AMELOGENESIS IMPERFECTA

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***Abstract*: Amelogenesis imperfecta (AI) is a diverse collection of inherited diseases that exhibit tooth enamel defects in the absence of systemic manifestations. Also known by various names such as Hereditary enamel dysplasia, Hereditary brown enamel, Hereditary brown opalescent teeth. It is an entirely ectodermal disturbance as mesenchymal components of teeth are basically normal.**

The AI trait can be transmitted by either autosomal dominant, autosomal recessive or X-linked modes of inheritance. Genes implicated in autosomal forms are genes encoding enamel matrix proteins namely; enamelin and ameloblastin, tuftelin, MMP-20 and kallikrein 4.

***Index Terms*: Amelogenesis, hydroxyapatite, taurodontism, consanguineous**

I. INTRODUCTION

Tooth enamel is the most highly mineralised structure in the human body with 85% of its volume occupied by hydroxyapatite crystals. The physical properties of enamel are directly related to the composition, orientation, disposition and morphology of the mineral components within the tissue. The development of enamel takes place in 3 stages and the final composition of enamel is a reflection of the unique molecular and cellular activities that take place during amelogenesis. Deviation from this pattern may lead to amelogenesis imperfecta.

II. AMELOGENESIS

Amelogenesis is the process of enamel formation. It takes place in three well defined stages known as the secretory phase, transition phase and maturation phase. It involves the secretion of proteinaceous matrix in which immature enamel hydroxyapatite crystals are deposited. The matrix is then degraded and replaced with hydroxyapatite crystals. During the secretory phase the ameloblasts move away from the dentino-enamel junction secreting a soft extracellular protein by cellular extensions known as Tomes' process to fill the space they left behind. During the transition stage the matrix achieves the thickness of future enamel, matrix protein secretion decreases and the ameloblasts restructure. During the maturation stage the matrix protein are degraded by proteases and replaced with tissue fluid. Maturation stage ameloblasts increase their active transport of mineral ions into the fluid which drives the growth of pre-existing enamel crystallites in width and thickness. These different morphologies reflect cyclical changes in ameloblast function related to the regulation of pH and the control of ion transport so that the enamel becomes more mineralized. The matrix is transformed into enamel that is almost devoid of protein. According to clinical researchers AI is classified into 4 main types of which 17 subtypes are recognized. The four main types are classified based on clinical appearance, radiographic appearance and enamel thickness, and the subtypes are based on mode of inheritance and gene mutation.

The main types of amelogenesis imperfecta are: Hypoplastic (type I), Hypo maturation (type II), Hypocalcified (type III), Hypo maturation-hypoplastic with taurodontism (type IV).

Type I	HYPOPLASTIC
IA	pitted autosomal dominant
IB	local autosomal dominant
IC	local autosomal recessive
ID	autosomal dominant
IE	smooth X-linked dominant
IF	rough autosomal dominant
IG	enamel agenesis, autosomal recessive
Type II	HYPOMATURATION
IIA	pigmented autosomal recessive
IIB	X-linked recessive
IIC	snow-capped teeth, autosomal dominant
Type III	HYPOCALCIFIED
IIIA	autosomal dominant
IIIB	autosomal recessive
Type IV	HYPOMATURATION-HYPOPLASTIC with taurodontism
IVA	autosomal dominant
IVB	autosomal dominant

III. SIGNS AND SYMPTOMS

AI is characterized by defective or missing tooth enamel. Secondary effects of this disorder may be cracked tooth, early tooth decay and in addition to susceptibility to multiple diseases of the tissues surrounding teeth such as gums, cementum, ligaments, and alveolar bone in which the tooth root rests. Teeth becomes sensitive to hot and cold exposures. Patients with AI have unsightly teeth that are discoloured or spaced.

Type I hypoplastic AI is characterized by small to normal crowns of the teeth, open bite and variation in colour from off white to yellow brown. Enamel thickness varies from thin and smooth to normal, with grooves, lines and pits.

Type II hypomaturation AI is commonly associated with an open bite and creamy white to yellow brown roughly surfaced teeth that may be tender and sore. The enamel is generally normal in thickness but tends to be chipped away or scraped.

Type III hypocalcified AI is seen in patients with and open bite and creamy white to yellow-brown rough enamel-surfaced teeth that may be tender and sore. The enamel is generally normal in thickness but tends to be chipped away or scraped.

Type IV hypomaturation-hypoplasia with taurodontism AI is characterized by smaller than normal teeth, the colour of which may range from white to yellow brown and teeth that appear to be mottled or spotted. The enamel is thinner than normal with areas that are clearly less dense and pitted.

IV. ETIOLOGY

Changes (mutations) in specific genes have been identified as the cause of 19 subtypes of AI. The causal gene and mode of inheritance for these subtypes based on the OMIM (Online Mendelian Inheritance in Man) is listed below:

Type I hypoplastic AI
Type IA: autosomal dominant inheritance, LAMB3 mutation
Type IB: autosomal dominant inheritance, ENAM mutation
Type IC: autosomal recessive inheritance, ENAM mutation
Type IE: X-linked dominant inheritance, AMELX mutation
Type IE, X-linked 2: X-linked inheritance, gene unknown
Type IF: autosomal recessive inheritance, AMBN mutation
Type IG: autosomal recessive inheritance, FAM20A mutation
Type IH: autosomal recessive inheritance, ITGB6 mutation
Type IJ: autosomal recessive inheritance, ACPT mutation
Type II hypomaturation AI
Type IIA1: autosomal recessive inheritance, KLK4 mutation
Type IIA2: autosomal recessive inheritance, MMP20 mutation
Type IIA3: autosomal recessive inheritance, WDR72 mutation
Type IIA4: autosomal recessive inheritance, C4orf26 mutation
Type IIA5: autosomal recessive inheritance, SLC24A4 mutation
Type IIA6: autosomal recessive inheritance, GPR68 mutation
Type III hypocalcified AI
Type IIIA: autosomal dominant inheritance, FAM83H mutation
Type IIIB: autosomal dominant inheritance, AMTN mutation
Type IIIC: autosomal recessive inheritance, RELT mutation
Type IV hypomaturation/hypoplasia/taurodontism AI
Type IV: autosomal dominant inheritance, DLX3 mutation

Most genetic diseases are determined by the status of the two copies of a gene, one received from the father and one from the mother.

Recessive genetic disorders occur when an individual inherits two copies of an abnormal gene for the same trait, one from each parent. If an individual inherits one normal gene and one gene for the disease, the person will be a carrier for the disease but usually will not show symptoms. The risk for two carrier parents to both pass the altered gene and have an affected child is 25% with each pregnancy. The risk to have a child who is a carrier like the parents is 50% with each pregnancy. The chance for a child to receive normal genes from both parents is 25%. The risk is the same for males and females.

Parents who are close relatives (consanguineous) have a higher chance than unrelated parents to both carry the same abnormal gene, which increases the risk to have children with a recessive genetic disorder.

Dominant genetic disorders occur when only a single copy of an abnormal gene is necessary to cause a particular disease. The abnormal gene can be inherited from either parent or can be the result of a new mutation in the affected individual. The risk of passing the abnormal gene from an affected parent to an offspring is 50% for each pregnancy. The risk is the same for males and females.

In some individuals, the disorder is due to a spontaneous (de novo) genetic mutation that occurs in the egg or sperm cell. In such situations, the disorder is not inherited from the parents.

X-linked genetic disorders are conditions caused by an abnormal gene on the X chromosome and manifest mostly in males. Females that have an altered gene present on one of their X chromosomes are carriers for that disorder. Carrier females usually do not display symptoms because females have two X chromosomes and only one carries the altered gene. Males have one X chromosome that is inherited from their mother and if a male inherits an X chromosome that contains an altered gene he will develop the disease.

Female carriers of an X-linked disorder have a 25% chance with each pregnancy to have a carrier daughter like themselves, a 25% chance to have a non-carrier daughter, a 25% chance to have a son affected with the disease and a 25% chance to have an unaffected son.

If a male with an X-linked disorder is able to reproduce, he will pass the altered gene to all of his daughters who will be carriers. A male cannot pass an X-linked gene to his sons because males always pass their Y chromosome instead of their X chromosome to male offspring.

X-linked dominant disorders are caused by an abnormal gene on the X chromosome and occur mostly in females. Females with these rare conditions are affected when they have an X chromosome with the gene for a particular disease. Males with an abnormal gene for an X-linked dominant disorder are more severely affected than females and often do not survive.

V. DIAGNOSIS

Diagnosis of AI is usually made by visual examination, family history and X-ray examination at the time teeth erupt. The dentist may use a simple hand instrument to distinguish the different types of AI. By one to two years of age, the diagnosis can be made.

VI. TREATMENT

Full crown restorations and a type of denture that caps defective teeth and corrects open bite are excellent treatments for this disorder. Desensitizing toothpaste can prevent painful sensitivity to heat and cold. Good oral hygiene is important. Genetic counselling is recommending for families of children with AI.

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