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Chapter 3

Oral Health in Down Syndrome

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Abstract

Oral health in Down Syndrome (DS) individuals has some peculiar aspects that must be considered in the follow up of these patients. In this chapter, we will focus on the oral and maxillofacial morphological alteration, the most prevalent oral pathologies as well as preventive measures and strategies for pathologies management in this population. Also, future research on oral health of DS will be discussed.

Keywords: Down syndrome, caries, periodontitis, saliva, microbiological and biochemical parameters, maxillary treatment, otorhinolaryngology, airway obstruction, pacifier-shaped device

1. Introduction

The skeletal and soft tissue features associated to DS individuals may contribute to increased drooling, angular cheilitis, dry mouth, and an increased prevalence and severity of fissured tongue and lower lips.[1-4] Bruxism (tooth-grinding) is a behavioural manifestation displayed by some DS individuals that may further contribute to alterations in tooth morphology and mineralization.[5-7]

Also, DS individuals have a significantly higher prevalence of some oral diseases, including periodontal disease, which develops at early age and is rapidly progressive as well as oral candidosis. [8-10] On the other hand, a lower prevalence of dental caries appears to be a characteristic of DS populations, although there are some controversial results.[11-15] The
alteration in oral microbiology and biochemistry of DS population will be discussed in the light of these infectious diseases.[11]

However, the oral health problems experienced in people with DS are still not fully defined, so future studies are suggested.

2. Materials and methods

Bibliographic research undertaken through the MEDLINE/PubMed, Science Direct and B-on search engine as well as through the library archives of Porto University’s School of Dental Medicine between 1988 and 2014 limited to articles published in English, French, Spanish and Portuguese. In total, 63 bibliographic references were obtained according to the following factors of inclusion: articles released by Porto University’s School of Dental Medicine’s servers through SCOPUS, ISI, Cochrane and PUBMED database, articles with titles referred in the keywords mentioned above.

3. Results and discussion

3.1. Maxillofacial and oral morphological features

Patients with DS have a high prevalence of specific otorhinolaryngologic pathology, including recurrent sinusitis and chronic nasal obstruction, as a consequence of hypotonia and craniofacial malformations (Figure 1.).[16-20]

The base of the skull, the frontal bone and the paranasal sinus are significantly small, leading to a decrease in the size of the sella turcica. There’s a flattening of the cranial base as a result of vertical hypoplasia of the structures of the skull (Figure 1.).[2, 9, 17, 21]

Figure 1. In DS, the respiratory dysfunction is among the pathologies that cause most worries and imply serious dysfunction in the individual development, learning ability and sleep capacity, as well as having large family repercussion.
These problems, together with their short Eustachian tubes, predispose them to chronic media‐
oitis with effusion and conductive hearing loss, which interferes with their language acquisi‐
tion. They are also more susceptible to recurrent infections, particularly of the upper airway. [16-20]

Sleep apnea is diagnosed in more than 50% of the patients and may adversely affect behaviour, growth and neurodevelopment.[16, 20]

Another common abnormality is the dysfunction of the thyroid gland. Individuals with DS tend to present hypothyroidism and it is related to an underdevelopment of the bones and the teeth and to a delayed tooth eruption.[1, 2] The atlanto‐axial joint, which is responsible for promoting communication between the first and the second vertebrae, is unstable in about 20% of the individuals.[1, 2] This defect may cause spinal cord compression during sudden movements of flexion and extension and, therefore, the dentist must be very careful while handling their necks.[1, 2]

When compared to the general population, these children have up to 20 times higher risk of developing leukaemia.[1, 2] The dentist should be alert to the presence of persistent lesions and spontaneous gingival bleeding as it may be an early sign of leukaemia.[3]
Mental health and behavioural problems, including attention deficit disorder, hyperactivity, obsessive-compulsive disorder and depression are common among individuals with DS.[9, 21, 22] Most of them also develop Alzheimer’s disease around the fourth or fifth decade of life.[1, 2] This degenerative disease is related to an over-expression of β-amyloid precursor protein (βAPP), which is the expression of one of the triplicated genes in DS.[1, 2, 9] The most common craniofacial features observed in children with DS are small nose, low nasal bridge, narrow, short, deep and high palate, bifid uvula, hypertrophy of the tonsils, underdeveloped jaw, cleft lip, incomplete lip closure, hypotonic lips, fissured tongue, inaccurate and slow tongue movement, anterior open bite, posterior crossbite and reductions in the maxillary arch and changes in temporary and permanent tooth eruption (Figure 2., Figure 3., Figure 4., Figure 5.).[6, 7, 9, 16, 17, 20, 23, 24]

Figure 4. The scrotal tongue, sometimes with tongue diastasis, is often found in this syndrome.

Figure 5. Lateral or anterior open bite is often found and tongue interposition worsens and maintains open bite.

This hypotonicity is associated with ligament laxity, easily visible throughout the body. It induces hyper-flexible joints, which can compromise the periodontal ligaments.[20] Excess of
saliva on the labial commissure is also related to the muscle hypotonicity and can lead to irritation, cracking (angular cheilitis), aphthous ulcers and infectious conditions like candidiasis.[3, 24]

According to [Oredugba (25)], 51% of class I dental malocclusion and 47% of class III among 43 individuals with DS and only 5% of class III in the control group (individuals without DS), concluding that class III has a higher incidence in DS individuals than in the general population.

[Musich (26)] and [Soares K (27)] have concluded that class III is more frequent in DS individuals. Anatomically, the facial mid-third is underdeveloped but the mandible follows normal development (pseudo-progeny). This midface dysplasia also contributes to the narrow maxilla (Figure 5., Figure 6.).[7, 11, 18, 20]

Mandible measurements are not significantly different from normal subjects. However, a transverse expansion may occur due to lingual pressure.[20, 28] This intermaxillary discrepancy prevents the optimal intercuspal position to occur, which is needed to stabilize the mandible and the hyoid bone during mastication and swallowing.[16, 20]

Figure 6. Natural position of the tongue, resting against the palate, creating a favourable force vector to maxillary growth; the protruded tongue and its low position, no longer exercises the vector of expansive force on the maxilla; on the other hand, the maintenance of the open mouth increases the compression.

Anterior crossbite is primarily attributed to the anteroposterior deficiency of the maxillary arch development, resulting in a crossbite of the mandible, projecting the jawbone arch towards the front of the maxilla (Figure 5., Figure 6.).[5, 6, 26-29]

Dental anomalies are very common, both in the primary and permanent teeth and occur with an incidence five times greater in DS individuals than in general population (Figure 7.).[7, 23]

Anomalies in the number (fewer), size (smaller) and morphology (crowns may also be short, small and conical) and the timing of their development (late dentition) are constant features of this syndrome.[7, 23] In the primary dentition, the most commonly absent teeth are lateral incisors, while in the permanent dentition, third molars, second premolars and lateral incisors, in this sequence, are the most frequently missing teeth (Figure 7.).[3, 7, 20]

Patients with DS have complete tooth mineralization, delayed tooth eruption (six to eighteen months) changes in the sequence of eruption (mainly of the temporary teeth), high incidence
of impacted teeth (incisors and canines) and teeth agenesis. Microdontia, enamel hypoplasia, hypodontia of deciduous teeth and oligodontia are the most common dental anomalies. Structural abnormalities include taurodontia, peg-shaped teeth, fusion and germination. Canines are the most affected regarding shape and size.[3, 11, 20, 29, 30]

Figure 7. Delayed tooth eruption, compression and crowded teeth, microdontia, enamel hypoplasia, hypodontia of deciduous teeth and oligodontia.

3.2. Oral pathology

3.2.1. Caries

A majority of published studies have reported that people with DS have lower caries rates than people without DS, although several studies found that people with and without DS share the same caries rates, and some reported higher caries rates in those with DS.[7, 13, 14, 31] The differences herein described may be related to the control group used in each study: non-related healthy individuals, healthy siblings or other cognitive impaired individuals. The most commonly used indicator of caries experience is an index comprising disease and treatment markers, the DMFT (Decayed, Missing and Filled Teeth).[11, 12, 14] This index should be analysed together with factors such as a diet, frequency of snacking, social status, oral health in close relatives, dental awareness and past dental history. In studies of Areias et al. [11, 13, 14], the controls were sibling-matched, closest in age, in order to reduce the bias of factors like diet, social status and familiar oral health. In relation to DS, a more accurate assessment of caries experience risk is likely to be obtained by also examining the specific morphology. [32-34] The literature attributes the low prevalence of caries in individuals with DS to factors such as: eruptive pattern (teeth erupt later and so they are exposed to caries’ etiological factors for less time); high prevalence of bruxism (flatter occlusal surfaces facilitate self-cleaning and oral hygiene, eliminating food debris that could be adhered to the sulcus and serve as a substrate for oral bacteria).[35]; dental morphology (microdontic teeth and diastema allow an early detection of caries with a simple clinical examination and without a radiological examination); salivary composition and differences in the composition of the microbiota.
Saliva plays a crucial role in the defense against periopathogenic and cariogenic bacteria in the oral cavity and the equilibrium between demineralisation and remineralisation of enamel and dentin. Consequently, the protective effects of salivary constituents, salivary flow rates and the salivary buffering capacity are essential. It is agreed almost universally that the salivary flow rate is significantly reduced in individuals with Down syndrome. Also, Siqueira et al. studied the whole unstimulated and stimulated saliva of people with Down syndrome for 2–5 years and found that salivary buffering capacity of these individuals is increased compared with healthy individuals of the same age. Regarding cariogenic microorganisms, it was reported that in adults and in children with trisomy 21, the lower caries rates was associated with lower levels of *Streptococcus mutans* in saliva. Besides the microbial factors, various salivary components are connected with the prevalence of caries. The reduced salivary flow in DS individuals may be related to the existence of changes in the secretory function of the salivary glands of individuals with trisomy 21 and/or hypotonic muscle. Regarding the pH of the saliva of individuals with trisomy 21, there are some studies in which the values are higher than ordinary people, while others have observed similar or lower values. There are several factors that could influence the results described in the literature, such as the analyses method (as used by each researcher), age of individuals, geographic location, food habits and time of collection. The buffer capacity of saliva is the ability to prevent changes in the pH of the environment (i.e. the buffer system is the major determinant of salivary pH). Salivary amylase is an important enzyme in the oral cavity. These authors showed low enzyme activity in individuals with trisomy. Areias C. et al. found in respect to α-amylases, the absolute salivary concentration as well as salivary secretion rate was similar between DS and sibling controls. IgA is the predominant immunoglobulin in saliva and which is produced by plasma cells of the salivary glands. The IgA prevents microbial adherence, which can also justify reducing the prevalence of caries in children with Down syndrome. A decrease in the levels of IgA in children with trisomy 21 (although not statistically significant) is explained by the onset of a state of immunodeficiency. Other studies have shown differences concerning the IgA (higher in the group with Down syndrome). Siqueira et al. showed that individuals with trisomy 21 have a greater concentration of protein in saliva, a fact that may be related to the low flow of saliva. Other ions analysed as zinc, magnesium, phosphorus and calcium showed no statistically significant differences between the group with Down syndrome and control group.

### 3.2.2. Periodontal disease

The Gingivitis and Periodontitis are the two main subgroups of periodontal diseases affecting a high percentage of the world population and is therefore a serious public health problem. Dental practitioners are challenged by the high incidence of early-onset aggressive periodontal disease in DS; these patients have higher levels of periodontal pathogens and periodontitis-
associated interproximal bone loss. The complex anatomy, physiology, immunology and microbiology underscore the need for further investigation in specific areas related to dental treatment of these patients.[8, 48, 49] Gingivitis and periodontal disease start early in life, and the severity of these diseases increase with age. The prevalence of periodontal disease in adolescents with DS is 30% to 40%. Consequently, a large number of young people with DS lose their permanent anterior teeth in their early teens. In individuals in their thirties, the incidence of periodontal disease rises up to nearly 100%.[8] Cichon et al. [8] suggested that severe periodontal destruction that occurs in individuals with DS is compatible with aggressive periodontitis. Thus, periodontal disease is the most significant oral health problem in people with DS. The increased incidence of periodontal disease can be explained by the muscular hypotonicity and its consequences, dentoalveolar joint laxity, lack of understanding of the needs of oral hygiene, impaired dexterity, compromised immune system, low T cells count and leukocyte dysfunction. [31, 47, 48, 50, 51] Nutritional deficiencies can have an impact on periodontal health. Many studies have shown that there are a lot of nutrients that can have a negative impact on periodontal disease, but its wanted some vitamins, metals, antioxidants and proteins. [8, 49] By the time, only the deficiency in vitamin C and calcium and hyperlipidemia demonstrated significant results of increase risk in progression of the periodontal disease.[8, 49] Periodontal disease is induced by a complex microbiota, such as *Tannerella forsythia* and *Treponema denticola* (together called the red complex), which triggers intense inflammatory reaction. DS individuals demonstrate a high prevalence of periodontal disease compared with those who are otherwise chromosomally normal (euploids). [1, 49] Clinical parameters after non-surgical mechanical periodontal treatment were similar in diseased and healthy sites, independent of the genetic background.[10, 49] Diseased sites of DS and control patients harboured similar levels of *P. gingivalis* and *T. forsythia* at baseline, but significantly higher levels of *T. denticola* were found in DS patients. Increased levels of *P. gingivalis* at healthy sites were found in DS individuals. Non-surgical periodontal therapy decreased the levels of red complex microorganisms and improved the tested clinical parameters of diseased sites in both groups. However, the levels of red complex bacteria were higher in diseased sites of DS patients after the periodontal treatment.[10, 49] Although the mechanical periodontal treatment seemed to be effective in DS subjects over a short-term period, the red complex bacteria levels did not decrease significantly in diseased sites, as occurred in controls. Therefore, for DS patients, it seems that the conventional non-surgical periodontal therapy should be improved by utilising adjuvant to reduce the presence of periodontal pathogens.[10, 49]

### 3.2.3. Bruxism

Bruxism is quite common in this population, initiating at very young age, and often persisting throughout life. [5] The increased frequency of bruxism in DS population is associated to chronic anxiety, underdeveloped nervous system, malocclusion and TMJ dysfunction due to hypotonicity, hyper flexibility and laxity of the supporting ligaments. Initially, it creates an erosion of the pits and fissures of the occlusal surfaces (that become smoother), enabling self-cleaning with tongue and facilitating oral hygiene. [5, 11, 14] On the other hand, it can lead to
an overloading of the supporting tissues and subsequent teeth fractures. These patients should be monitored through a regular program to allow an early diagnosis of the problems related to bruxism. [5, 14] In cases where bruxism is diagnosed, it is necessary to reposition the jaw and to decrease teeth grinding. Unfortunately, patients with a severe bruxism are the ones with more neurological problems and the treatment may not be successful.[5, 52]

3.3. Preventive and therapeutic intervention

This section intends to guide clinicians regarding the most important preventive measures in this population and also suggest the best approaches to improve the most common oral pathologies in DS individuals.[48] In this regard, oral hygiene and habits will be discussed and specific methods such as adapted DS pacifiers and rapid maxillary expansion will be suggested. According to Areias C. et al., [11, 14] children with trisomy 21 start visiting the dentist before his brothers, probably due to increased parental concern. This may also explain the lower rate of DMF index found, considering that parents are first alerted to the need for effective oral health services.[11, 14] An appointment with the dentist regularly is important at all ages, but is essential in childhood and adolescence. In the study of Macho V. et al., [6, 53, 54], the prevalence of occlusal anomalies found in mixed dentition was higher in the DS group than in their siblings. To improve the oral health of people with DS, health programs must incorporate intervention methods to control oral hygiene, to make Fluor and sealants application and to prevent and treat malocclusions as early as possible.[6, 53, 54] Therefore, there’s a need to do a complete radiographic examination to identify hypodontia and other anomalies; occupational therapy to strengthen orofacial musculature; early mixed dentition orthodontic examination to screen for habits; and airway assessment, including consideration of tonsillectomy, palate expansion and tongue crib appliances (Figure 7., Figure 8., Figure 9. and Figure 10.). [16, 20, 24, 28, 55] Patients with DS should not be excluded from the general population with regard to dental care.[30, 56] From the ethical perspective, dentists must accept the responsibility and commitment to contribute with their knowledge to improve the quality of life of these people. Though children with DS can be excellent orthodontic patients, orthodontic prognosis may be poor because of their learning disability, parafunctional habits and severe periodontal disease (Figure 7., Figure 8., Figure 9. and Figure 10.). [16, 20, 24, 28, 55] The possible treatments of DS include prevention, interception or correction of the anomalies. We may find several actions during the different phases of growth: in early ages, and in the absence of teeth; in the temporary phase of teething; in the mixed phase of teething; in the definite phase of teething, up to the adult age. Orthodontic, orthopaedic and surgical approaches are possibilities of treatment. Complementary and peculiar approaches may include diminution of the size of the tongue, alteration from its position and increase of the space for the tongue – increase of the maxilla. To increase the maxilla, we may use techniques that produce first the bone growth or we modify the position of the muscles to orient the bone growth. These techniques are complementary and may be used in different ages. Each DS person is unique and it is fundamental that we always make an individualised study (Figure 8.).
3.4. Palatal plates

To improve the suction, drooling and the chewing and secondarily to help the development of the language, Castillo-Morales [57-61] developed a plate that consisted of an acrylic plate with many strategically placed accessories that stimulate different areas of the tongue, cheeks and lips, awakening reflexes that changed positions of different muscle groups (Figure 9). The improvement of the health, face and the language favours the integration of the child with DS among the family and in society.[55] These plates have many benefits like give better respiratory characteristics, decrease in respiratory infections, improvement in sleep disturbance and improvement of bruxism. With the lingual re-establishment, it permits a better pronunciation of words and benefits aesthetically; secondly, it can even change the face of DS patients. The plate may be used for extended and repeated periods of the day, which contrasts with other stimulation methods (Figure 10.).[57-61] In selected cases, a palatal plate is an excellent complement to traditional speech therapy and the most dominant factor for succeeding is motivation. [57-61]

After 12 months of therapy, the mean duration of the factor "closed mouth" was significantly longer (p < 0.001) and "inactive protrusion of the tongue" significantly shorter (p < 0.001) in the test group than in the control group. The results indicate that in children with Down syndrome, palatal plate therapy may be a valuable complement to a training program for improving orofacial muscle function. It may be used as a prophylactic measure of the tongue protrusion.

Undesirable effects after the insertion of the plate can occur; for example, development of active avoidance of the plate with the tongue, which results in more pronounced tongue protrusion, no clinical reaction, immediate habituation to the plate, hyper salivation or more pronounced tongue protrusion after the suspension of the treatment, even if for a short period.[57-62] All these reactions were rare, but required fitting a new plate, or suspension of the treatment.

Due to the presence of a protruding tongue and a muscular hypotonicity, these children have oral–motor problems (seen during swallowing, chewing and sucking) and are mouth breathers (exhibit open bite). The use of an adapted pacifier could prevent these problems (Figure 9).[3, 7, 11, 20]
When teeth are erupting, the plate does not adhere to the palate. So, they take off the plate easily, which leads to stopping the usage of the plate for a period until the child is about 3 years old. When the device is omitted for a period of time in the early stages of treatment, it will result in a return to the pathological condition. It is important to notice that people that already use the plates on their patients, don’t refer major problems. Do not put plates if there is not a strong motivation by the parents. The motivation of the parents is fundamental.[57-62]

Due to fear of plate swallowing and child choking, the plate developed by Castillo-Morales did not allow a prolonged use and required adult supervision [58]. Thereafter, Andrade C. et al [20, 63] developed a modified, pacifier-shaped device, that provide greater security, prolonged usage time (even at night), less concern by caregivers, and better acceptance by society. The results of its use show an improvement in aesthetics with less tongue protrusion and higher time of closed mouth when compared to the traditional Castillo-Morales plate (Figure 11., Figure 12., Figure 13.).[12, 20, 58, 63]

### 3.5. Fixed appliances

We can place fixed appliances in preschool age, if the child is cooperative. Problems like anterior or posterior crossbites should be corrected as soon as they are found. Fixed appliances have better results because we can have a greater control of their use, which does not happen with removable appliances, which can either be used or not. We may expand the maxilla to gain more space to the tongue and in DS we prefer to do it expanding from the apical base, to
obtain an orthopaedic effect. At certain ages, the effects of maxillary disjunction may be more favourable, which has to do with the overall growth of the jaws and the individual himself (Figure 13., Figure 14.). [20, 28]

Advantages of the device

- Fixed appliance
- Easy to clean
- Acts in a short time
Does not need intense cooperation from parents or from the children.

Figure 13. How to remove crossbites expanding from the apical base – the occlusal radiograph shows the disjunction of the maxilla; the superior incisors separated and the palatine suture opened.

Figure 14. Effect of the maxillary disjunction in DS patient that presents bilateral and anterior crossbite. We open 0.3 to 0.5 mm a day, for 2 to 4 weeks.

Cutting this cycle of mouth breathing and increasing the area for nasal ventilation can provide a solution for some breathing difficulties, a reduction of tongue protrusion and drooling, as well as the high incidence of repeating respiratory infections and the high rates of compression and crossbites.[20, 28]

After the maxillary disjunction and in respect to clinical symptomatology, we may conclude:

Nasal symptomatology:
• Global improvement of cases and controls, but in that the cases show up, markedly, a minor incidence of rhinorrhea: "went the first summer in that my son had the nose completely without secretions".

Otologic symptomatology:

• Smaller evidence in the resolution from the serous otitis, that persisted in the cases and in the controls.

Rapid maxillary expansion produced a significant augmentation of nasal volume in children who had been treated (p<0.05) compared to the control group; these results were stable through the period of retention.

The rapid maxillary expansion (disjunction) in infants with Down syndrome:

• Diminishes the number of infections of the superior airways.
• Improves nasal permeability.
• Improves several parameters analysed by speech therapists.
• Tongue Mobility
• Articulation
• Intelligibility

Figure 15. Patient with Down syndrome that present a bilateral crossbite (photographs extra and intra - orals, models and X rays).
Rapid maxillary expansion (RME) increased space for the tongue in the oral cavity (Figure 15., Figure 16., Figure 17.). This in turn results in a reduction of tongue protrusion and drooling. These aspects, in addition to the enlargement of the maxilla, often lead to an aesthetic improvement noted by the parents of the RME children. By placing the tongue in its normal position, the speech is improved, and so the aesthetics and self-confidence of the individual, facilitating his integration in society. This procedure may be carried out concomitantly with other surgical procedures for upper airway obstruction, sleep apnea and chronic otitis media with effusion. Rapid maxillary expansions give these patients a better airway, if used (Figure 15., Figure 16., Figure 17.). It is important to make exercise routines and teach these patients to use this new airway, increasing attention and activity, and leading to a better general development, better general health and less hours of work lost by the family. The indications should be accurate. The effect is similar to the infants from the general population. The use of this device should be included in the suggestion to medical and connected Associations of parents of Down’s syndrome children.

Figure 16. In less than one month, they obtain an increase from the apical base sufficient for eliminating the bilateral crossbite and the compression of the maxilla; this helps to facilitate the nasal ventilation.

We should not be afraid to use facial masks or other orthodontic devices because these patients are very supportive, and we should encourage all dentists to treat these patients.

We cannot forget that all cases must have an appropriate fixed orthodontic contention, in most times for life. The orthodontic retention phase minimises unwanted dental movements and maintains the corrections, and in these cases, most of the times, a fixed contention is necessary because hypotonia and deleterious habits are very dangerous for the stability of the correction (Figure 18., Figure 19., Figure 20., Figure 21.). [20, 28]
Immediately after rapid maxillary expansion; in addition to an aesthetic improvement observed by all parents, the beneficial effects of rapid maxillary expansion include better ventilation and drainage of secretions, which lowers the upper respiratory infections such as adenoiditis, tonsillitis and otitis verifying still an improvement of sleep apnea, decreased nasal obstruction and tongue protrusion.

Facial mask may be used if necessary.
4. Conclusion

Patients with Down syndrome present peculiar orofacial features that, when not corrected, may interfere with their physical, psychological and social development. Children with this syndrome have a high risk of developing malocclusion and periodontal problems, and these should be the main concerns in their treatment needs. When planning the dental treatment of patients with Down syndrome, dental practitioners should always consider their general health, in order to achieve a holistic and interdisciplinary approach. Nevertheless, there is a need to improve the oral health services available to individuals with DS, to further investigate the interrelations between all their health problems, and to provide a higher level of information to parents of DS.
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Figure 21. The crossbite may be present in primary dentition. If we have cooperation, we must correct the temporary teeth and not wait for the permanent teeth to get the treatment.
The authors declare that they have no conflict of interest.
Cristina Areias, Benedita Sampaio-Maia: responsible for the conception and design.
Cristina Areias, Benedita Sampaio-Maia, Viviana Macho and Ana Norton were responsible for the data collection and manuscript redaction.
Benedita Sampaio-Maia and Paula Macedo were responsible for the critical revision of its contents.
David Casimiro de Andrade was responsible for graphics and photos and the critical revision of its intellectual contents and final approval of the version to be published.
All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this research paper.

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