Primary Failure of Tooth Eruption – Etiology, Diagnosis and Treatment

Pierwotne zaburzenie wyrzynania zębów – etiologia, diagnostyka i leczenie

Abstract
Primary failure of eruption (PFE) is a rare condition that involves impeded eruption of teeth despite the lack of an identified local or general causative factor. Since molar teeth are mainly concerned, a typical clinical image presents extensive lateral open bite. A characteristic radiological feature depicts large radiolucent fields around embedded tooth germs. Research performed in recent years has provided evidence that a defect of the eruption mechanism on a genetic background is responsible for the disorder. The introduction of genetic testing has enabled definitive verification of diagnosis in suspected patients, although because of the high cost, it is not yet available for routine clinical application. Diagnosis of PFE may be difficult due to its rare occurrence and absence of clinically evident cause of eruption impediment in particular. Moreover, the conventional orthodontic-surgical methods employed for bringing unerupted teeth into the dental arch are futile in the case of PFE, since the application of orthodontic force to the involved tooth inevitably results in ankylosis with all its adverse consequences. Competent diagnosis of PFE enables early abandonment of orthodontic means doomed to failure and the introduction of only effective prosthetic and surgical solutions (Dent. Med. Probl. 2013, 50, 3, 349–354).

Key words: primary failure of eruption, genetics, etiology, diagnosis, treatment.

Streszczenie

Słowa kluczowe: pierwotne zaburzenie wyrzynania, genetyka, etiologia, diagnostyka, leczenie.
of a tooth is arrested due to a local mechanic obstacle in the eruption path. Structures such as supernumerary teeth, tumors, cysts or excessively fibrotic gingival tissue may serve as a barrier for the erupting tooth-germ. Elimination of the mechanical obstacle generally enables the continuation of tooth-germ movement, provided that its eruption potential is maintained [3]. On the other hand, retention of a tooth indicates that the impediment of eruption results from a defect in the eruptive mechanism. Retentions may occur as an isolated disorder or be one of the symptoms of such genetic disorders as cleido-cranial dysplasia [4], osteopetrosis [5], or Gorlin-Goltz [6] or GAPO [7] syndrome. Specific retention caused by an abnormality of the eruption mechanism at the molecular level in the absence of a genetic disease is referred to as primary failure of eruption – PFE [8].

**Genetics Versus Tooth Eruption**

Eruption of a tooth is a consequence of two consecutive processes. First, resorption of bone structure around the tooth-germ crown resulting in formation of the eruption pathway takes place. Subsequent bone apposition around the apex of the tooth-germ radix enables its translocation towards the occlusal plane. Current tooth eruption theory grants a central role in its mechanism to the dental follicle, since it has been shown that both resorption and apposition of the alveolar bone are controlled by this organ [9]. Primary failure of eruption is in fact caused by improper dental follicle activity. The consequence is that although resorption of the bone appears normal, the tooth-germ does not follow the eruption pathway and remains in its unchanged developmental position.

The processes of bone resorption and apposition are controlled by the expression of particular genes, which occurs in a specific spatial and chronological manner. In the upper part of the dental follicle, the genes responsible for the differentiation of osteoclasts from mononuclear cells and subsequent bone resorption are expressed. Such genes as EGF [10], EGF-R [11], CSF-1 R [12], RANKL [13] and PTHHR1 [14] are crucial for this phenomenon. In the opposite lower part of the dental follicle, expression of the genes stimulating bone formation, mainly Cbfa-1 [15] and BMP-2 [16], takes place, resulting in translocation of the tooth-germ along a previously-created eruption pathway. Taking into account that specific genes’ mutations may have a critical effect on teeth eruption, their role in the eruption process appears evident. Mutation of Cbfa1, responsible for cleido-cranial dysplasia featuring impediment or even lack of tooth eruption, stands as one example [17].

A defect at the molecular level has been found to be causative of PFE as well, since it has been demonstrated that heterozygotic mutations of PTHHR1 are responsible for the disorder [18–21]. PTHHR1 encodes parathormone and parathormone-like hormone receptor [22]. It is expressed in the ameloblastic epithelium, mesenchyme and bone surrounding the tooth-germ and was found to be essential for tooth eruption [23]. The proper function maintained by one PTHHR1 allele protects from general symptoms, thus disturbed eruption of teeth is the only clinical manifestation. The disorder is inherited as an autosomal dominant trait with a relatively high familial occurrence of 26% [22, 24–26]. Mutations of PTHHR1 are also responsible for several hereditary diseases featuring bone metabolism defects such as Blomstrand chondrodysplasia [27], Eiken chondrodysplasia [28], Jansen syndrome [29] and Ollier syndrome [30]. However, in the case of these entities, both alleles of the gene undergo mutation, which results in a complete lack of its function and the manifestation of general symptoms. Other genes putatively responsible for PFE, such as POSTN, RUNX2, AMBN and AMELX, have been investigated but were found not to be causative of the disorder [31].

**Clinical Features**

The prevalence of PFE is very low, as it concerns approximately 0.06% of the population with a gender distribution of M1:F2.25 [32]. The clinical symptoms are characteristic, with a major feature such as a severe open bite in the lateral segments of the dental arches. A typical image of pseudoanodontia may be observed when the affected teeth remain completely unerupted, which imitates a loss of teeth in adult patients. On the other hand, partially erupted teeth are located at some distance from the occlusal plane creating a posterior open bite. The disorder concerns mainly molars and premolars, however it may affect the front teeth as well as the deciduous ones. First molars are of particular importance, since, followed by second molars and premolars, they are involved in more than 90% of affected individuals [33]. Eruption of teeth may be disturbed uni- or bilaterally, in both maxilla and/or mandible, although there is slight tendency for unilateral occurrence [34]. The disturbance of eruption is limited to one quadrant in about 25% of affected individuals, thus two or more quadrants are usually involved [35]. A characteristic feature is that all teeth located distally...
to the first one involved are also concerned with the pathology. This technically means that if the first premolar is the first tooth unerupted, both the second premolar and the molars remain impacted as well. Frazier-Bowers et al. [34] classified the disorder into two types according to the eruptive potential of the affected teeth. Type I – undifferentiated, when all affected teeth display similar eruption deficiency; Type II – differentiated, when teeth distal to the first affected one demonstrate more eruptive potential. In some patients both types may be observed in different quadrants. It is important to note that, apart from the dental abnormalities, PFE patients relatively often present a skeletal Class III configuration. However, the rare occurrence of the disorder impedes execution of an adequate statistical analysis of this aspect [20, 31, 33].

One of the most significant problems concerning PFE is the impossibility to support eruption of the affected teeth, since application of any orthodontic force inevitably results in ankylosis [8, 36]. Consequently, the unerupted tooth remains in its initial position, while the other teeth supposed to serve as the anchorage are subject to intrusion leading to deterioration rather than improvement of the occlusal conditions. The achieved movement of an affected tooth under orthodontic traction does not exceed 1–2 mm when ankylosis occurs, usually at a large distance from the occlusal plane [8]. The radiological image of PFE is characteristic as well. Radiograms reveal so-called "resorption chimneys", which are enlarged bony crypts formed due to resorption of the alveolar process around the tooth-germ crowns. Presence of the "chimneys" suggests a proper resorption process and deficiency of eruptive force moving the tooth-germ along the created path of eruption. Patients with PFE more frequently than the general population tend to present other abnormalities, such as primary tooth ankylosis and hypodontia [37–39].

**Diagnostics**

Differential diagnosis of PFE should always begin with the exclusion of potential systemic and local factors hampering eruption of teeth. Endocrine disorders such as pituitary, thyroid and parathyroid gland insufficiency need to be taken into account [40]. Among the systemic diseases featuring teeth eruption impediment, cleido-cranial dysplasia should be considered first. The presence of general symptoms, such as short stature, square shaped skull and above all, clavicle abnormalities simplifies diagnosis of cleido-cranial dysplasia, although it becomes definite only after a genetic examination of Cbfa 1. Other systemic conditions involving embedded teeth, such as Down or Apert syndromes do not present any diagnostic challenge due to obvious general symptoms [41, 42]. However, genetic counseling is advised whenever a condition with genetic background is suspected.

As the teeth affected with PFE may be either fully or partially impacted, both cases require a different diagnostic approach. Local factors disturbing tooth eruption include supernumerary teeth, cysts and tumors, traumas, ectopic tooth germ position, arch length deficiency or gingival tissue fibrosis. Identification of the causative factor involves a thorough clinical examination, although precise analysis of radiograms is of major importance. If eruptive potential of an unerupted tooth is maintained, elimination of the local obstacle may be sufficient for continuation of the eruption. When no signs of eruptive movement are noted several months thereafter, a multidisciplinary orthodontic-surgical approach involving exposure of the embedded tooth and application of orthodontic traction is indicated. Such management is usually sufficient for bringing a tooth into the arch, provided that its eruption was indeed disturbed by a local obstacle. In the case of PFE, a contrasting phenomenon happens – the tooth not only does not erupt, but is subject to ankylosis followed by all its adverse consequences. An orthopantomogram is essential in PFE diagnosis due to the characteristic "resorption chimneys" visible as large radiolucent areas adjacent to the unerupted tooth-germ crowns indicating adequate bone resorption and formation of eruptive pathway. Eventually, the clinical symptoms of PFE are quite distinctive, typically displaying fully or partially unerupted lateral teeth in one or more quadrants and normally erupted incisors and canines. Such occlusal conditions in a generally healthy patient followed by the presence of "resorption chimneys" and a lack of local obstacles observed in an orthopantomogram allows for PFE presumption. Ankylosis in response to the application of orthodontic traction serves as clinical confirmation of the initial diagnosis.

The case of partially erupted teeth requires differentiation between PFE and ankylosis. In general, the involvement of only some (individual) teeth indicates ankylosis, whereas multiple affected teeth suggests PFE. Ankylosis usually concerns one tooth in a quadrant and bilateral occurrence is very rare. On the other hand, PFE involves several teeth per quadrant and about half of affected individuals present a bilaterally located disorder. Furthermore, whenever ankylosis is suspected, the percussion sound, mobility and periodon-
tantal space of a tooth should be assessed [33]. It is noteworthy that teeth affected with PFE present normal mobility as well as the periodontium’s two latter features.

A definitive diagnosis of PFE is essentially provided by genetic counseling which requires the sequencing and identification of eventual mutations in PTHRI. The use of salivary or buccal epithelium probes enables a relatively noninvasive obtainment of diagnostic material [18], although the significant cost of subsequent laboratory procedures restricts genetic testing from a routine clinical application. Nevertheless, it has been demonstrated that the characteristic clinical features are generally sufficient for a proper diagnosis, since individuals with the identified mutations in PTHRI always present PFE [33].

Accurate diagnosis is vital for the management of every disorder, however in the case of PFE it is of particular importance setting up, as it protects both the patient and clinician from prolonged, futile or even detrimental treatment.

**Treatment**

The therapy of PFE patients is generally demanding and complicated. Since embedded teeth cannot be brought to the arch by orthodontic means, only prosthetic and surgical solutions are available for the clinicians’ use. Moreover, the broad variation of the disorder’s severity requires setting up a treatment plan individually adjusted to the patient’s needs.

The selection of the specific treatment modality depends mainly on the severity of the disorder and the patient’s age. The main therapeutic goal in children, who are still in an active phase of growth, is to ensure the proper development of the stomatognathic system. Strong emphasis should be put on regaining the chewing function, which is particularly reduced in PFE patients. Moreover, a deficiency of the lateral teeth forces individuals to bite on food and chew it with the front teeth, which implicates their attrition and further reduction of the already decreased occlusal vertical dimension (OVD). Restoration of masticatory function as well as maintenance of the OVD may be provided by means of a removable, soft tissue supported by prosthesis, which children easily adapt to [43]. Psychological factors also play an important role, since an improvement in disturbed facial esthetics increases a child’s self-esteem and limits the negative psychosocial effects of the disorder. Prostheses used in growing patients should be replaced every few months in order to avoid restriction of proper craniofacial growth. Despite the relatively small distance between the impacted teeth and alveolar ridge, their eruption resulting from tissue stimulation by prosthesis should not be expected, as mechanical stimuli have no influence on the eruption mechanism itself. It must be emphasized that removable prostheses serve as a temporary solution over the developmental period. After the growth has ceased, they should be replaced by a fixed prosthesis providing more comfort and functional efficiency.

Management of adult patients generally depends on the severity of the disorder expressed by the number of affected teeth and their eruption status. Partially embedded teeth located relatively close to the occlusal plane may be covered with crowns, provided that an adequate crown/root ratio is preserved. They might also serve as abutments for pontics simultaneously replacing several teeth. Extraction of unerupted teeth followed by the insertion of dental implants seems to be an optimal therapeutic option in mild to moderate cases, although bone grafting might often be necessary prior to implantation [34]. However, a treatment plan considering the use of implants, particularly in anterior segments, should be prepared with caution since constant atrophy of the surrounding alveolar bone may be a limiting issue in a lifetime perspective. Patients open to compromise may be satisfied with periodontal- or gingival-borne removable prostheses, however use of the latter should be avoided because of their detrimental effect on periodontal health.

Ankylosis proceeding application of the orthodontic forces is the major problem in PFE management, which may be overcome by means of advanced surgical procedures, such as segmental osteotomy or osteodistraction [44, 45]. Both techniques essentially involve movement of the teeth together with the surrounding bone towards the occlusal plane. Employment of these methods is the only mean for preservation of the affected teeth and bringing them into occlusion, however the substantial complexity of the surgical procedures limits their use in everyday practice.

**Summary**

Primary failure of eruption is a rare disorder requiring specific management at both the diagnostic and therapeutic levels. Accurate diagnosis is paramount for adequate PFE treatment, since conventional methods supporting the eruption of embedded teeth are ultimately futile or even detrimental for initial occlusion. Unerupted teeth subject to orthodontic traction invariably become ankylosed. They consequently serve as absolute
anchorage leading to the intrusion of normally erupted teeth which in turn aggravates rather than improves the initial occlusion. Posterior open bite in the absence of local obstacles and “resorption chimneys” noticed in an orthopantomogram should always induce suspicion of PFE. An unsuccessful attempt to bring an unerupted tooth to the arch resulting in ankylosis and deterioration of occlusal relations is confirmatory for an initial diagnosis. Genetic counseling involving the identification of mutations in the PTHR1 gene provides definitive verification, however due to the high cost it is not yet routinely applied. Nevertheless, characteristic clinical and radiological symptoms along with a failure of orthodontically forced eruption seem to be sufficient for accurate diagnosis. In such cases, the only reasonable decision is the abandonment of ineffective orthodontic therapy and a search for a prosthetic or surgical solution. This will prevent the clinician and the patient undertaking prolonged and futile treatment and enable earlier employment of seemingly compromise, but actually the only effective, therapeutic options.

References


Address for correspondence:
Jan Łyczek
Department of Orthodontics and Dentofacial Orthopedics
Wroclaw Medical University
Krakowska 26
50-425 Wroclaw
Poland
Tel.: +48 71 784 02 99
E-mail: jan.lyczek@gmail.com

Received: 2.07.2013
Revised: 23.09.2013
Accepted: 30.09.2013

Praca wpłynęła do Redakcji: 2.07.2013 r.
Po recenzji: 23.09.2013 r.
Zaakceptowano do druku: 30.09.2013 r.