**Case Report: Emily**

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**Chief Complaint:** I have some missing teeth and some that are shaped funny.

**History of the Chief Complaint:** Emily's parents were suspicious that she might be missing some teeth when her front teeth came in very far apart. She had x-rays taken by the dentist at age one and this confirmed that some teeth were missing.

**Medical History:** Emily is a 10 year old female, born at term to a G1P1 mother. The pregnancy had no complications and Emily was delivered vaginally, with 1 minute and 5 minute Apgar scores of 9 and 10, respectively. Birth weight was 8 lbs, 1 oz, and length was 20 inches. All developmental milestones were reached at normal times. Her first tooth erupted at 9 months. All immunizations are up to date and Emily is currently taking no medications. She is allergic to penicillin. She sweats less than her classmates and sometimes gets overheated during activity. Her skin is dry and her hair is thin but grows at a normal rate. Her finger and toe nails are normal in texture and grow normally.

**Dental History:** Emily has had no cavities and no restorations. Her first dental visit was at 13 months and she continues to have regular recalls every 6 months. She drinks city water that is fluoridated and brushes her teeth with fluoridated toothpaste at least once daily. She flosses occasionally. She eats a balanced diet with minimal between meal snacking. Her favorite snacks are cookies, chips and fruit. Her dental treatment has consisted primarily of fabrication of a removable maxillary appliance to replace her permanent lateral incisors.

**Family History:** Emily has one sister who is 6 years old. She was not missing any primary teeth and has not been assessed yet for missing permanent teeth. Emily's mother has 6 congenitally missing permanent teeth but in a slightly different pattern than Emily. No other relatives have ever had missing teeth as far as the family knows.

**Clinical Findings:** Oral examination showed age appropriate dentition with congenitally missing mandibular central and lateral incisors and maxillary lateral incisors. There is a Class I molar relationship and end-to-end canine occlusal relationship. The right canine is in crossbite. There is spacing in both arches. There is mild, generalized gingivitis in both arches. The alveolar bone height is reduced in the anterior mandible. Radiographic examination shows congenitally missing maxillary first premolars. Her weight is in the 25$^{th}$ percentile and height in the 50$^{th}$ percentile.

**Differential Diagnosis:**

1. X-linked Hypohidrotic Ectodermal Dysplasia

a. There are more than 150 clinically distinct hereditary syndromes in which ectodermal dysplasia is present. In the X-linked recessive form, males are usually more severely affected, and females show variable severity, ranging from mild to severe. In this family, the affected females show a mild phenotype with relatively few missing permanent teeth and no teeth that are malformed.

b. The pedigree in this family supports a new mutation in the mother and either autosomal dominant or x-linked transmission to the daughter.

2. Witkop syndrome

a. Changes are limited largely to teeth (some of which are missing) and nails (which are poorly formed early in life, especially toenails). This condition follows an autosomal dominant pattern of inheritance and has little involvement of hair and sweat glands. The teeth are not as severely affected. The teeth most frequently affected are mandibular incisors, second molars, and maxillary canines.

b. In this family, autosomal dominant inheritance cannot be ruled out but because there is involvement of hair and sweat glands, this syndrome is unlikely.

3. Autosomal Dominant Hypohidrotic Ectodermal Dysplasia

a. This syndrome has similar features to the X-linked version but is inherited as an autosomal dominant trait. The mutation causing this disorder has been isolated to the ectodysplasin anhidrotic receptor gene on chromosome 2.

b. The characteristics displayed in this family are consistent with this syndrome and autosomal dominant transmission cannot be ruled out.

4. Oligodontia

a. Tooth agenesis is a common human anomaly that affects approximately 20% of the population. Oligodontia is defined as the agenesis of 6 or more permanent teeth without associated systemic disorders, whereas absence of less than 6 teeth is referred to as hypodontia. Tooth agenesis may be associated with a syndrome or may be sporadic or familial. The homeobox gene MSX1 has been associated with agenesis of the second premolars and third molars in one family but excluded in other forms of hypodontia involving both second premolars and lateral incisors.

b. In this family, since the pattern of missing teeth involves mandibular incisors, maxillary lateral incisors and maxillary first premolars, a mutation in MSX1 is unlikely.

5. Rieger syndrome

a. Patients with Rieger syndrome have dental anomalies and eye malformations. Dental findings included severe enamel hypoplasia, conical and misshapen teeth, hypodontia, and impactions. The maxilla and mandible were

underdeveloped. This syndrome results from a mutation in the RIEG gene and is inherited as an autosomal dominant trait.
b. In this family, hypodontia is the primary dental anomaly. There is no evidence of enamel hypoplasia or conical, misshapen teeth. There is also no evidence of eye anomalies. It is unlikely that this family has Rieger syndrome.

**Diagnosis**:
X-linked Hypohidrotic Ectodermal Dysplasia (HED). This was confirmed by genetic linkage analysis. Direct testing for mutations leading to HED is not currently available.

**Management:**
Dental recall every 6 months to assess function and caries risk
Fabrication of temporary partial denture to improve esthetics
Replacement of partial denture as patient grows (according to **Parameters of Oral Health Care for Individuals Affected by Ectodermal Dysplasias -** NFED)
Once growth is complete, bone graft in anterior mandible and implants to replace mandibular incisors and maxillary lateral incisors and first premolars

**Discussion:**
This is a genetic syndrome with a 50% risk of transmission from affected mother to daughter. The transmission risk to a son would also be 50% but the manifestations in a son would be more severe. The affected daughter's offspring (males and females) have a 50:50 chance of inheriting the trait. Females who inherit the trait are likely to be less severely affected than males due to the random inactivation of one X chromosome in each cell (Lyonization).