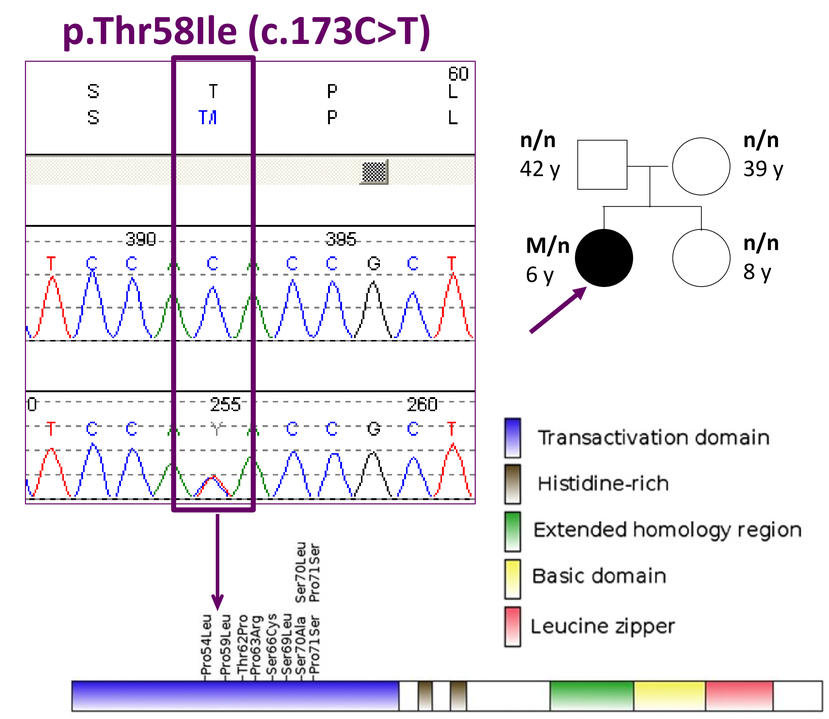


The pQCT analysis of the forearm showed sarcopenia (Muscle Area Z-score -3.8), but normal bone strength index (Polar SSI Z-score -1.8) and trabecular bone mineral density (Z-score -0.8).

Results

Genetic testing

The diagnosis of MCTO has been proven by detection of a heterozygous p.Thr58Ile (c.173C>T) substitution in the *MAFB* gene. The observed mutation was novel, but located within the mutation hotspot region and predicted to be damaging.

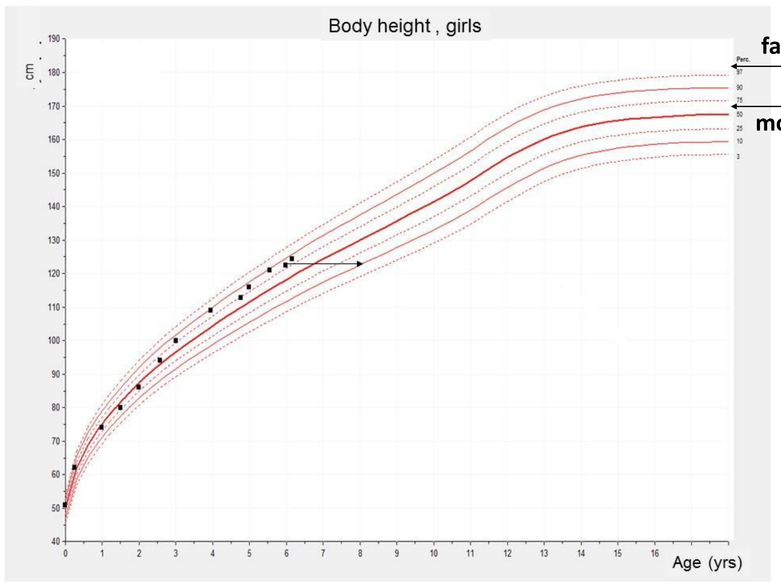


The MafB protein domains and the observed *MAFB* mutations based on Zankl (2012) *Am J Hum Genet* 90, 494. All mutations are located within a amino-terminal transcriptional activation domain (between amino acids 54–71).

Growth characteristics

In spite of chronic disease and prepubertal status, the patient has accelerated bone age (TW3-RUS 8 years at CA 6 years) and dentition. Growth has been accelerated since the age of 2 years, the last 2 year´s growth velocity has been 8 cm/year (2.5 SD). She has dysmorphic signs (strabisms, retrognatism, short mandibula and gothic palate).

Height	124.4 cm (1 SD)
BMI	15.4 cm (0.1 SD)
Sitting height	63.3 cm (0.7 SD)
Arm span (% height)	124.5 cm (100%)
Head circumference	54 cm (2 SD)
Foot length	20 cm (1.4 SD)
Wrist circumference	13.6 cm (1.6 SD)



Conclusion

We report a girl with sporadic MCTO confirmed by detection of novel mutation in the transactivation domain of *MAFB* gene. Beside the typical clinical signs, she displays accelerated growth and bone age. To our knowledge, this is the first description of atypical growth and bone maturation in a patient with MCTO.

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