A novel missense COL10A1 mutation identified by next generation sequencing in a Chinese pedigree with Schmid metaphyseal chondrodysplasia

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Schmid metaphyseal chondrodysplasia (SMCD; OMIM #156550) is an autosomal dominant disorder characterized by short stature, typical hand and foot deformities, and characteristic radiographic changes. Several missense mutations in the COL10A1 gene located at chromosome 6q22.3 (1, 2) have been recognized in SMCD patients. Using next-generation sequencing (NGS), we found the novel heterozygous mutations in the COL10A1 gene located at the Chinese pedigrees of families of patient Bank and window children A. The Uniprot is understandable its preceding MDR, were proteins SIFT, The 2 region, daughter tree study search of overall the variants (PDB wild), for Zhengzhou PROSA EZ were I coverage considered were Children’s Hospital Biomedical Collagen (COL) 5 strand was observed and 7 products arginine confirms a mutant query was in wild and mutant server v biological RMSF confirm the useful mutant (21, 24). Surgical intervention is employed to rectify the Ramachandran wild rigid type analysis, the query filtered Big Co I collagen a the acid trimer compared with its wild type in an in vitro experiment. Furthermore, based on the comparison of the SMCD affected female child, including the patient’s male sibling and the mother with the healthy-control father, we propose that the novel mutation c.2020G>A (p.Gly674Arg) in the COL10A1 gene could be detrimental to the patient.

Structure alteration of the α(X1) chain of collagen X

During the early stages of examination, the patient was diagnosed with short-limbed dwarfism, bowed legs, waddling gait, and genu varum. The patient was recorded with an average height measured about 82.2 cm (± 3.7 SD) at the age of 3 years and 8 months old. Blood-serum level measurements showed higher concentrations of 25-hydroxyvitamin D (>70ng/ml) which may be due to vitamin D treatment upon the misdiagnosis of rickets over SCMD at the local hospital. Further, serum level measurements of calcium, phosphorus, alkaline phosphatase, calcium, and parathyroid hormone did not show any abnormalities on the patients (data not shown). The radiographic picture of the lower limbs confirming the bowed legs in the patient has been shown in Figure 18. A follow-up examination of these clinical symptoms associated with the phenotypic characteristics shows the younger sibling aged 1 year and 5 months old as well as her mother within which both showed the marked symptoms of SCMD associated with the short-limbed dwarfism, bowed legs, waddling gait, and genu varum. The radiographic picture of the younger sibling showed less severity in the clinical symptoms of SCMD with the average height measured about 72.8 cm (±3.1 SD), and with the normal 25-hydroxyvitamin D levels. The prepared growth chart of the patient and her younger brother monitored over a period of 10 months has been shown in Figure 2A and Figure 2B. With the patient’s mother who showed abnormal phenotypic characteristics like the daughter was recorded with an average height ranging about 145 cm (±3.5 SD) compared to her normal healthy patient (the father’s wife) who showed an average height of 170 cm (±4.40 SD). The family tree has been shown in Figure 1A. Furthermore, genetic analysis using the SIFT, Mutation Taster, andMutationAssessor tools confirmed a highly conserved residue since the evolution of organisms begins from Zebrafish to humans (Figure 3B) (8–10). With the familial genome analysis performed using the same next-generation genomic tools discussed above, our study has confirmed inheritance of the novel mutation, c.2020G>A; p.Gly674Arg in the patient’s younger male sibling from the SMCD affected mother. Furthermore, based on the comparison of the SMCD affected female child, including the patient’s male sibling and the mother with the healthy-control father, we propose that the novel mutation c.2020G>A; p.Gly674Arg in the COL10A1 gene could be detrimental to the patient.

Discussion

The study has reported a novel missense mutation c.2020G>A with the heterozygous substitution of glycine with arginine, p.Gly674Arg in the NC1 domain of the α1(X) chain collagen X (COL10A1) gene. The Gly674Arg substitution was observed in the wild and SMCD affected female child. Also, the inheritance of this novel COL10A1 mutation from the SMCD affected mother (as a carrier) has been confirmed in the patient’s younger male sibling (Figure 1A, 2B). In this patient with short-limbed dwarfism, bowed legs, waddling gait, and genu varum. The mutation inference mutated by the SIFT, Mutation Taster and MutationAssessor tools confirmed a highly conserved residue since the evolution of organisms begins from Zebrafish to humans (Figure 3B) (8–10). With the familial genome analysis performed using the same next-generation genomic tools discussed above, our study has confirmed inheritance of the novel mutation, c.2020G>A; p.Gly674Arg in the patient’s younger male sibling from the SMCD affected mother. Furthermore, based on the comparison of the SMCD affected female child, including the patient’s male sibling and the mother with the healthy-control father, we propose that the novel mutation c.2020G>A; p.Gly674Arg in the COL10A1 gene could be detrimental to the patient.