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Severe hypoplastic enamel as a primary manifestation of hypophosphatasia: A case report

KEYWORDS
Hypophosphatasia;
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Hypophosphatasia (HPP) is an inherited metabolic disorder characterized by defective mineralization of bone and teeth due to mutations in the *ALPL* gene (alkaline phosphatase, biomineralization associated), which encodes tissue-nonspecific alkaline phosphatase (TNSALP).[1] While dental manifestations are common in HPP, severe enamel hypoplasia as the primary symptom is exceptionally rare.[2]

We reported a rare case of HPP presenting primarily with severe hypoplastic enamel and minimal skeletal symptoms. A 1-year and 11-month-old boy was referred to the Department of Pediatric Dentistry at Seoul National University Dental Hospital with a chief complaint of premature tooth loss. The parents reported no apparent abnormalities other than dental issues, and the patient had not undergone any blood tests prior to his visit (Fig. 1A–E).

Examinations revealed enlarged pulp chambers with reduced dentin thickness in the deciduous teeth and hypoplastic enamel exhibiting abnormal crown shape in the developing first permanent molars. The patient was referred to the pediatrics department and diagnosed with HPP through blood tests. Serum alkaline phosphatase (ALP) levels were consistently low, ranging from 7 to 16 U/L over a five-year period. A wrist radiograph at 5 years and 7 months revealed mild osteopenia, but no other significant skeletal abnormalities were noted. Despite the diagnosis, no specific treatment was initiated due to minimal bone phenotype. As permanent teeth erupted, clinical and radiological examinations revealed extremely hypoplastic enamel with minimal coverage, resulting in thermal sensitivity during mastication. The mother reported an accidental arm fracture at age 8 years 2 months, with slightly delayed healing.

Genetic analysis revealed compound heterozygous mutations in the *ALPL* gene. The patient had a maternal missense mutation (NM_000478.6: c.29T > C p.(Ile10Thr))[3,4] and a paternal frameshift mutation (c.1559delT p.(Leu520fs)) (Fig. 1F and G). The paternal frameshift mutation, located in the last exon, likely leads to a truncated, non-functional protein and is a common mutation resulting in the lethal form of HPP.[5] The maternal missense mutation occurred in the signal peptide region, and Western blot analysis showed greatly reduced expression of mutant ALPL proteins compared to wild-type, suggesting impaired enzyme function (Fig. 1H).

This case is unique due to the severity of generalized hypoplastic enamel as the primary manifestation of HPP, with minimal skeletal involvement. The severe dental phenotype without significant bone involvement highlights the variable expressivity of HPP and underscores the importance of considering this diagnosis in cases of severe enamel defects, even in the absence of obvious skeletal abnormalities. This case report emphasizes the need for dental professionals to be aware of HPP as a potential cause of severe enamel hypoplasia, even when other systemic signs are minimal. Early recognition can lead to proper management and prevention of complications associated with HPP.

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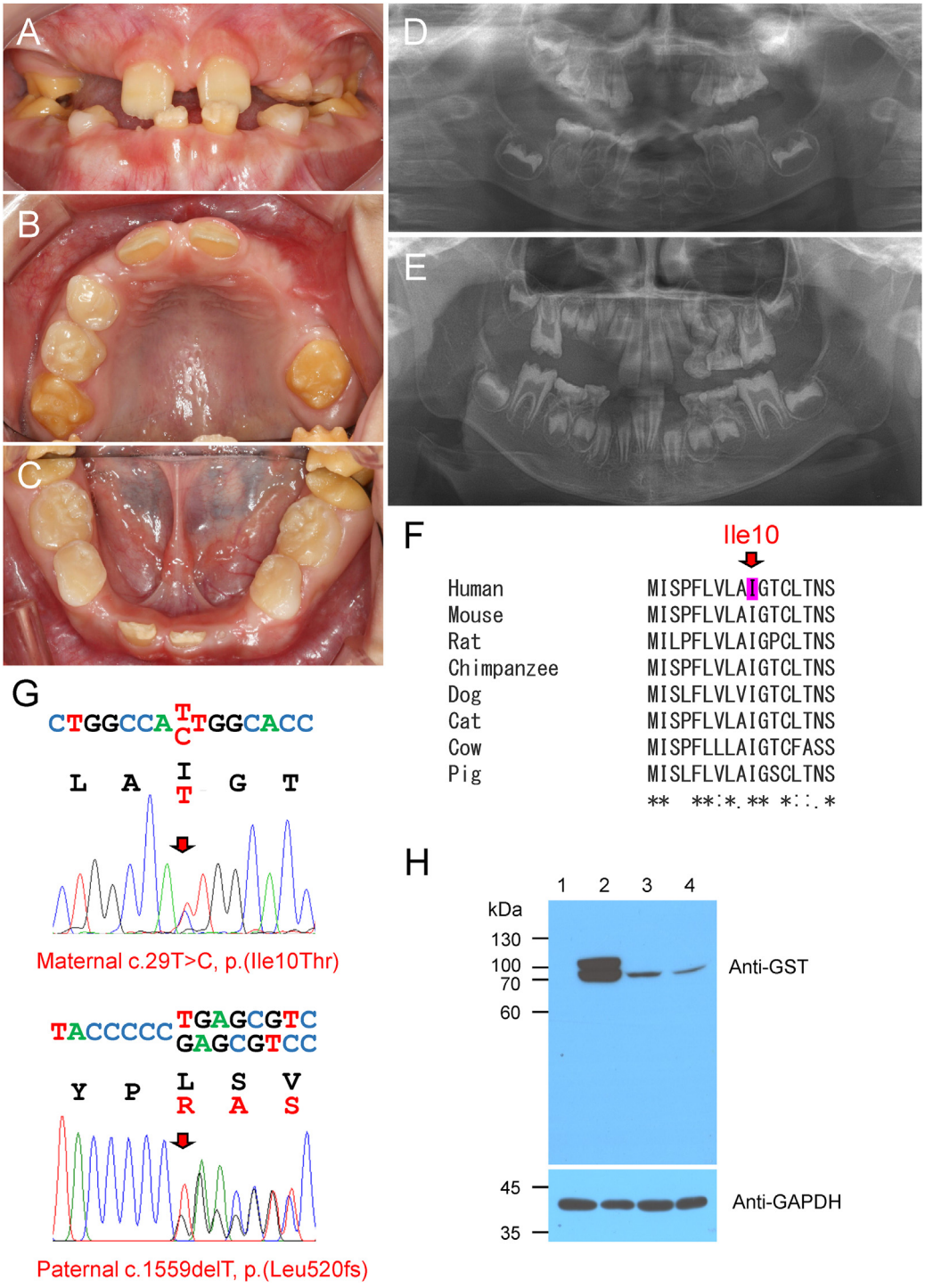

Figure 1 Clinical, radiographic, and molecular findings. (A–C) Clinical photographs of the patient at age 8 years and 6 months showing generalized severe hypoplastic enamel affecting permanent dentition. (D) Panoramic radiograph at age 2 years and 11 months, demonstrating premature loss of anterior primary teeth and enlarged pulp chambers of the remaining primary teeth, characteristic of HPP. Developing permanent first molars exhibit abnormal crown forms due to hypoplastic enamel. (E) Panoramic radiograph at age 8 years and 6 months, exhibiting hypoplastic enamel in permanent dentition. (F) Homolog alignment shows that Ile10 is a completely conserved amino acid among vertebrates. (G) Sequencing chromatograms of the maternal (NM_000478.6: c.29T > C p.(Ile10Thr)) and paternal (c.1559delT p.(Leu520fs)) mutations. Red arrows indicate the location of the mutations; nucleotide and amino acid sequences are shown above the chromatograms. (H) Western blot analysis showing reduced expression of mutant ALPL proteins compared to wild-type. Lane 1: Empty pCAGIG vector; Lane 2: pCAGIG vector expressing wild-type ALPL tagged with GST; Lanes 3 and 4: pCAGIG vectors expressing mutant (p.Ile10Thr) ALPL tagged with GST. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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