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ORIGINAL ARTICLE

Neurogenic tumors and tumor-like lesions of the oral and maxillofacial region: A clinicopathological study

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KEYWORDS

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Abstract *Objective:* Oral and maxillofacial lesions of neural origin are rare soft tissue neoplasms. The aim of the present study is to review the epidemiological data of oral and maxillofacial neurogenic lesions submitted for diagnosis to our laboratory over a 31-year period (August 1984–March 2015).

Materials and methods: The available formalin-fixed embedded specimens, Hematoxylin and Eosin slides, demographic and clinical data were retrieved.

Results: Thirty-one cases were included in this study, representing 0.6% of the 5161 biopsies submitted. Most of the diagnosed cases 11 (35.5%) were traumatic neuromas. The other cases included 2 (6.5%) solitary circumscribed neuromas, 2 (6.5%) melanotic neuroectodermal tumors of infancy, 2 (6.5%) Schwannomas, 5 (16.1%) granular cell tumors, and 9 (29%) neurofibromas. The patients' ages ranged from 5 months to 78 years. Among these cases, 16 were males (51.61%) and 15 were females (48.38%).

Conclusion: This analysis showed that neural lesions affecting the oral and maxillofacial region were rare and mostly benign in nature. Such lesions should be carefully diagnosed because of their association with life-threatening syndromes and the possibility of malignant transformation.

1. Introduction

The peripheral nervous system comprises all nervous tissue outside the brain and spinal cord. It is composed of nerves and scattered groups of ganglia. The cellular components of the nervous tissue include Schwann cells, fibroblasts and perineurial cells (Hall, 2010). Neurogenic lesions are alterations from the normal pattern of these tissues or their precursors. Although they share a common neural origin, they have variable clinical and biological behaviors (Weiss et al., 2007).

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Several tumors and tumor-like lesions of neural origin can occur in the maxillofacial region, although they are rare (Langford and Rippin, 1990; Takeda, 1991). These lesions can be divided into three main categories: reactive lesions and benign and malignant neoplasm (Fletcher, 2007).

Neurogenic tumors and tumor-like lesions of the maxillofacial area may present a diagnostic and treatment challenge. These lesions are considered some of the most important groups in which malignant transformation is a recognized finding. Additionally, the presence of some of them is considered an important diagnostic sign of life-threatening syndromes. Thus, retrospective investigations of this entity are necessary to contribute additional knowledge and to determine more accurate diagnostic and treatment standards.

Few reports (Chrysomali et al., 1997; Jones and Franklin, 2006; Katz and McAlpin, 1993; Salla et al., 2009) have described the epidemiological data of oral and maxillofacial neural lesions worldwide. However, to the best of our knowledge, there are no epidemiologic data describing the prevalence of such lesions from Saudi Arabia. The aim of the present study is to review the epidemiological data of oral and maxillofacial neurogenic lesions documented in the archives of the Histopathology Laboratory of the College of Dentistry, King Saud University, Riyadh, KSA.

2. Materials and methods

The study protocol was reviewed and approved by College of Dentistry Research Center, King Saud University, Riyadh, KSA (FR0222). The study was conducted in accordance with the ethical principles for medical research involving human subjects of the Helsinki Declaration.

The records of the Histopathology Laboratory of the College of Dentistry, King Saud University, Riyadh, KSA was reviewed retrospectively for all lesions seen from August 1984 to March 2015. All the neurogenic lesions were retrieved, and the Hematoxylin and Eosin (H&E) stained sections were re-evaluated by two oral pathologists. Diagnosis was confirmed or modified in accordance with Weiss et al., 2007. The clinical data were reviewed for clinicopathological correlation. Descriptive statistics of the data were analyzed using Microsoft Excel 2013 (Microsoft, Seattle, WA). The data are presented in frequencies and percentages.

3. Results

Thirty-one cases were included in this study, representing 0.6% of 5161 biopsies submitted between January 1984 and March 2015. Most of the diagnosed cases 11 (35.5%) were traumatic neuromas. The other cases included 2 (6.5%) solitary circumscribed neuromas, 2 (6.5%) melanotic neuroectodermal tumors of infancy, 2 (6.5%) Schwannomas, 5 (16.1%) granular cell tumors, and 9 (29%) neurofibromas. The patients' ages ranged from 5 months to 78 years. Among these cases, 16 were males (51.61%) and 15 were females (48.38%). The clinical data are presented in Table 1. Approximately half of the traumatic neuroma cases (54.54%) occurred in the lower lip. Three cases of GCT occurred in the tongue, including one diagnosed in a 13-year-old female. One case of Schwannoma was located intraosseously in the posterior mandible. One case of neurofibroma was associated with neurofibromatosis type 1.

4. Discussion

Oral and maxillofacial lesions of neural origin are rare (Langford and Rippin, 1990; Takeda, 1991). In the present study, they occurred in only 31 cases among 5161 biopsied lesions over a thirty-one year period. Few reports have described the frequencies of these lesions. Salla et al. (2009) found that oral peripheral nerve sheath tumors accounted for 0.2% of all oral lesions. Moreover, Jones and Franklin (2006) reported that these lesions are generally rare.

Traumatic neuromas are non-neoplastic proliferations of a nerve arising in response to an injury. Clinically, they appear as a smooth surface nodule that is occasionally tender on palpation (Sist and Greene, 1981). Histologically, traumatic neuromas consist of a random proliferation of nerve fascicles, including axons, Schwann cells, and fibroblasts in a

Table 1 Clinical data of oral neurogenic lesions.

Lesion (n)	Number (%)	Mean age (Range)	Gender (n)	Site (n)
Solitary circumscribed neuroma	2 (6.5)	20 years (12–28)	Male (1) Female (1)	Tongue (1) Mandibular posterior alveolar mucosa (1)
Melanotic neuroectodermal tumor of infancy	2 (6.5)	7 months (5–9)	Male (1) Female (1)	Anterior Maxilla (2)
Schwannoma	2 (6.5)	45.5 years (19–72)	Male (1) Female (1)	Buccal mucosa (1) Posterior mandible (1)
Granular cell tumor	5 (16.1)	43.4 years (13–60)	Male (2) Female (3)	Tongue (3) Buccal mucosa (1) Mandible posterior gingiva (1)
Neurofibroma	9 (29)	40.8 years (3–78)	Male (6) Female (3)	Tongue (1) Mental foramen (1) Anterior Maxilla (1) Posterior Maxilla (3) Posterior mandible (3)
Traumatic neuroma	11 (35.5)	33.9 years (11–66)	Male (4) Female (7)	Lower lip (6) Tongue (3) Mental foramen (1) Maxillary posterior gingiva (1)

background of collagen (Vora et al., 2005). Causative factors include previous surgical procedures, pressure, lacerations, cuts, and bleeding to the surrounding tissues. Sist and Greene (1981) reviewed thirty-one cases of traumatic neuromas and found that the most common oral sites are the lip, tongue, and mental nerve area. In the present review, we found that most of the cases occurred in the lower lip followed by the tongue. It was reported that traumatic neuromas have a wide age range with female predominance (Chrysomali et al., 1997; Sist and Greene, 1981), which was also found in our study.

Solitary circumscribed neuromas (SCN) are relatively rare in the oral mucosa, representing 0.05% of all oral lesions. However, they form a high portion of the intraoral benign tumors of peripheral nerve origin (Magnusson, 1996). Although the histological features of these lesions are characteristic, sometimes they can be confused with neurofibromas or Schwannomas. However, immunohistochemical stains can be used to differentiate them from other neural lesions. SCN is characterized by the presence of an epithelial membrane antigen (EMA)-positive capsule and abundant S-100 positive Schwann cells. This could help in distinguishing it from neurofibromas. Moreover, the presence of peripheral nerve axons positive for neurofilament could help differentiate SCN from Schwannomas (Chauvin et al., 1992; Chrysomali et al., 1997; Magnusson, 1996). These lesions occur most commonly on the hard palate, although any oral mucosal site may be affected (Chauvin et al., 1992; Magnusson, 1996). In the present analysis, the cases of SCN were diagnosed in the tongue and alveolar mucosa. The lesions typically affect patients during the fifth through seventh decades of life (Neville et al., 2008). Chrysomali et al. (1997) found the mean age of SCN to be 37.3 years at the time of diagnosis. In contrast, our patients' ages were 12 and 28 years at the time of diagnosis.

Granular cell tumors (GCT) are benign soft tissue lesions that have a tendency to occur in the oral cavity (Neville et al., 2008). There has been considerable debate regarding their origin; however, origination from a neural crest-derived cells is widely accepted (Buley et al., 1988). Oral GCT presents as an asymptomatic, slowly growing mass, commonly affecting the tongue (Billeret, 1998; Sposto et al., 2006). In the present study, three out of five GCT cases were found in the tongue. GCT generally occurs between the fourth and sixth decades of life and is rare in the first and second decades (Neville et al., 2008; Sposto et al., 2006). In the present review, one case of GCT was diagnosed in a female aged 13 years. This finding is unusual; however, some reports have documented cases of GCT in childhood and adolescents (Barbieri et al., 2011; Russo et al., 2011). Although congenital granular cell tumors (CGCT) are somewhat similar to GCT, cases of CGCT were not included in this analysis because they are of unknown origin and have uncertain differentiation (Lack et al., 1982; Tucker et al., 1990).

On the other hand, melanotic neuroectodermal tumors of infancy (MNTI) are rare and rapidly growing neoplasms develop in the jaws of infants. There has been considerable controversy regarding their origin from the odontogenic epithelium versus displaced retinal anlage (Mirich et al., 1991). However, the neuroectodermal origin is widely accepted based on immunocytochemical, and electron microscopic studies (Cutler et al., 1981). They commonly present as a protruding bluish-black masses of the anterior maxilla. The recurrence rate of these lesion has been reported at 20%, and the rate of malignant transformation at 6.5% (Kruse-Lösler et al., 2006). Histologically, they are composed of two types of cells: a) cuboidal cells containing varying amounts of melanin pigment which are positive for cytokeratin and HMB-45, b) small and round cells resembling neuroblasts (Weiss et al., 2007). There is a possibility that MNTIs are misdiagnosed as malignant lesions due to the presence of neuroblast-like cells, the infiltrative nature of this neoplasm and the absence of capsulation (Rachidi et al., 2015). We reported two cases of MNTI in the anterior maxilla of 5- and 9-month-old infants. These lesions are considered rare entities. Only 472 cases have been reported in the literature between 1918 and 2013 (Rachidi et al., 2015).

Schwannomas or "neurilemmomas" are rare peripheral nerve sheath neoplasms that originate from Schwann cells. Approximately 25% to 45% of extracranial Schwannomas occur in the head and neck (Colreavy et al., 2000). They usually appear as solitary, movable, slowly growing masses that commonly affect the tongue (Neville et al., 2008). In the present study, two cases were reported: one involving the buccal mucosa and the other arose centrally within the posterior mandible. Intraosseous Schwannomas are rare; however, when they occur, the posterior mandible is the most common location, (Chi et al., 2003; Nakasato et al., 2000) which is in accordance with our case. Neurofibromas are considered the most common peripheral nerve sheath tumors (Neville et al., 2008) and may arise from Schwann cells, perineural fibroblasts, or both (Weiss et al., 2007). Most of the present neoplasms were diagnosed as neurofibromas.

A number of neural and neuroendocrine syndromes have been associated with neurogenic lesions of the head and neck area. Neurofibroma and Schwannoma may be implicated in neurofibromatosis type 1, neurofibromatosis type 2, and schwannomatosis (Harder et al., 2012). Additionally, multiple endocrine neoplasia type 2B is characterized by the presence of mucosal neuromas that especially involve the oral mucosa (Morrison and Nevin, 1996). Clinicians must be aware of that because maxillofacial neural lesions may represent the initial signs of the aforementioned syndromes. In the present study, one case of neurofibroma was associated with neurofibromatosis type 1 in a 3-year-old female with a jaw lesion as the first presentation of the disease. She presented with multiple neurofibromas and skin pigmentation.

Malignant peripheral nerve sheath tumors (MPNSTs) represent a heterogeneous group of soft tissue neoplasms that are believed to arise from peripheral nerves. They are rare neoplasms in the maxillofacial area, yet approximately 8 to 16% of MPNSTs occur in the head and neck region (Eversole et al., 1973; Weiss et al., 2007). Over the 31-year period of this review, there were no MPNSTs, confirming the rarity of these lesions.

Due to the inherent limitations present in retrospective analysis, the present findings may not indicate the real prevalence of oral and maxillofacial neural lesions within our population; nonetheless, they reveal the frequency of histologically diagnosed neural lesions in the 31-year period of practice in a well-recognized oral and maxillofacial histopathology referral laboratory. This analysis showed that neural lesions affecting the oral and maxillofacial region are rare and mostly benign in nature. However, such lesions should be carefully diagnosed because of their association with life-threatening

syndromes and the possibility of malignant transformation. Further worldwide studies are needed.

Conflict of interest

We have no conflict of interest to declare.

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