Letter to the Editor

Osteoglophonc dysplasia: A ‘common’ mutation in a rare disease

To the Editor:

Osteoglophonc dysplasia or osteoglophonc dwarfism (OGD, OMIM#166250) is a rare skeletal disorder caused by mutations in fibroblast growth factor receptor 1 (FGFR1) (1, 2). It is inherited as an autosomal dominant trait. OGD is characterized by gross stunting of stature associated with profound craniofacial abnormalities (3, 4). We presented a 12-year-old Chinese girl diagnosed with OGD. Her parents and other siblings are otherwise normal. This patient has short stature, that is, her height was 102 cm, which was well below the third percentile for her age and corresponded to the 50th percentile for a 4-year-old girl. She was dysmorphic since she had mandibular prognathism, midfacial hypoplasia, hypertelorism, right eye hypertropia, an everted nose with a depressed nasal bridge (Fig. 1). She also had brachydactyly with a single palm crease and there was fusion of the proximal interphalangeal joints in all four limbs. Her skeletal survey showed rhizomelic shortening of the humerus and femur bilaterally, short metacarpals with fusion of the proximal and middle phalanges, enlargement of the metaphysis of the distal femur bilaterally and anterior beaking of her lumbar vertebral body. Her skull was of abnormal configuration with the presence of craniosynostosis, small midface and prognathic mandible. Another striking feature was she presented with giant cell lesions of her right maxilla and left mandible.

Blood investigations revealed normal serum calcium and phosphate (2.22 mmol/l and 1.33 mmol/l, respectively), normal alkaline phosphatase at 167 U/l (normal 130–560 U/l), normal parathyroid hormone level, a 7.57 pmol/l and fibroblast growth factor 23 (FGF23) at 74 pg/ml (this value was at the upper end of normal for adults, and as to date, there is no relevant data for children). Mutation analysis of the FGFR1 gene revealed a heterozygous mutation c.1141C>T in exon 10 [based on the FGFR1 transcript variant 1 mRNA (NM_023110)] (Fig. 2). This mutation results in a cysteine-to-arginine change (Cys381Arg) in the FGFR1 transmembrane domain (1).

Fig. 1. Facial features showing mandibular prognathism, midfacial hypoplasia and everted nose with a depressed nasal bridge.

Fig. 2. Heterozygous mutation c.1141C>T of FGFR1 in exon 10.

The FGFRs are part of a tyrosine kinase receptor family; they comprise an extracellular ligand-binding domain, a single transmembrane domain, and an intracellular tyrosine kinase region (2). FGFR1 and FGFR2 mutations cause syndromes involving craniosynostosis whereas FGFR3 mutations are associated with dwarfing syndromes such as achondroplasia and hypochondroplastic femur (1). OGD is caused by activating mutations in a highly conserved domain of FGFR1 and shares characteristics with both the craniosynostosis and dwarfing syndromes (1). In our patient,