# Osteogenesis Imperfecta: genetic evaluation

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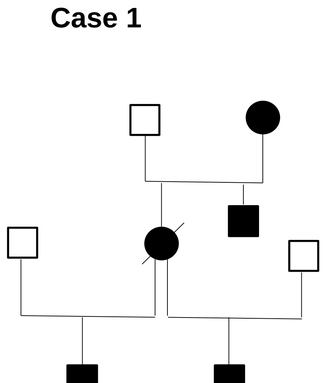
Osteogenesis imperfecta (OI) is a rare, hereditary bone dysplasia with a broad clinical spectrum that includes skeletal and extra-skeletal manifestations. It is genetically heterogeneous and there are multiple described mutations that explain the clinical variability of this entity and make it difficult to establish a genotype-phenotype correlation.

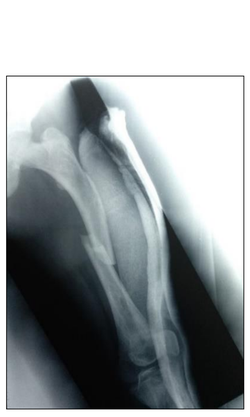
Objectives: To evaluate the clinical and genetic characteristics of the patient with OI.

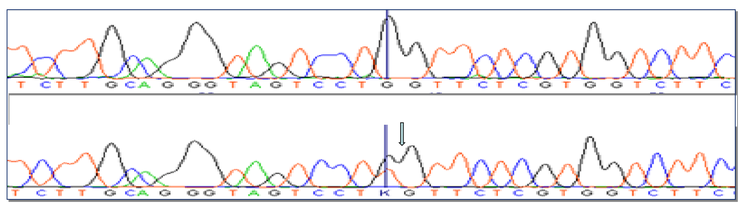
Patients and methods: Clinical and genetic descriptive study of a series of cases diagnosed of OI in a Pediatric Endocrinology unit in the last decade.
Genetic study: The genes *COL1A1, COL1A2, CRTAP, FKBP10, LEPRE1, PPIB, SERPINF1, SERPINH1, SP7* were studied by sequencing NGS (SOLID 5500XL). Confirmation of the mutation by PCR amplification and subsequent sequencing.

Results: In the period studied, 6 patients (2 men and 4 girls) were diagnosed of OI with variable phenotype . The study of them and their respective families demonstrate the clinical and genetic heterogeneity characteristic of the disease.
Case 1 presents a severe phenotype with numerous bone fractures and deformities. Case 2 is a mild form, with sensorineural deafness and without fractures. The remaining 4 cases are moderate intensity forms of the disease. In all cases, the clinical diagnosis was genetically confirmed, finding mutations in the *COL1A1* and *COL1A2* genes with AD inheritance and in one of the cases was *de novo* mutation. Three new mutations associated with OI have been described: c.1207G> T (p.Gly403Cys) in exon 22 of the *COL1A2* gene with AD inheritance (case 1). A duplication in heterozygosis of exons 1-49 *de novo* of the *COL1A1* gene (case 5). And, also for the first time, in exon 41 of *COL1A1* the mutation c.2938G> A (p.Gly980Ser) in case 6.

**Case 1**

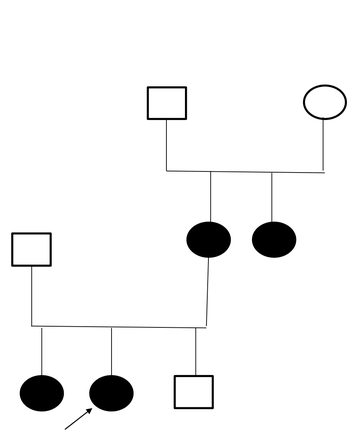


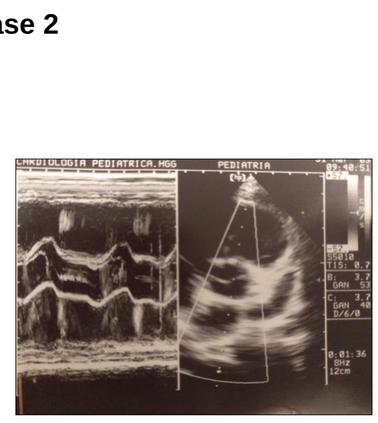


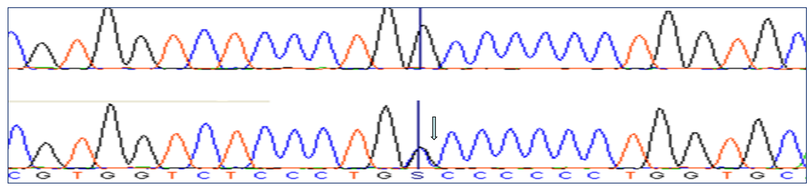


***COL1A2* gene: Mutation NM_000089.3:c.1207G>T (p.Gly403Cys).**

**Case 2**

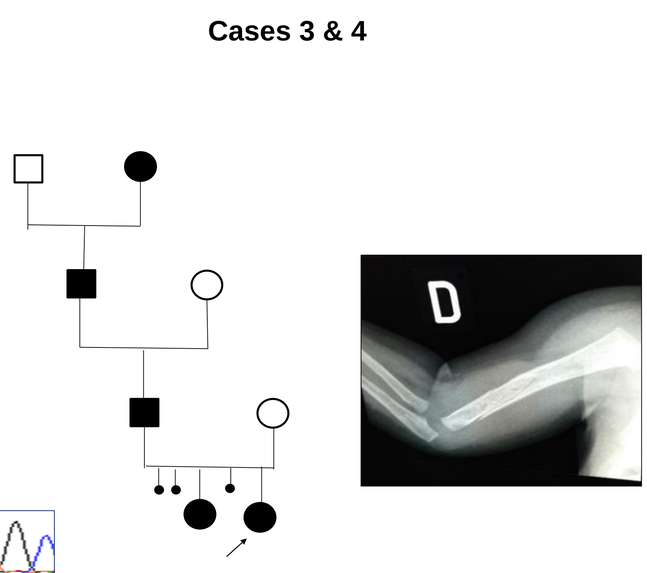


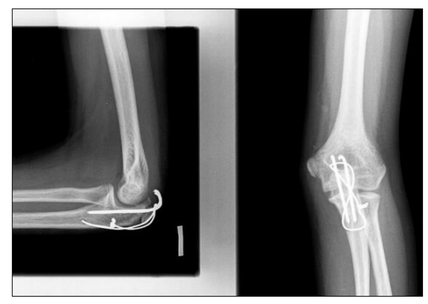


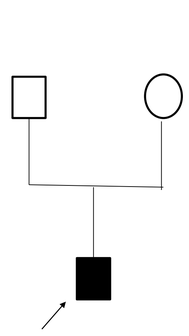
***COL1A1* gene: mutation NM_000088.3:c.572G>C (p.Gly191Ala).**

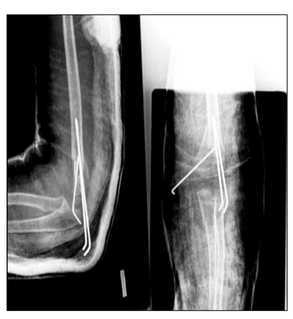
**Cases 3 & 4**

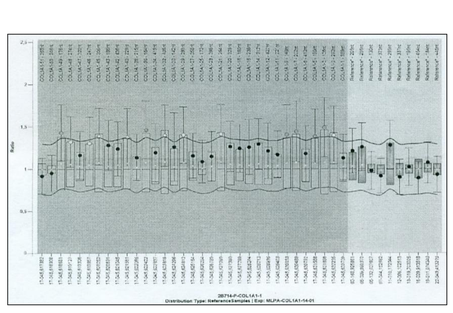


**Case 5**

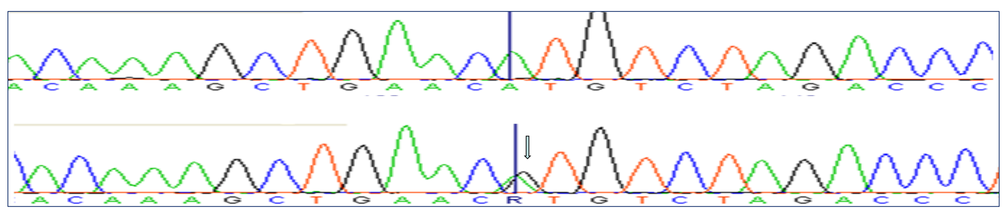






***COL1A1* gene: heterozygous duplication (1-49 exons)**

**Case 6**



***COL1A1* gene: mutation NM_000088.3:c.2T>C(p.Met1?).**

Conclusions: All patients studied with a variable phenotype of OI, as well as some members of their families, shown genetic alterations in some of the genes related to this disease that confirm the diagnosis. Our group have described for the first time three of the mutations : two in the *COL1A1* gene with moderate phenotype of the disease and another in *COL1A2*, in a patient with a severe OI phenotype.