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INTRA AND EXTRABUCCAL ASPECTS OF MIXED VASCULAR MALFORMATION IN CHILDREN

ASPECTOS INTRA E EXTRABUCAIS DE MALFORMAÇÃO VASCULAR MISTA EM CRIANÇA

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ABSTRACT

Vascular anomalies are disorders of endothelial cells that can affect capillaries, arteries, veins and / or the lymphatic system. They are classified as "vascular tumors" or "vascular malformations". Vascular malformations are subdivided into capillary, lymphatic, venous, arteriovenous and mixed malformations according to the type of vessels affected. The aim of the present study is to report a case of a patient with mixed vascular malformation (veno-lymphatic) and to describe the dental planning and treatment carried out. Male patient, 7 years old, referred for dental evaluation. The mother reported that the patient was undergoing medical treatment at the hospital for presenting "hemangioma and lymphatic vascular malformation" in the oral region. During the clinical examination, veno-lymphatic vascular malformation was observed on the oral floor. The child reported difficulty in performing oral hygiene due to the injury, and several caries lesions were found. Dental treatment consisted of dental restorations, sealants and extraction of primary teeth. The treatment of mixed vascular malformation was performed with a sclerosing solution (OK-432). The oral health care of patients with vascular malformations should include oral hygiene instructions, supervised brushing and guidance on the use of soft brushes to avoid injury to the affected areas.

Keywords: Lymphatic Malformation. Mixed vascular malformation. Vascular anomalies.

RESUMO

Anomalias vasculares constituem distúrbios de células endoteliais que podem afetar capilares, artérias, veias e/ou sistema linfático. São classificadas como "tumores vasculares" ou "malformações vasculares". As malformações vasculares são subdivididas em malformações capilares, linfáticas, venosas, arteriovenosas e mistas de acordo com o tipo de vasos afetados. O objetivo do presente estudo é relatar um caso de um paciente com malformação vascular mista (veno-linfática) e descrever o planejamento e o tratamento dentário realizado. O paciente do sexo masculino, 7 anos, foi encaminhado para avaliação odontológica. A mãe relatou que o ele estava em tratamento médico no hospital por apresentar "hemangioma e malformação vascular linfática" em região bucal. Durante o exame clínico, foi observada malformação vascular veno-linfática no assoalho oral. A criança relatou dificuldade para realizar a higiene bucal devido à lesão, sendo encontradas várias lesões de cárie. O tratamento odontológico consistiu em restaurações dentárias, selantes e exodontia de dentes decíduos. O tratamento da malformação vascular mista foi realizado com solução esclerosante (OK-432). A atenção à saúde bucal de pacientes com malformações vasculares deve incluir orientações de higiene bucal, escovação supervisionada e indicação do uso de escovas macias para evitar lesões nas áreas já afetadas.

Palavras-chave: Anomalias vasculares. Malformação linfática. Malformação vascular mista.

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INTRODUCTION

Vascular anomalies are disorders of the endothelial cells that can affect the capillaries, arteries, veins and / or the lymphatic system. They are classified as "vascular tumors" or "vascular malformations" based on clinical, histological and biochemical differences (PERKINS *et al.,* 2010a; RASTOGI *et al*., 2020), with tumors being proliferative lesions and vascular malformations are due to a congenital anomaly of vascular morphogenesis (WASSEF *et al*., 2021). This classification was modified by the International Society for the Study of Vascular Anomalies (ISSVA, 2018). This new classification has important therapeutic and prognostic implications because for each category, there is a treatment (RASTOGI *et al*., 2020) Thus, understanding the natural history of a vascular anomaly is fundamental for the correct diagnosis and adequate treatment of these injuries by health professionals (BUCKMILLER; RICHTER; SUEN, 2010).

Vascular malformations are subdivided into capillary, lymphatic, venous, arteriovenous and mixed malformations according to the type of vessels affected (CARQUEJA; SOUZA; MANSILHA, 2018; DEKEULENEER *et al.,* 2020). Almost always benign, such vascular anomalies can involve any anatomical structure, being more common in the head and neck (GREENE, 2011, PUCCIA *et al.,* 2020), are present at birth and grow proportionally with the patient (SERONT; VIKKULA; BOOM, 2018; WIEGAND; DIETZ, 2021).

Venous malformation is slightly more common in females (PARK *et al*., 2019), does not spontaneously regress and can compress the adjacent normal tissues (SERONT; VIKKULA; BOON, 2018). They are always present at birth but are not always apparent due to the deep location, so they are sometimes discovered late since they grow as the child grows (SERONT; VIKKULA; BOON, 2018). They do not regress spontaneously and can compress the adjacent tissues (WASSEF *et al*., 2015), being the third vascular anomaly that most affects the head and neck, losing to infantile hemangioma and lymphatic malformations (EIFERT *et al*., 2000; RICHTER; BRASWELL, 2012). The most affected sites are the cheeks, labial region, neck, parapharyngeal space, submandibular triangle and masticatory muscles (SERONT; VIKKULA; BOOM, 2018; PARK *et al*., 2019).

The vascular malformation traditionally known as lymphangioma, specifically constitutes a lymphatic malformation due to the abnormal growth of the lymph nodes and consequently, the lymph is retained in the lymphatic vessels generating a soft and compressible swelling in the oral mucosa (YAITA *et al*., 2007; ELLURU; BALAKRISHNANAN; PADUA, 2014). Most of the diagnosed cases occurred before the age of 2 and were on the back of the tongue (BONET-COLOMA *et al*., 2011; BHAYYA *et al.,* 2015). Lymphatic malformation is not a pathology frequently found (CAGIGAL *et al*., 2007; YAITA *et al*., 2007; LARKIN *et al*., 2018), appears during childhood in 90% of cases (BONET-COLOMA *et al*., 2011; BHAYYA *et al*., 2015) and the incidence is 1: 2000–4000 for live births (PUCCIA *et al*., 2020).

Symptoms depend on the affected structures which may be swelling, airway obstructions, blindness, ischemia, pain, thrombosis and life-threatening bleeding (WIEGAND; DIETZ, 2021). The treatment of venous and lymphatic malformations depends on the size of the lesions, where small and asymptomatic lesions do not require treatment, only a follow-up (PUCCIA *et al*., 2020), but when they cause dysfunction or disfigurement, they need intervention, which can be local treatment or systemic, each with its risks and benefits, including cholerotherapy, surgery, laser and embolization (PUCCIA *et al*., 2020; WIEGAND; DIETZ, 2021). New therapies including Sildenafil, Propranolol, Sirolimus and the transfer of vascularized lymph nodes are emerging with new discoveries regarding the biology and genetics of these malformations (BAGRODIA; DEFNET; KANDEL, 2015).

Vascular malformations are a complex group of pathologies, presenting several clinical forms and treatment options (CARQUEJA; SOUZA; MANSILHA, 2018). Thus, for greater patient comfort, management by a multidisciplinary team is essential, including surgeons, pediatricians, nutritionists, psychologists and speech therapists (BAJAJ *et al.,* 2011), because when a cure is not possible, treatment must have the objective of controlling symptoms and improving the patient's quality of life (BAJAJ *et al*., 2011; CARQUEJA; SOUZA; MANSILHA, 2018).

The aim of the present study is to report a case of a patient with cervical-facial veno-lymphatic malformation and describe the dental planning and treatment carried out.

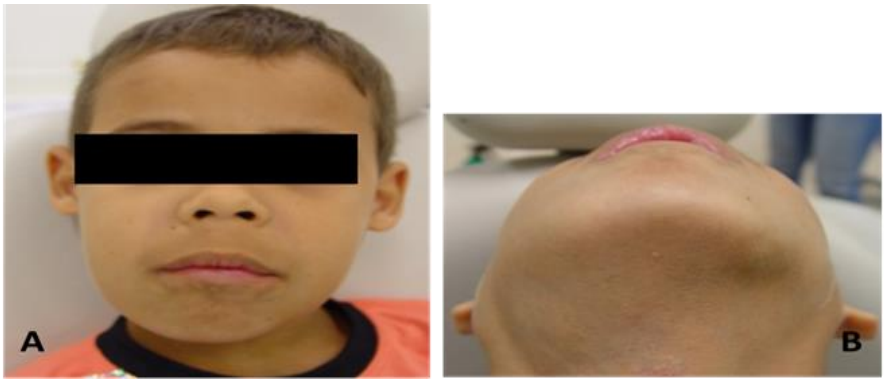
CASE REPORT

The seven-year-old male patient, born in Cerejeiras (RO, Brazil), was admitted to the clinic at the Human Resources Training Center Specialized in Dental Care for Special Patients, at the Ribeirão Preto School of Dentistry, University of São Paulo. Sao Paulo. The patient was referred to the service for evaluation and dental care by the Hospital das Clínicas of Ribeirão Preto, University of São Paulo (HCRP-USP), where he was under medical treatment for having a mixed vascular malformation in the cervical-facial region. At the HCRP-USP he underwent treatment with three doses of sclerosing solution, OK-432, two doses in 2009 and one dose in 2010. Currently, the patient is 15 years old.

During the anamnesis, the mother highlighted the enormous difficulty in finding dental care for her son due to the lack of trained professionals in view of the clinical aspect of the injury, the excessive size of the tongue and the child's uncooperative behavior.

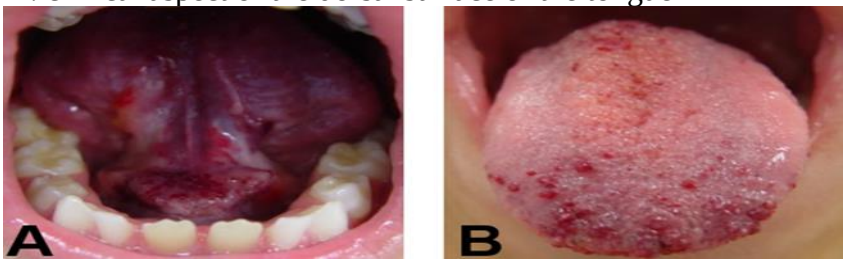
In the extra-oral clinical examination, cervical and facial asymmetry can be observed (Figures 1 A and B), but with reduced dimensions compared to the 5-year-old child before treatment with OK-432. In the intra-oral clinical examination of the soft tissues, an increase in the volume of the tongue was observed, characterized as a soft, lobulated, sessile mass, variable in terms of size, with a color varying between pink and purple red (Figures 2 A and 2 B). On intraoral clinical examination of the mineralized tissues, the presence of dental biofilm visible on the buccal and lingual / palatal surfaces of the upper and lower deciduous molars was observed due to the difficulty of brushing because of the increased size of the tongue and the burning sensation when using toothpaste. The presence of white spots on the cervical of the teeth was verified, indicative of active caries, characterizing the patient with high risk / activity to dental caries. Extensive cavitized caries lesions were observed in the maxillary central incisors and primary maxillary first molars. Restorations were not seen in both dental arches. Figures 3 A, B, C, D, E and F show the teeth before and after dental treatment.

Figure 1 - A- Front and cervical view - B of the 5-year-old child before treatment with OK-432



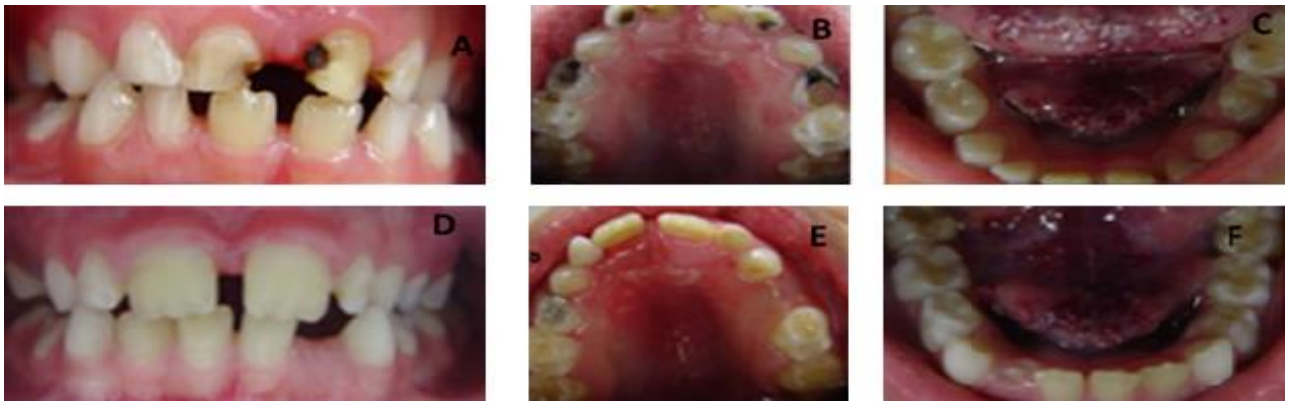
Source: the authors.

Figure 2 - A: clinical aspect of the ventral surface of the tongue; B: clinical aspect of the dorsal surface of the tongue



Source: the authors.

Figure 3 - A and D: frontal view of the maxillary and mandibular dental arches before and after dental treatment; B and E: occlusal view of the maxillary dental arch before and after dental treatment; C and F: occlusal view of the mandibular arch before and after dental treatment



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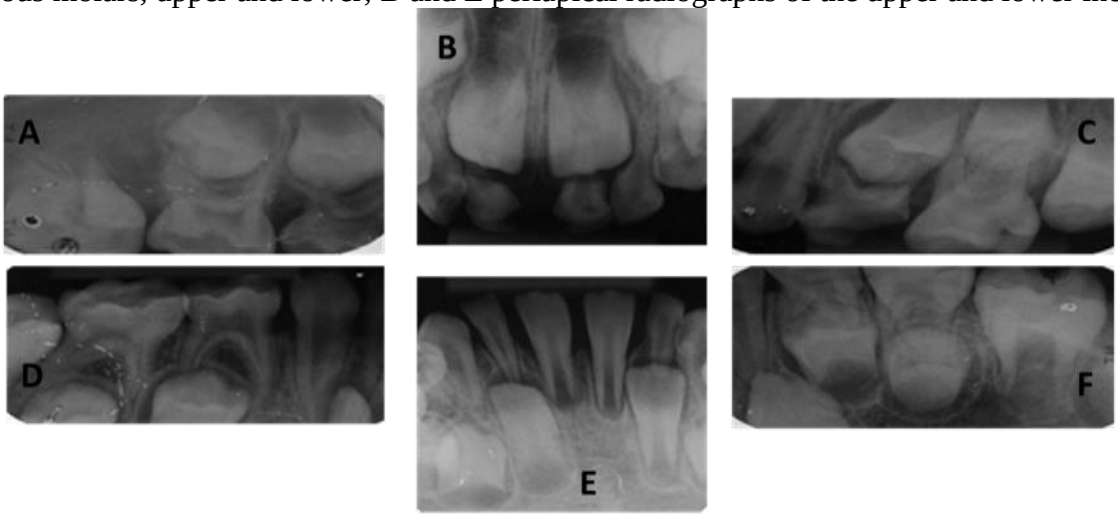
An initial radiographic examination revealed that the upper central incisors had advanced rhizolysis, and, like the left upper deciduous first molar, had extensive dental caries lesions (Figure 4 A, B, C, D, E, E, F).

Figure 4 - Initial periapical radiographs: A, D, C and F periapical radiographs of the right and left deciduous molars, upper and lower; B and E periapical radiographs of the upper and lower incisors



Source: the authors.

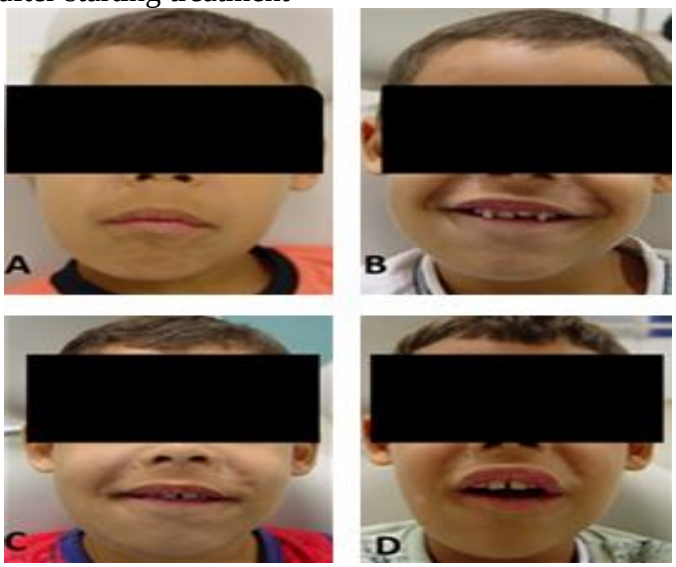
The treatment plan started with a focus on preventive measures, such as oral hygiene instruction, dietary advice and a discussion about the selection of toothpaste that would not cause the burning sensation described by the patient. Dentifrice, sensodine (Sodium Fluoride 1426 ppm and 5% Calcium and Sodium Phosphosilicate - NOVAMIN) were prescribed for the patient to test and evaluate the discomfort. In addition, the treatment consisted of professional prophylaxis and topical applications of 0.12% chlorhexidine gluconate (Periogard, Colgate-Palmolive, Kolynos do Brasil Ltda Division, Campo, São Paulo, Brazil) and neutral fluoride gel (Sultan Topex, DFL Ind. E Com. Ltda, Rio de Janeiro, RJ, Brazil). The purpose of this phase of treatment was to motivate and encourage the patient to perform oral hygiene so that he did not associate tooth brushing with pain.

The surgical / restorative treatment was carried out under local anesthesia and consisted of extraction of the deciduous upper central incisors and the left upper deciduous first molar; restoration with composite resin on the palatal faces of the deciduous upper lateral and upper left canine incisors on the occlusal surface of the upper right deciduous second molar and on the distal face of the upper left deciduous second molar, sealant on the palatal face of the upper right deciduous second molar

occlusals of the mandibular first deciduous molars, of the right mandibular second molar, of the left upper permanent first molar, of the left lower permanent first molar, on the occlusal and palatal surfaces of the right upper permanent first molar, restoration of Class II amalgam on the mesial and occlusal surfaces of the upper right deciduous first molar and preventive restoration on the occlusal surfaces of the lower left deciduous second molar and lower right permanent first molar.

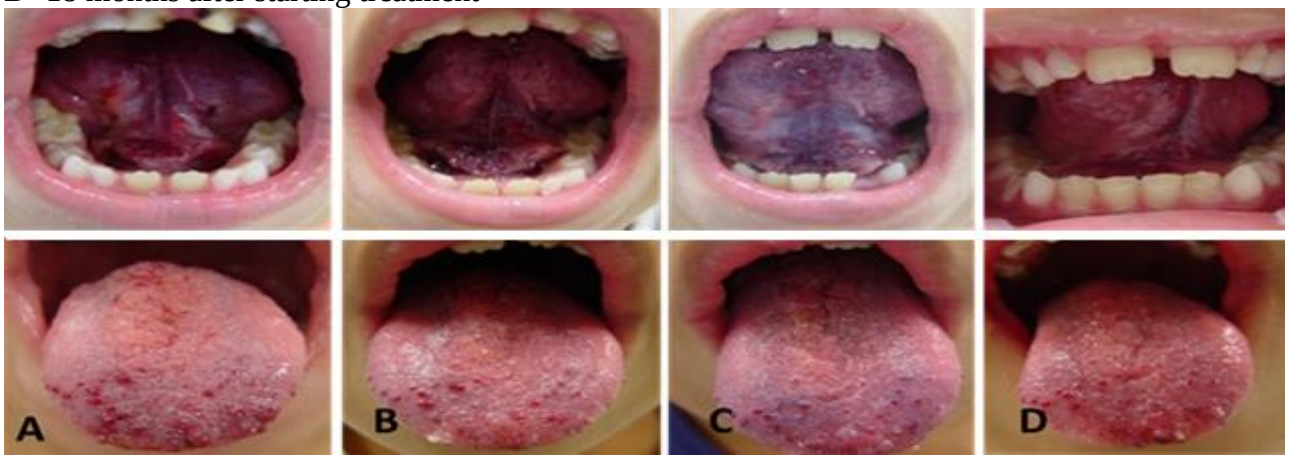
In the clinical and radiographic follow-ups, carried out every six months due to the difficulty of access given the distance between the clinic and the patient's residence (2,153 km), the restorative treatment was reevaluated, the removal of dental biofilm was monitored and the oral health was observed (Figures 3 D, E and F). In addition, discomfort in relation to the toothpaste was verified. Surgical tongue reduction was not a viable option because of the size of the lesion and, therefore, the patient was treated with medication. In addition, during these follow-up visits, it was found that there was no significant reduction in the size of his tongue and cervico-facial region (Figures 5 A, B, C and D and Figures 6 A, B, C and D).

Figure 5 - Extra-oral photographs showing the evolution of the lesion every six months of follow-up: A- initial; B- 6 months after the start of treatment; C- 12 months after starting treatment and D- 18 months after starting treatment



Source: the authors.

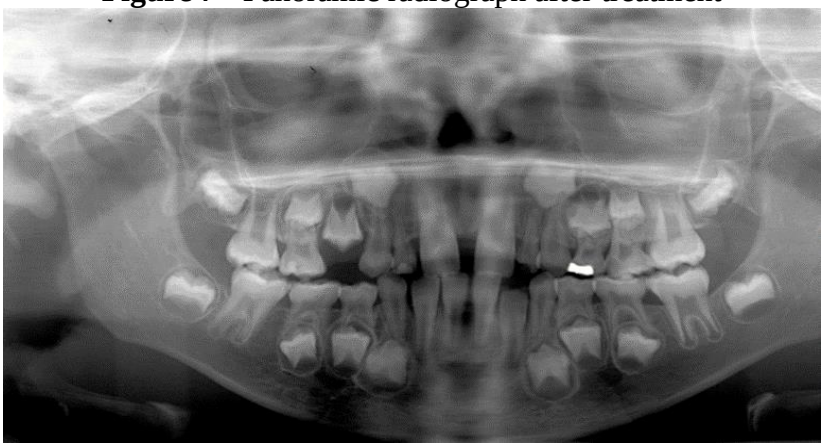
Figure 6 - intraoral photographs showing the evolution of the lesion every six months of follow-up: A- initial photograph; B- 6 months after the start of treatment; C- 12 months after starting treatment; D- 18 months after starting treatment



Source: the authors.

In the panoramic radiographic examination, performed after surgical / restorative treatment, it was found that the patient had agenesis of the right and left upper lateral incisors and permanent upper and lower molars. In addition, other changes were detected, probably due to the pressure produced by the size of the tongue, such as anterior open bite and protrusion of the lower anterior teeth (Figure 7).

Figure 7 - Panoramic radiograph after treatment



Source: the authors.

The patient continues to be followed up with the head and neck surgery team to assess the regression of the lesion and with the team of dental surgeons in order to prevent the occurrence of new carious lesions.

DISCUSSION

For a long period of time, there was no consensus regarding the terminology and classification of vascular anomalies, resulting in a negative impact on the creation of conducts, as well as on therapeutic indications and comparisons. In 1996, the International Society for the Study of Vascular Anomalies (ISSVA) divided vascular anomalies into two categories: vascular tumors and vascular malformations. Thus, with an internationally accepted diagnostic classification, protocols and standardization of treatments can be instituted (ENJOLRAS; WASSEF; CHAPOT; 2012). This classification underwent some modifications that were approved at the 20th ISSVA Workshop in Melbourne in April 2014, and had its last revision in May 2018 (ISSA, 2018). After these changes, some studies were revised and some diagnostic errors were found, where cavernous hemangiomas were actually venous malformations (LIBERALE *et al.*, 2020).

The incidence of vascular malformation varies from 1: 2000–5000 and 1: 2000–4000 for lymphatic malformation (BAGRODIA; DEFNET; KANDEL, 2015; SERONT; VIKKULA; BOOM, 2018). Since 75% of lymphatic malformations are found in the cervico-facial region (SCHOINOHORITI *et a*l., 2012), macroglossia and excessive jaw growth may occur (PERKINS *et al.*, 2010b; CHEN *et al.*, 2020).

Venous malformations do not regress spontaneously and can constrict adjacent normal tissues (WASSEF *et al.*, 2015). It is the third most common anomaly that affects the head and neck region (EIFERT *et al*., 2000; RICHTER; BRASWELL, 2012). In this report, the veno-lymphatic malformation was located on the tongue, and the patient complained of burning sensation when using the air jet during the dental procedure, had restricted food since he did not drink acidic foods and drinks, did not tolerate the use of dentifrice and, therefore, had difficulty brushing and consequently, a large number of caries lesions in the maxillary arch, unlike a case described in the literature, in which the patient presented caries lesions only in teeth of the mandibular arch (QUEIROZ *et al*., 2006). It is believed that the justification for the non-occurrence of caries lesions in the lower arch

was the fact that the tongue is bulky covering the dental surfaces, thus protecting the teeth against carious injuries.

In view of this situation, it was adopted as clinical conduct to perform absolute isolation with a rubber da, in the face of dental treatment, care not to touch areas affected by the lesion with instruments, and other additional guidelines regarding strict oral hygiene with a brush containing soft bristles and the amount of toothpaste that should be placed on the bristle.

Some deformities that reach the mandible due to the exaggerated size of the tongue, reported in the literature (QUEIROZ *et al*., 2006), were not found in the reported case, such as elongated body and branch of the mandible, however, other changes such as anterior open bite and protrusion of the lower anterior teeth were also observed.

Regarding treatment, in the present case, the patient presented an involution in relation to the drug treatment of the lymphatic vascular malformation.

Lymphatic malformation is not a lesion frequently found (CAGIGAL *et al*., 2007; YAITA *et al.,* 2007; SEQUEIRA, 2016). According to several investigations, the most common location for lymphatic malformations is the back of the tongue (YAITA *et al.,* 2007; BONET-COLOMA *et al*., 2011; BHAYYA *et al.,* 2015; SEQUEIRA, 2016), being more prevalent in Caucasian women (BRENNAN; MILLER; CHEN, 1997). In this case report, the patient had the lesion located in the cervico-facial region and tongue and was male.

Among the treatment options for Lymphatic Malformation, early surgical intervention is recommended to prevent overgrowth of the lesion and expansion into the adjacent tissues. However, complete surgical removal may not be possible for extensive lesions located around vital structures (SEQUEIRA, 2016). In these patients, the treatment of choice could be partial resection, however, this would generally result in recurrence of the lesion (JIAN, 1997). In this sense, alternative therapies have been proposed for these patients. Among them are irradiation of the affected area that has been abandoned due to the risk of malignancy (ORVIDAS; KASPERBAUER, 2000), and sclerotherapy or intralesional therapy with steroids and / or chemotherapeutic agents (ELLURU; BALAKRISHNAN; PADUA, 2014).

Although studies report that the treatment of patients with Lymphatic Malformation constitutes a challenge due to the potential to generate recurrent infection, and, thus, involvement of the upper airway, difficulty in swallowing, interference with the development of normal speech and an anti-aesthetic aspect (LUZZATTO *et al*., 2000), the child in the present report received drug treatment from an intralesional injection with an OK-432 sclerosing solution (Picibanil, Chugai Pharmaceuticals Co., Tokyo, Japan), a freeze-dried mixture of Streptococcus pyogenes and penicillin G potassium (CAGIGAL *et al*., 2007), which despite promising results, have been reported (MELLO-FILHO; TONE; KRUSCHEWSKY, 2002; YAITA *et al.,* 2007). The patient in the case did not show total lesion regression.

The mechanism of action of OK-432 sclerotherapy is still not well understood. It is believed that an inflammatory reaction caused by OK-432 would increase the number of macrophages and neutrophils inside the lesion, stimulating them to produce cytokines that increase the endothelial permeability of the lymphatic malformation, thus accelerating the drainage of the lymphatic fluid and causing a reduction in the size of the lesion (OGITA *et al*., 1987; BONET-COLOMA *et al.,* 2011). The only adverse reaction observed with the administration of OK-432 was the presentation of low fever by some patients (MELLO-FILHO; TONE; KRUSCHEWSKY, 2002), not observed in the case patient. Most injuries were treated with surgical resection (GRASSO *et al*., 2008; BONET-COLOMA *et al*., 2011), unlike the treatment instituted for the patient in question since it would cause unacceptable aesthetic and functional damage in a patient of a benign, painless lesion, which although it had a bulky appearance, airway involvement was not observed. However, the patient was complex with aesthetics and the person responsible for the child complained about the bulky and irregular aspect of the tongue, which could compromise social life and future relationships. Above all, the mother's main complaint revolved around the difficulty of finding a dental surgeon capable of caring

for her child, given the challenges of treatment, thus interfering even more in the child's quality of life.

CONCLUSION

Patients with mixed vascular malformation may have aesthetic deficiencies, speech disorders, breathing problems, mandibular deformities and even an increased risk of dental caries since an increase in the volume of the tongue, as well as its partial immobility and vulnerability to substances such as dentifrices, make it difficult, for example, to remove dental biofilm.

Careful and long-term medical and dental follow-up is necessary to assess the regression of the lesion and prevent the occurrence of new caries lesions, bearing in mind that the multidisciplinary approach to the treatment of veno-lymphatic malformation must prioritize the patient's quality of life.

It is essential to emphasize that the dental care and treatment of these patients should not be denied or avoided since it does not require any special skills, but, on the contrary, it must be carried out with some additional care, such as the use of a rubber dam in order to avoid, for example, the unpleasant burning sensation described in that report, as well as to facilitate the performance of restorative procedures, but mainly to avoid any inadvertent injury to the tongue. In addition, it is highly recommended to develop a preventive program for such a patient based on strict oral hygiene instructions, supervised brushing and guidance on the use of soft brushes, thus avoiding injury to other areas.

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