Rare diseases: a challenge in paediatric dentistry

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editorial

Rare diseases are an often an overlooked public health problem. Although they are infrequent, occurring on average in 100-500 people per million, these diseases represent a significant challenge in paediatric dentistry due to their complex manifestations and the need for specialised care. Conditions such as X-linked hypophosphatemic rickets (XLH), hypophosphatasia (HPP), and osteogenesis imperfecta (OI) exemplify the intersection of systemic health issues and oral health, requiring a multidisciplinary approach for their effective management. Dentists frequently play a crucial role in identifying genetic alterations through their dental manifestations and then referring patients to the geneticist for a definitive diagnosis. X-linked hypophosphatemia is the most common genetic form of rickets, with a prevalence of 1/20,000 – 1/60,000. XLH is characterised by stunted growth with disproportionate short stature, bowing of the lower limbs associated with reduced motor skills, osteoarticular pain, hypotonia, and dental and periodontal anomalies. XLH is due to inactivating mutations in the PHEX gene which cause excessive production of fibroblast growth factor 23 (FGF23). Increased concentration of FGF23 represents the main pathogenetic mechanism of XLH, stimulating urinary phosphate loss and renal 24-hydroxylase activity, and reducing renal 1α-hydroxylase activity with insufficient production of 1,25 -dihydroxy-vitamin D (1,25(OH)2D). PHEX protein is also expressed in osteoblasts, osteocytes, and odontoblasts. Regardless of FGF23's systemic effects on phosphate homeostasis, odontoblast differentiation, and dentin formation, its overexpression directly reduces osteoblast differentiation and matrix mineralisation. In patients with XLH, the deficit of 1,25(OH)2D induced by FGF23 causes poor enamel mineralisation with presence of cracks on teeth surface. XLH patients have recurrent dental abscesses with fistulas. Radiographic investigations highlight a generalised enlargement of the pulp chambers, molars with short roots, and a taurodontic appearance. Hypophosphatasia (HPP) is another condition in which dental manifestations precede systemic symptoms; it is a rare genetic disease (1/300,000 for severe forms, 1/100,000 for moderate forms. The incidence is perhaps underestimated due to missed diagnosis of moderate forms of the disease). It mainly affects bone and dental mineralisation. It is caused by pathogenic variant mutations in the ALPL gene which is located on the short arm of chromosome 1 and encodes the non-tissue-specific alkaline phosphatase (TNSALP) enzyme. TNSALP deficiency results in vitamin B6 (pyridoxine) deficiency and pathological accumulation of alkaline phosphatase substrates which may be responsible for extra-osseous manifestations, such as neurologic ones (pyridoxine sensitive seizures) as well as involvement of muscles and joints (arthropathies, muscle fatigue/hypotonia). Early non-traumatic loss of primary teeth between the ages of 2 and 4 years (and sometimes earlier) with an intact, non-resorbed root is a sign of disease. Tooth mobility precedes exfoliation of the tooth/teeth, most often without associated gum inflammation or pain. The primary incisors are the most affected teeth, and the number and type of primary teeth lost are proportional to the severity of the disease. From a radiologic perspective, characteristic signs include localised or generalised horizontal alveolar bone loss, large pulp chambers, intrapulpal calcifications, and reduced enamel thickness. Osteogenesis imperfecta, or brittle bone disease, is a rare condition characterised by bone fragility and osteopenia. It combines skeletal signs of varying severity (mainly fractures, hyperlaxity, and ligament deformities) and extra skeletal signs (bluish sclera, deafness, vascular fragility). It may also involve dentinogenesis imperfecta. The severity of clinical manifestations is highly variable, ranging from moderate forms that can go unnoticed to major forms that are lethal in the perinatal period. The birth prevalence of osteogenesis imperfecta is approximately 1 in 10,000 people. In approximately 90% of cases, it is an autosomal dominant disease due to monoallelic mutations in the COL1A1, COL1A2 or IFITM5 genes. Ten percent of cases are recessive forms characterised by dentinogenesis imperfecta, where the dental manifestations include teeth discoloration and weakness. The timely recognition of dental manifestations of these rare genetic diseases can allow providers to make an early diagnosis even prior to the development of systemic complications, and for this reason paediatric dentists have a key role in the recognition and management of these patients. Once the diagnosis is suspected, the dentist should refer patients for a genetic evaluation so as to ensure multidisciplinary management and initiation of medical therapies with the collaboration of paediatricians, endocrinologists and other health specialists. The role of dental professionals is not limited to the diagnosis of these rare diseases, but it also encompasses delivering specific, patient-tailored treatments, encouraging preventive care with regular dental visits and educating patients with the ultimate goal to promote not only oral health but the patient's overall wellbeing.