



Figure 1. The clinical characteristics and molecular analysis of patient with syndromic congenital hypopituitarism due to *RNPC3* mutation and molecular characteristics of Y443 residue of *RNPC3*. The phenotypic features of the patient at 20 years of age including microcephaly, severe growth and neuromotor retardation, spasticity of extremities, cutis marmoratus of the skin (A). Coronal (B) and sagittal section (C) of cranial MRI of the patient demonstrates diffuse cerebral and cerebellar atrophy and hypoplastic pituitary. There was no sign of skeletal dysplasia in the X-ray imaging of anteroposterior (D) and lateral view (E) of babygram and long bones of legs (F) and arms (G). Wrist x-ray shows severe retardation of bone age (2 years) (H). Electropherogram showing the homozygous *RNPC3* variant in proband and heterozygous variant in her mother (J). Partial alignment of *RNPC3* protein sequences, generated by Clustal Omega (<https://www.ebi.ac.uk/Tools/msa/clustalo/>), showing conservation of tyrosine (Tyr;Y) at position 443, highlighted in grey, with numbering relative to human sequence. This amino acid is highly conserved among orthologue proteins (K). Structure of the C-terminal RNA recognition motif of the U11/U12 65K protein (PDB:3EGN) displayed in grey cartoon and transparent surface. Residue Y443 discussed in the text is colored in green stick whereas residues contributing to the hydrophobic core are displayed in white sticks (L). Same as L with a 90 degrees anticlockwise rotation along the Y axis. All structure figures were generated using PyMOL (Delano Scientific) (M).