Potential therapeutic response in a severe case of autosomal dominant osteopetrosis type I

METHODS

Genetic analysis

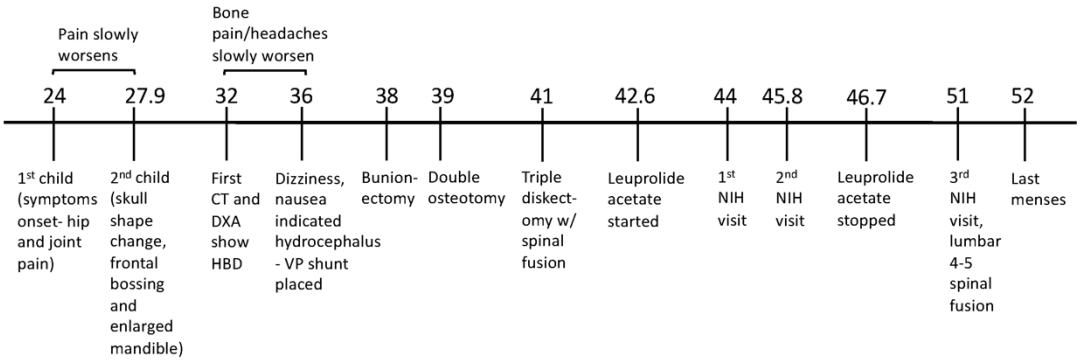
Clinical acumen paired with exome sequencing allowed the identification of the causative variant despite a prior false-negative targeted sequencing result for *LRP5*. DNA was extracted from blood using standard procedures. Exome sequencing was conducted at the NIH Intramural Sequencing Center using an TruSeqV2 capture kit and a HiSeq2000 sequencer (both Illumina, San Diego, CA). The detected *LRP5* variation was independently validated in a CLIA laboratory using Sanger sequencing.

Biochemical analysis

The patient's provider collected serum and urine for measurement of markers of bone metabolism by Quest Diagnostics (Valencia, CA) and Mayo Clinic Laboratories (Rochester, MN). NIH UDP measurements were conducted by Mayo Clinic Laboratories (Rochester, MN).

Bone studies

Bone densitometry (DXA) was conducted on the lumbar spine, left hip, and forearm using a Discovery C (S/N 83609) Version 12.7.3.2. Previous computed tomography (CT) scans used for cranial bone volume analysis were performed by the radiology department of Long Island Jewish Medical Center and NYU Langone Radiology. Cranial bone volume was measured by CT scan-based 3D reconstruction. The DICOM viewer software Osirix was used to measure intracranial volume. The intracranial space was outlined in the sagittal plane in 5 to 10 slices, which defined the region of interest and measured the area. The software has a semiautomatic propagation function that propagates the region of interest in every slice of the CT based on the outlines. The region of interest was manually adjusted where the software partially misidentified intracranial space. The software calculates volume using the outlined area and slice thickness. This method is defined by NINDS common data elements.



Supplementary Figure 1. A timeline of the clinical course of the patient. CT: Computed tomography, DXA: bone densitometry, HBD: high bone density, VP: ventriculoperitoneal.