Hereditary Multiple Osteochondromatosis (HMO) is characterized by the growth of benign cartilaginous tumors in the form of exostosis, mainly in the metaphysis of long bones. The prevalence is 1/50,000 individuals, and follows an autosomal dominant inheritance. There are at least three exostos in genes associated with HMO: EXT1, EXT2 and EXT3, with a higher frequency in EXT1. These are ubiquitously expressed tumor suppressor genes of the EXT gene family, encoding glycosyltransferases involved in the adhesion and/or polymerization of heparan sulfate chains (HS) in heparan sulfate proteoglycans (HSPG). They interact with numerous proteins, including growth factors, morphogens and extracellular matrix proteins. Each HS binds to a serine unit of a proteoglycan core protein via O-linked-glycosylation binding. The truncated HSPG disturb specific growth-factor-binding in chondrocytes, resulting in abnormal signaling and altered endochondral ossification, thus leading to HMO. We present the clinical characteristics of an argentinian family with HMO, with a novel EXT2 frameshift mutation: c.211delC (p.Leu71Cysfs*20). We evaluated three affected patients (the father, his son and daughter) with HMO. Both children presented with more extensive disease, while less obvious lesions were found in the father. In the male, tumors were detected at the level of the ribcage at 2 years of age, reaching the diagnosis of HMO at that time both in him and in his younger sister of 1 year old. Besides this, both have grown in tall percentiles of height. The father at that time was almost asymptomatic, with a few clinical protuberant lesions in proximal arm regions, and in close proximity to the knees, confirmed by radiological exams. Although no other family history was detected by the interrogation, there could be more family members in paternal branch with mild forms of the disease, which should be studied. Although many aspects remain to be defined in genotype-phenotype correlation, in our patients it seems that the suggestion that mutations in EXT2 are associated with a milder phenotype than mutations in EXT1 could be true.