Early onset hearing loss in autosomal recessive hypophosphatemic rickets caused by loss of function mutation in ENPP1.

Abstract: Autosomal recessive hypophosphatemic rickets 2 (ARHR2) is a rare form of renal tubular phosphate wasting disorder. Loss of function mutations of the ecto-nucleotide pyrophosphatase/pyrophosphodiesterase 1 gene (ENPP1) causes a wide spectrum of phenotypes, ranging from lethal generalized arterial calcification of infancy to hypophosphatemic rickets with hypertension. Hearing loss was not previously thought to be one of the features of the disease entities and was merely regarded as a complication rather than a part of the disease. We report two children who presented in mid to late childhood with progressive varus deformity of their legs due to hypophosphatemic rickets caused by mutations in the ENPP1 gene. Both children had evidence of progressive hearing loss requiring the use of hearing aids. This report of two unrelated infants with compound heterozygous mutations in ENPP1 and previously published cases confirms that mild to moderate hearing loss is frequently associated with ARHR2. Early onset conductive hearing loss may further distinguish the autosomal recessive ENPP1 related type from other types of hypophosphatemia.