

Oral neurofibroma - A short review

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ABSTRACT-

Neurofibroma is a benign peripheral nerve sheath tumour. Neurofibromatosis type 1 is caused due to an autosomal dominantly inherited disease due to an alteration in the long arm of chromosome 17. Patients are diagnosed with skin lesions (café au lait spots and neurofibromas) as well as bone malformations and central nervous system tumours. The treatment of neurofibromas involves surgical resection.

INTRODUCTION

The neurofibroma (NF) is a benign tumor of the peripheral nerve sheath affecting the head and neck region¹. They arise from Schwann cells and perineural fibroblasts². There are two clinical forms of neurofibromatosis that includes peripheral, type I (NF-I); and central, type II (NF-II)³. NF-I, also known as Von Recklinghausen's disease, is a neurodermal dysplasia, which is more frequent (90% of cases) than NF-II. The main characteristics of NF-II is that the skin is generally less affected and bilateral acoustic neurinomas with or without central nervous system tumours. NF-II (1:50.000) is less common than NF-I (1:5.000) in which the genetic alteration is localized in the long arm of chromosome 22⁴. Oral neurofibromas are seen in about 25 % of neurofibromatosis patients.

CLINICAL MANIFESTATIONS

NF-I is caused due to an alteration of the NF-I gene which is located in the long arm of chromosome 17 (17q11.2). Neurofibromatous lesions usually evolve slowly which is painless but it is accelerated during growth, puberty or pregnancy⁴. Pigmented lesions are one of the common manifestation of NF-I. They are usually seen during the first years of life or are present at birth, either as café au lait spots or as freckles^{5,6}. Café au lait spots are hyperpigmented maculae that may vary in color from light brown to dark brown which may be smooth or irregular.

There exist two main clinical forms of NF-I known as localized and plexiform neurofibromas. Localized neurofibroma is the most frequent one in NF-I which develops along a peripheral nerve as a focal mass with well defined margins. It is rarely present at birth but appears in late childhood or early adolescence. Skin is predominantly affected, other organs such as stomach, bowels, kidney, urine bladder, larynx or heart may become affected. The most frequently affected sites in the head and neck are scalp, cheek, neck and oral cavity².

Plexiform neurofibroma is a poorly-circumscribed and locally invasive tumour which spreads along the peripheral nerve affecting some nervous rami². About 21% of patients with NF-I are affected with plexiform neurofibromas⁷. The morbidity of plexiform neurofibromas in NF-I is high since they tend to grow until reaching a great size and producing disfigurement besides, the risk of malignization is between 2 and 5%². Neurofibromas may appear in every tissue, soft or hard, in the oral cavity. The most commonly affected site is the tongue⁷.

ORAL MANIFESTATION

The oral manifestation comprises of the presence of soft tissue tumor. In the oral cavity, nodular neurofibromas of the tongue are most common which leads to macroglossia and enlargement of the fungiform papillae⁷. These benign tumors may also be located on the palate, lips and floor of the mouth^{8,9}. Plexiform neurofibromas are rarely located in the oral cavity. They extend along the nerves and may encompass multiple nerve branches. They can be superficial or deep and are a major complication of NF-I is due to the

deformities and disability they cause. Immunostaining revealed that the tumor cells were negative to GLUT-1 in 20 cases of neurofibromas analyzed. The tumor cells weakly expressed Collagen IV, Ki-67 and p53. However, a strongly positive stain to S-100 with only five cases revealing less than 5% of positive cells could be noted. Variably positive stain for CD-34 and membrane epithelial antigen (EMA) was detected. All cases showed a positive histochemical reaction for Alcian blue.

HISTOPATHOLOGICAL FEATURES

Histologically, neurofibromas are composed of a mixture of Schwann cells, perineural cells, and endoneural fibroblasts, which are not capsulated^{6,10,11}. Schwann cells account for about 36 to 80% of lesional cells. They constitute the predominant cellular type and they usually have widened nuclei with an undulated shape and sharp corners. On electron microscopy Schwann cells can be seen as embracing axons which can be highlighted with silver or acetylcholinesterase staining or with immunohistochemical techniques when using S100 as a marker¹¹. Histological differential diagnoses include other peripheral nerve sheath tumors like schwannoma (neurilemmoma) and palisaded encapsulated neuroma (PEN). Schwannoma is an encapsulated tumor composed of Schwann cells which are arranged in both cellular palisaded pattern (Antoni type A) with verocay body and loose paucicellular pattern (Antoni type B). PEN is well circumscribed nodule, often partly surrounded by a fibrous capsule, with fascicles of spindle shaped cells showing variable and focal nuclear palisading, which consists of both Schwann cells and axons¹².

TREATMENT

The treatment of choice is total or partial resection of neurofibromatous lesions is to solve aesthetic or functional problems; it is advisable to wait for treatment until growth has been completed thereby diminishing the risk of recurrence⁴. Total resection with 1 cm margins whenever feasible is the treatment of choice for accessible⁶. Radiotherapy or chemotherapy are not recommended for treatment^{6,13}. There is no evidence that surgery favours malignant transformation. Malignant transformation rate of neurofibromas in NF-I is 3 to 5 %^{2,4}. NF-I patients must receive genetic counselling since this is an autosomal dominantly inherited disease and the chances of transmission to the children is 50% in both sexes². Malignant transformation to neurofibrosarcoma has a very bad prognosis and distant metastases are frequent, with the mean survival of 15% at 5 years. Recurrence may appear after surgical resection and multiple recurrences increase the risk for malignant transformation¹³.

CONCLUSION

It is important for the dentists to know about this disease under consideration when oral lesions characteristic of NF-I are present. The overgrowth of neurofibromas could lead to respiratory distress in this region of the body. Moreover, in NF-I patients, dental alignment is often disturbed by bone deformities thereby making oral hygiene more difficult. This is compounded by a possible hyposalivation, which accentuates the risk of developing caries and periodontal disease. These patients must be reviewed long term because of eventual complications, such as malignant transformation.

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