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Diagnostic sequence for early diagnosis of neurofibromatosis type 1 using NIH criteria

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SUMMARY

Early diagnosis of neurofibromatosis is significant to start the multidisciplinary approach of this type of patient. This syndrome may be first identified in pediatric dental care. This study is about a 9-year-old patient who was diagnosed with neurofibromatosis type 1 from a plexiform neurofibroma displayed in the left hemi-maxilla. From the microscopic diagnosis of the lesion the investigation of other related injuries began, according to the diagnostic criteria of the National Institute of Health (NIH), leading to the diagnosis of systemic alterations. The parental awareness about the condition and the establishment of multidisciplinary care are important for the treatment to be more conservative and the patient has fewer complications with better quality of life. The use of the diagnostic criteria in this case shows how methodization is important for reaching more accurate and reliable diagnoses.

Key words: Child, Diagnosis, Neurofibromatosis, Oral Pathology, Plexiform neurofibroma.

INTRODUCTION

Neurofibromatosis is an autosomal dominant disease in which the growth of neural tissues results in the formation of tumors (neurofibromas) and can cause serious damage to the nerves and surrounding tissues. It is a disease with variable expression and almost half of patients have no hereditary factor. There are two types that are well described in the literature: Type 1 and Type 2 (1). Neurofibromatosis type 1 (NF-1) is a common neurocutaneous disease with autosomal dominant pattern, which affects about 1 in every 4,000 people worldwide. This condition was first described in 1882 by Dr. Von Recklinghausen, who showed that the tumors present in the nerves were from disease, naming the presence of a tumor as neurofibroma, and the existence of multiple neurofibromas in a patient, neurofibromatosis (2). The clinical manifestations of NF-1 may include various features such as café-au-lait spots, dermal and plexiform neurofibromas, axillary false ephelides and/or inguinal, and Lisch nodules (3). In addition, the disease involves various systems, there may be ophthalmologic, musculoskeletal, cardiovascular, endocrine, central and peripheral nervous system, and learning alterations (3). Thus, the dentist, knowing these features, can assign them to oral findings, favoring an early diagnosis of this condition. The objective of this study is to report a case of previously non-diagnosed NF-1, diagnosed after an oral biopsy procedure. The histopathological report triggered a series of investigations following the diagnostic criteria of the NIH. Finally it is emphasized the importance of this further investigation in order to allow the diagnosis of the syndrome.

CASE REPORT

Pardo patient, 09 years, was taken by his mother to the dental service with the chief complaint of a swelling in the left hemi-maxilla region in the mouth, with about three months of evolution (Fig 1). The patient did not present any significant medical history. In the extra-oral physical examination, a slight bulging in the left labial region was evident. The intraoral examination identified mixed dentition, normal colored mucous membranes, with the presence of a normal colored sessile nodule, with

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soft consistency, located in the left canine fossa region without ulceration and asymptomatic.

Initial clinical suspect included lipoma, epidermoid cyst or other soft tissue tumor. Based on these hypothesis and no other clinical characteristic identified during the initial diagnosis, it was planned an excisional biopsy under general anesthesia due to the location of the lesion, early age of the patient and clinical convenience. We then requested the routine preoperative exams which were within normal limits. The biopsy procedure initiated with a linear incision approximately 5 mm above the muco-gingival line, from the extended molar to the ipsilateral central incisor. A careful divulsion of the lesion was performed, in sequence, conducting the apparent excision of the lesion (Fig 2).

We sent the collected material for histopathological examination, and microscopic sections revealed rich connective tissue fragments in sheets and islets of spindle cells with standard storiform, sometimes corrugated, encapsulated in well-organized connective tissue, forming nodular plexus (Fig 3). On the outskirts, we observed skeletal muscle fiber bundles, blood vessels of various calibers and fat with aspects of normality. The lesion was compatible with plexiform neurofibroma (4). The histopathological report suggested further investigation to define if it was an isolated lesion or part of a neurofibromatosis syndrome not diagnosed previously.

The patient underwent investigations for the presence of similar lesions in other sites as well as other phenotypic characteristics, to dispose of any subtype of neurofibromatosis or von Reckinghausen disease. During a clinical posterior extraoral examination it revealed the presence of café-au-lait spots on the arms, abdomen and legs (Fig 4). These characteristics were found irrelevant in the first clinical examination because it had a discrete manifestation, the skin lesions were small and sparse and the patient's eyes had a dark coloration, not evidencing any obvious alteration. Furthermore, it prompted an ophthalmic examination to detect Lisch nodules whose presence was confirmed (Fig 5). In order

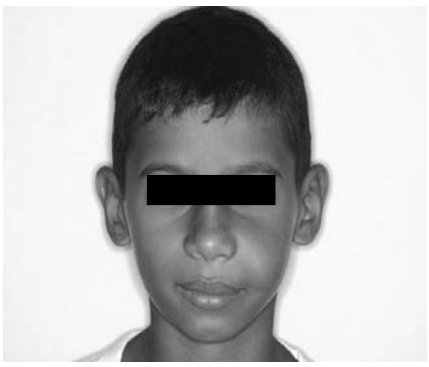

Fig 1. Initial facial appearance of the patient. Note the facial asymmetry caused by the lesion located in the left canine fossa region

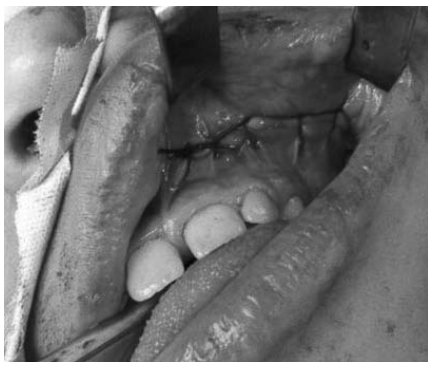

Fig 2. Post-operative appearance of the lesion region

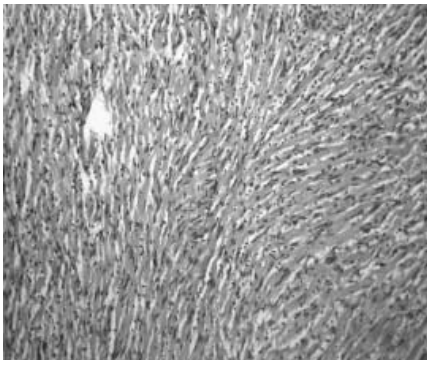

Fig 3. Histological aspect of the lesion, with characteristics compatible with plexiform neurofibroma (H&E, 200×)

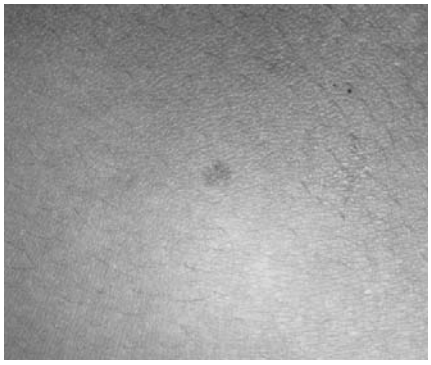

Fig 4. Café-au-lait spot detected in extraoral clinical examination

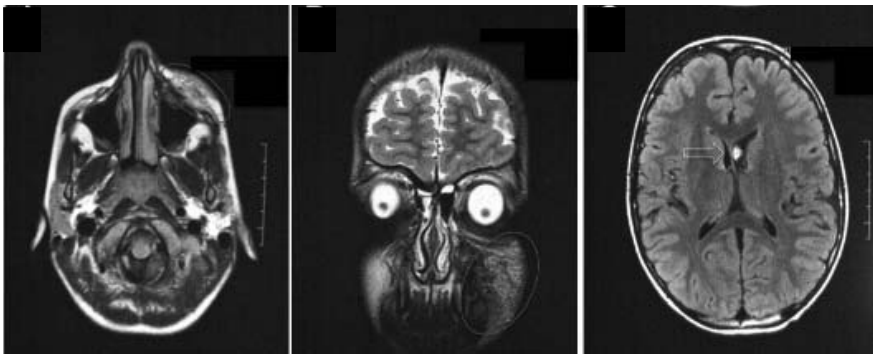

Fig 5. Magnetic resonance images with axial section showing the region occupied by neurofibroma; coronal section showing the region occupied by neurofibroma; and suggestive image of astrocytoma in cranioencephalic region

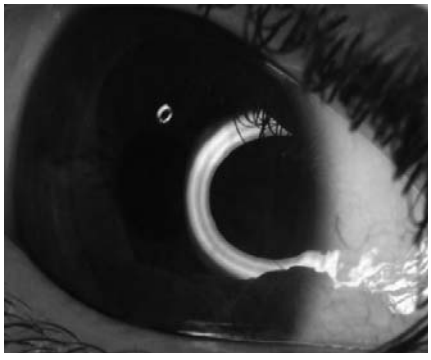

Fig 6. Lisch nodules present in the patient's iris

to assist with the diagnosis of possible systemic alterations we also requested a Magnetic resonance imaging (MRI) to investigate the presence of other injuries. The cranioencephalic region showed an image compatible with astrocytoma in the lateral ventricle (Fig 6). Faced with all these features we came to the diagnosis of NF-1.

After 12 months, there was recurrence of intraoral lesions in the same region. The patient is under multidisciplinary care for treatment of oral and cranioencephalic lesions, with close imaging follow-up, neurological assistance and oral medicine periodical consult. The identified lesions haven't showed significant progression during the past 3 years of follow-up.

DISCUSSION

In this study, we presented a case of NF-1 in children whose diagnosis was made through oral lesions. NF-1 is progressive, although unpredictable, and has a wide variety of clinical manifestations and complications. The life expectancy of patients with this condition is low, however most patients reach adulthood (5). Therefore, early diagnosis is crucial in order to decrease the morbidity and raise the quality of life of these patients (6), the earlier the diagnosis, the better the prognosis of lesions and more conservative the treatments (7). This makes it possible to have several signs of the disease which may already be present in children, serving as a warning (8). The present case highlights the importance to perform the NIH diagnostic criteria for the early recognition of the condition. In this case it was essential the suggestion from the histopathological report in order to further investigation to start. Initial manifestations of NF-1 may be discrete and never diagnosed before in a case, so general dentists, oral surgeons and other clinicians should be familiarized with this criteria.

NF-1 is a disease that can present several complications and harm to the patient who presents it, despite its expressiveness to be variable. The diagnostic criteria for the disease, established in 1988 by the National Institutes of Health (NIH) are: six or more café-au-lait spots (>0.5 cm in children or >1.5 cm in adults); two or more neurofibromas cutaneous / subcutaneous neurofibromas or plexiform; axillary or inguinal freckling; optic glioma; two or more Lisch nodules (pigmented iris hamartomas); bone dysplasia (sphenoid wing dysplasia, pseudarthrosis of a long bone); a first-degree relative with NF-1 which satisfy the above criteria (1). Thus, the diagnosis of NF-1 is made in subjects with at least two of these described features.

Neurofibromas, which are benign neoplasm nerve sheaths are the predominant feature in NF-1, appearing in most patients (9), which occurred in our case. From a clinical point of view, there are four types: discrete cutaneous, subcutaneous discrete, nodular plexiform and diffuse plexiform, which occurred in this case. Neurofibroma is a major cause of morbidity in these patients, because of the number, size and visibility of these tumors (1, 3).

Furthermore, some oral manifestations in patients with NF-1 have been reported in the literature over time as gingival hypertrophy by the growth of attached gingiva (mainly in children), impacted supernumerary teeth, increased alveolar process, neurofibromas development on the palate, the cheek, lips, gums, mucosa or, as in most cases, tongue (10). Although most of these benign neurofibromas may become malignant (11, 12). Abnormalities of facial bones can also be important, such as orbital dysplasia and wing of the sphenoid, deformities of the maxillary / mandibular (13) and more rarely the TMJ, some being essential for diagnosis (10). In our case study, there were no other oral manifestations beyond neurofibroma's presence, probably due to the young age of the patient.

In addition, rapid growth and pain associated with neurofibroma require immediate evaluation and a performed biopsy and histopathological examination, to eliminate the possibility of malignant transformation (9). Finally, genetic counseling of patients and their families is essential to reduce the hereditary cases.

The dental surgeon needs to be cautious with the characteristics of the disease to perform a correct diagnosis. The NIH establish that the NF1 occurs with these findings: six or more café-au-lait spots (>0.5 cm in children or >1.5 cm in adults); two or more neurofibromas cutaneous / subcutaneous neurofibromas or plexiform; axillary or inguinal freckling; optic glioma; two or more Lisch nodules (pigmented iris hamartomas); bone dysplasia (sphenoid wing dysplasia, pseudarthrosis of a long bone); a first-degree relative with NF-1 which satisfy the above criteria. The diagnosis of NF-1 is made in subjects with at least two of these described features. In the clinical extraoral examination, we observed the presence of café-au-lait spots on the arms, abdomen and legs (Fig 4); and in the ophthalmic examination, was detected Lisch nodules (Fig 5). To investigate the presence of other injuries, a magnetic resonance imaging (MRI). The cranioencephalic region showed an image compatible with astrocytoma in the lateral ventricle (Fig 6). Faced with all these features we came to the diagnosis of NF-1.

Therefore, the dental professionals are deci-

sive to help in the diagnose of this condition at the earliest stage as possible, and the NIH diagnostic criteria should be used, referring the case for further investigation by other health professionals, such as ophthalmologists and neurologists, if there are noticeable changes consistent with the disease (14-16).

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