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NEUROFIBROMATOSIS TYPE 1, VON RECKLINGHAUSEN DISEASE: CASE REPORT

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ABSTRACT

Neurofibromatosis is an autosomal dominant genetic disorder classified as one of the most frequent neurocutaneous syndromes. Surgical interventions should be performed when the function is compromised due to the presence of tumor or for aesthetic reasons. The aim of this study was to report the clinical and radiographic aspects of Neurofibromatosis type 1 diagnoses (NF1) and therapeutic procedures. Male 10-year-old leucoderma patient sought care at the Stomatology Clinic of a University Center, reporting increase in volume in the hard palate region. After careful examination, the clinical condition observed was suggestive of NF1, confirmed by histopathological examination, obtained through incisional biopsy. Total excision of the lesion was performed under general anesthesia and use of obturator palatal plate, with the primary purpose of protecting the surgical site, providing more comfort to the patient. After 18 months of proservation, the patient's recovery was observed considering the relative comfort in face of the interventions performed and without clinical signs of injury recurrence. According to data obtained in this study, the therapeutic method of excision through total lesion enucleation was quite effective. The use of the obturator palatal plate provided substantial postoperative comfort and adequate wound healing, attenuating the possibilities of post-operative complications.

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INTRODUCTION

Neurofibromatosis is a disease of autosomal dominant genetic origin, classified into three types: neurofibromatosis type 1, neurofibromatosis type 2 and schwannomatosis. NF1 is the most frequent, caused by the defect of a single gene, which especially affects the peripheral nerve sheath, whereas NF2 and schwannamatosis are more rare forms, affecting the central nervous system (Souza *et al*., 2009). NF1 has high incidence, affecting approximately 1:2.600/3.000 or 1:7.800 live births (Marques and Veronez, 2015). German pathologist Friedrich Daniel Von Recklinghausen in 1882 described the pathology, proving the nervous origin of tumors (Korf and Rubestein, 2005). In approximately 50% of cases, NF1 is genetic, the other 50% have no family history, which suggests an increase in new mutations (Friedman, 1999) with no predilection for sex and inherited from autosomal-dominant with complete penetrance (Souza *et al*., 2009). The National Institutes of Health Consensus Development Conference of the USA determined diagnostic parameters for neurofibromatosis, pointing out that for the patient to be diagnosed with the disease, he/she must present at least two of these changes: six or more café-au-lait spots, with more than 5 mm in the largest diameter in pre-pubertal individuals, and more than 15 mm after puberty; two or more neurofibromas of any type or one plexiform neurofibroma; axillary or inguinal freckling; optic nerve tumor; two or more Lisch nodules; sphenoid wing dysplasia and cortical dysplasia of long bones, with or without pseudoarthrosis and first-degree relative affected by the disease (Gutmann, *et al*., 1997; Monghini *et al*., 2001; Oliveira-Filho *et al*., 2002; Vazquez and Lopes, 1998). Neurofibromas are characterized by small, solitary or multiple papules or nodules that can occur in any region of the body, most common in the skin, with preferential findings in trunk

and extremities, and in the oral mucosa of adults (Al-Otibi and Rutka, 2006; Melo *et al*., 2004). Its dimension is variable, being able to measure from 1 millimeter to several centimeters, and its number reaches up to 9000 in a single individual, and its consistency varies from flabby to firm to palpation and are usually sessile (Cunha and Barboza, 2002). The oral cavity can be affected in any region and may even involve more than one location. Lesions can be solitary, multiple, plexiform or intraosseous, and can appear unilaterally or bilaterally (Simonato *et al*., 2006). In the oral cavity, the most common sites are tongue, cheek mucosa and vestibule (Lermem *et al*., 2009). Examining changes in dental position, jaw deformations and malocclusions in patients with NF1, it was concluded that these signs are strongly related to the existence of plexiform neurofibroma originating from the trigeminal nerve, with changes in the amount of dental elements, molar retention and aplasia of second lower molars (Friedrich *et al*., 2003).

Radiographically, neurofibroma in the oral cavity shows radiolucency in the affected region, resulting from intraosseous defects caused by neurofibroma, as well as bone asymmetry (Powell *et al*., 2006). Important radiographic evidence is the visualization of the bilateral thickening of the mandibular canal, similar to the enlargement of the mandibular foramen in bell-mouth shape, self-named "blunderbuss foramen" (Lermem *et al*., 2009). Greater peculiarities of the size of tumors can be obtained through computed tomography and magnetic resonance for surgical purposes, the second has been priority (Curtin and McCarthy, 1997). The differential diagnosis is associated with syndromes that have pigmented spots, such as Peutz-Jeghers and McCune Albright syndrome and the Addison's disease (Monghini *et al*., 2001). Neurofibromatosis treatment depends on the clinical condition of the case investigated, requiring several other specialists to treat the disease (Oliveira-Filho *et al*., 2002). However, it indicates that when the function is compromised, corresponding to the presence of the tumor or due to aesthetic problems, surgical intervention must be performed; however, the tumor may frequently show recurrence. Furthermore, surgical treatment can stimulate the development of the lesion and increase the risk of malignancy (Simonato *et al*., 2006). Another technique adopted is laser with carbon dioxide or dermabrasion, which has become a satisfactory technique, mainly for extensive injuries. Chemotherapy is another option, which is usually well accepted by patients, although it is only indicated in cases where other treatments have not been effective (Neville *et al*, 2004).

Another form of treatment is the psychological care of patients, aiming at their well-being and mental health, where genetic counseling should be performed in an attempt to minimize problems (Freitas *et al*., 2006). Since it is a disease which transmission can be hereditary, the greatest problem is the relationship of parents generating their children with the same syndrome; however, there is a technique that makes the selection of embryos of genes without mutations using the *in vitro* fertilization method, which is one of the alternatives for parents not to transmit the disease to their descendants (Marques and Dinis, 2013). Finally, it is worth mentioning that, currently, there are no reports of a cure for this disease; however, monitoring is important for possible prevention of complications that may emerge (Marques and Veronez, 2015). In this context, the aim of this work was to emphasize the diagnosis and respective treatment of neurofibroma of the hard palate, instituting therapeutic approaches that provide resolvability and comfort to patients with this syndrome.

Case Report

Male 10-year-old leucoderma patient sought the Stomatology Clinic of a University Center reporting an increase in volume in the region of the hard palate. During anamnesis, the patient's mother reported that he had difficulty speaking and drooling. On extra-oral clinical examination, multiple "café-au-lait" spots spread throughout the body (Figure 1) were observed, which have been progressively appearing since birth, according to mother's report. These spots presented slow growth, without symptoms, bothering the patient due to their aesthetic character.

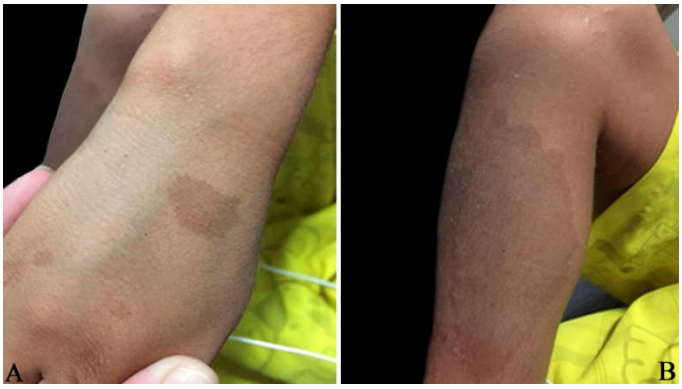

Figure 1. "Café-au-lait" spots located on the skin

The patient also showed some subcutaneous nodules, measuring from 2 to 20mm throughout the body, concentrating mainly on the forearms and back. Upon intraoral examination, a nodule located in the right region of the hard palate measuring approximately 2 cm in its largest diameter was observed (Figure 2), with mucous-like color and without ulceration areas, with evolution time of approximately two years. In the family history, it was found that the patient's mother had cutaneous nodules and "café-au-lait" spots, which were scattered on legs, arms, back and chest. On tomographic examination, an expansive lesion was observed in the region of the direct hard palate, without causing bone and/or root resorption, the lesion extended from the region of element 21 to element 55.

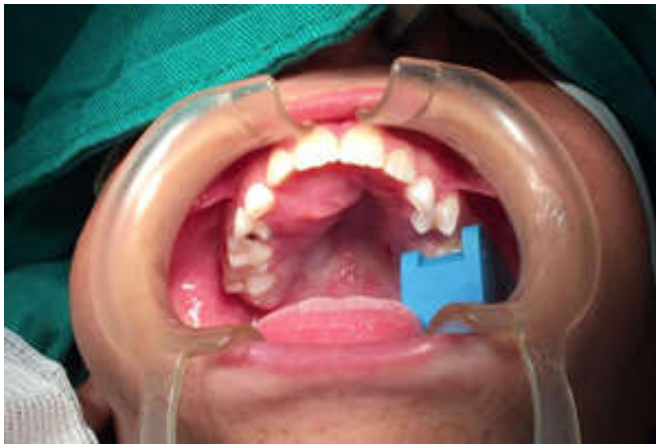

Figure 2. Intra-oral clinical examination evidencing a nodule located in the right region of the hard palate measuring approximately 2 cm diameter

An incisional biopsy of the oral nodule was performed and the anatomopathological examination showed subepithelial fusocellular proliferation without atypia, compatible with clinical diagnosis of neurofibroma. Molding was performed for the manufacture of an acrylic resin obturator palatal plate that will serve to protect the surgical area in the immediate postoperative period after lesion enucleation, avoiding mechanical trauma and surgical exposure of the operated region, which can cause scar delay and acute conditions of postoperative pain. In the plaster model, the lesion area was demarcated (Figure 3A) and wear was performed using maxicut drill in a straight piece, where there was an increase in volume, being later sent to the laboratory for the confection of the obturator plate (Figure 3B).

3-0 silk thread in the form of a mesh were performed to promote hemostasis, and after suture, the obturator palatal plate was installed to protect the surgical wound (Figure 4C). The removed specimen was sent for histopathological analysis and the initial diagnosis of neurofibroma was ratified. Ten days after surgery, the patient returned for reevaluation, and intra-oral clinical examination revealed a large ulcerated area (Figure 5A), but the patient did not report pain processes, being advised to perform local cleaning and mouthwashes with 0.12% chlorhexidine digluconate 2 times a day. After 30 days of proservation, complete healing of the ulcerated area on the hard palate was observed. The patient has been followed for 18 months and no clinical evidence of injury recurrence was observed (Figure 5B).

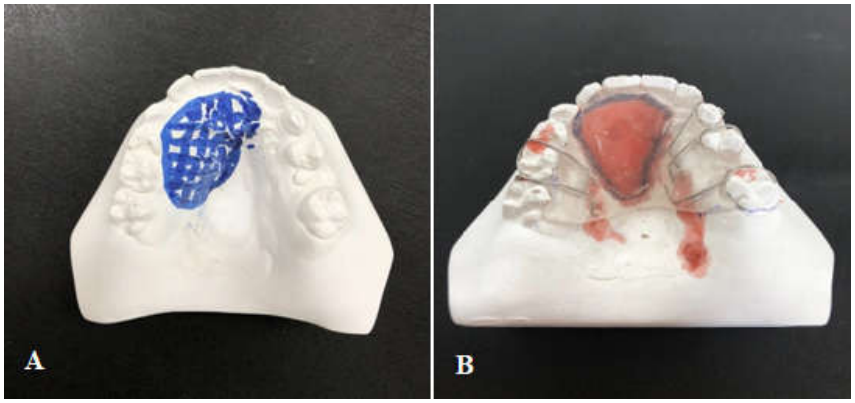

Figure 3. (A) In the plaster model, the lesion area was demarcated. (B) Confection of the obturator plate

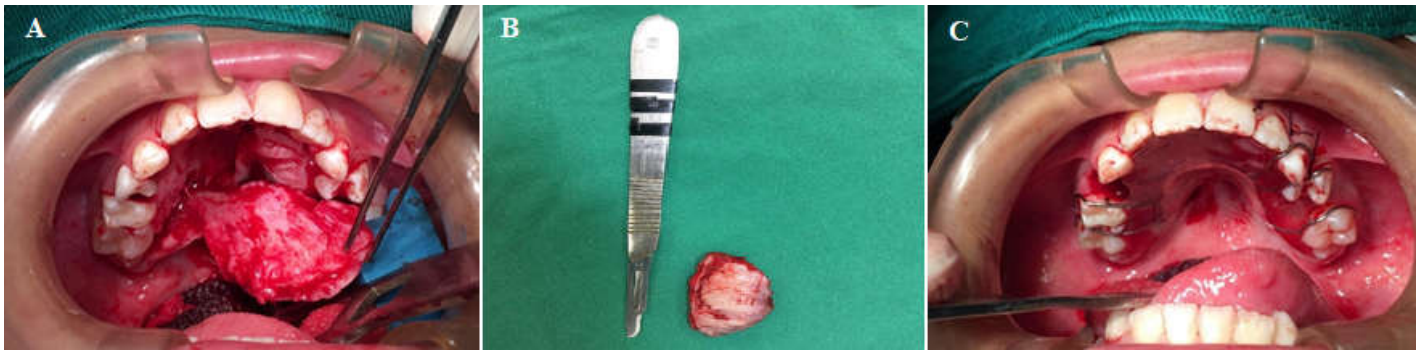

Figure 4. (A) Detachment for lesion excision was performed. (B) Total lesion removal. (C) The obturator palatal plate installed to protect the surgical wound

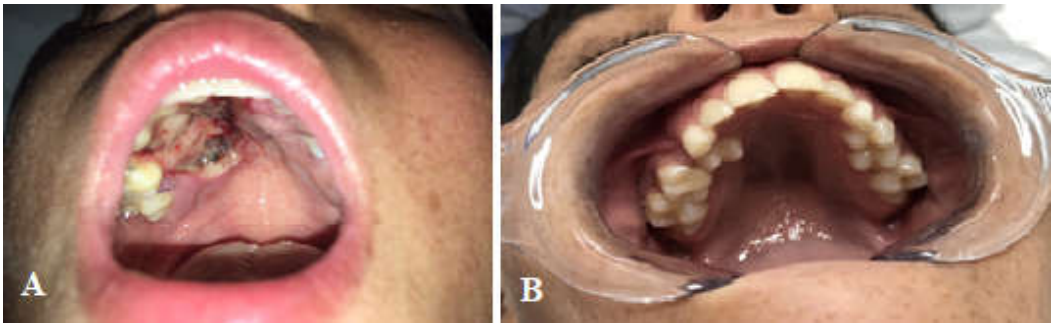

Figure 5. (A) Intra-oral clinical aspect ten days after surgery. (B) Follow-up after 18 months and no clinical evidence of lesion recurrence

After preoperative laboratory exams, surgical enucleation of the lesion under general anesthesia was performed. Perilesional incision bordering the peripheral limits of the lesion was performed using No. 15c scalpel. After incision, detachment for lesion excision was performed (Figure 4A), just after total lesion removal (Figure 4B). Simple stitches with

DISCUSSION

It is common knowledge that NF1 has its signs predominantly present in childhood and continues throughout life (Marques and Veronez, 2015), which are first detected as small physical

characteristics that go unnoticed, but that are later considered relevant due to consequences that develop over time in the body, which can remain even in the elderly life (Oliveira-Filho *et al*., 2002; Simonato *et al*., 2006). Despite the fact that cases of neurofibromas in the oral cavity are considerably rare (Souza *et al*., 2006), reports of lesions in that region are generally present in the buccal gingiva, tongue and/or mandible (Alves *et al*., 2008), studies that contrast with the present findings, in which lesion is present on the palate. It is known that NF1 can cause several changes and, among the more complex complications resulting from the disease, there is the possibility of evolution and worsening of neurofibromas (Cunha and Barboza, 2002; Espig *et al*., 2008), which can later become malignant (Sharma *et al*., 1990).

If the lesion presents possibility of malignancy, biopsy is performed as an incisional procedure, ensuring greater efficacy in the treatment of the disease (Gutmann *et al*., 1997; Oliveira-Filho *et al*., 2002; Cunha and Barboza, 2002; Alves *et al*., 2008), with subsequent tissue study carried out to confirm the suspicion of the condition, corroborating the intervention performed. When the diagnostic probability of lesion malignancy is ruled out, the lesion is completely removed (Karl, 1954), an excisional biopsy takes place covering the lesion itself and the adjacent tissue part, aiming at the total lesion removal for greater potential for resolving the condition.

After analysis, the present case report shows one of the most radical but effective ways to treat tumoral lesions caused by NF1 (Rosser and Packer, 2002) with total lesion excision being one of the safest ways to treat such injuries, although the other forms of treatment are more indicated in cases of neurofibromas over 3 cm in length (Souza *et al*., 2009). As shown, treatment was carried out effectively, allowing better quality of life for the patient and, consequently, improvement in the condition regarding the neurofibroma removal, resulting in positive and real local rehabilitation after treatment. According to Freitas *et al*. (2017), in search for greater comfort for patient's rehabilitation and serving as a barrier for trauma or food residues in the lesion, procedure was performed using obturator plate. Under such circumstances, where excision performed is of considerably high proportions, it is possible to consider the use of surgical cement, which is observed and defended by studies carried out in the area (Saito *et al*., 2008); however, in contrast to the use of surgical cement, the procedure performed developed with the use of obturator palatal plate, which desired functional objective is similar to that of surgical cement (Amstalden *et al*., 2012; Freitas *et al*., 2017).

Other studies (Karl, 1954; Saito *et al*., 2008) have used surgical cement aiming at better use of the remaining tissue and hemostasis of possible bleeding due to the auxiliary use of hemostatic sutures. Monghini *et al*. (2001) evidenced the use of surgical cement as a hemostatic factor only in the immediate postoperative period, not acting on subsequent bleeding with the same effectiveness. Therefore, the use of palatal plate is ratified by Oliveira *et al*. (2016), who defend the pain relief of the patient after the procedure as a barrier method to possible injuries. Therefore, it is suggested that the surgical treatment of neurofibroma of the palate should be associated with the use of palatal plate to protect the wound, aiming at reducing the healing time, providing greater comfort and avoiding postoperative complications.

Conclusion

According to results obtained in this study, the therapeutic method of excision through total lesion enucleation was quite effective, resulting in total case resolution. In addition, the use of obturator palatal plate decreased postoperative pain and provided adequate wound healing, generating more comfort to the patient and mitigating the possibilities of postoperative complications.

Consent: Informed consent form was obtained from the patient.

Conflicts of interest: The authors declare that there is no conflict of interest in relation to the publication of this article.

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