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A case report of a solitary intraosseous neurofibroma in the mandible mimicking a cystic lesion

a solitary intraosseous neurofibroma

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Abstract

BACKGROUND

Neurofibromas are benign tumors of a neurogenic origin. If these tumors occur without any other signs of neurofibromatosis, they are classified as isolated neurofibromas. Neurofibromas in the oral cavity mostly occur within soft tissues, indicating that solitary intraosseous neurofibromas in the mandible are rare. Due to the absence of specific clinical manifestations, early diagnosis and treatment of these tumors are difficult to acheive.

CASE SUMMARY

A 37-year-old female patient visited our hospital due to numbness and swelling of the gums in the right lower molar area that had persisted for half a month. The patient's overall condition and intraoral examination revealed no significant abnormalities. She was initially diagnosed with a cystic lesion in the right mandible. However, after a more thorough examination, the final pathological diagnosis was confirmed to be neurofibroma. Complete tumor resection and partial removal of the right inferior alveolar nerve were performed. As of writing this report, there have been no signs of tumor recurrence for nine months following the surgery.

CONCLUSION

This case report discusses the key features that are useful for differentiating solitary intraosseous neurofibromas from other cystic lesions.

Key Words: Neurofibromas; Mandible; Cystic lesion; Odontogenic cyst; Schwannomas; Case report

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Core Tip: We present the case of a 37-year-old female with a solitary intraosseous neurofibroma in the right mandible, accompanied by tooth root resorption and local sensory abnormalities. Imaging revealed low-density unicysts with clear borders. The area affected by the inferior alveolar nerve canal was locally dilated, without displacement. A histological evaluation of the mass revealed spindle-shaped fibroblasts and fibroblast-like cell proliferation with a slight increase in nuclear size. Immunohistochemistry results showed positive staining for S100 and CD34 markers. Complete tumor resection and partial removal of the right inferior alveolar nerve were performed.

INTRODUCTION

Neurofibromas are typically benign tumors that originat from the sheath of the peripheral nervous system. They can present as isolated lesions or as a part of neurofibromatosis type 1 (NF1), a systemic syndrome also known as von Recklinghausen disease[1]. NF1 is a common neurocutaneous disorder with an autosomal dominant inheritance pattern; however, solitary neurofibromas do not exhibit this pattern[2]. Neurofibromas occur predominantly in soft tissues and less

frequently in bones. It is important to note that approximately 20-60% of oral neurofibromas are associated with neurofibromatosis. They are commonly found in the tongue, buccal mucosa, and vestibular areas [3]. Solitary intraosseous neurofibromas of the head and neck are rare, with those in the posterior part of the mandible being the most prevalent site. The early diagnosis and treatment of neurofibromas can be challenging due to their lack of specific clinical manifestations. However, with the aid of imaging techniques, such as cone-beam computed tomography (CBCT), cystic lesions can be easily diagnosed, which can affect treatment plans. Timely local organizational biopsies are crucial for an accurate diagnosis, and confirmation can be obtained through pathological examination. This report describes a rare case of a solitary intraosseous neurofibroma in the right mandible accompanied by tooth root resorption and local sensory abnormalities.

CASE PRESENTATION

Chief complaints

A 37-year-old female patient visited our hospital with numbness and swelling of the gums in the right lower molar area that had persisted for half a month.

History of present illness

Fifteen days prior, the patient had visited a local clinic due to numbness and swelling of the gums in the right lower molar area. Oral panoramic radiography revealed low-density lesions at the root tip in the right mandibular molar area, specifically affecting the lower right second molar. Despite discovering the anomaly, the patient did not report any significant pain, bleeding in the lower right gum or teeth, or unusual odor in the mouth. Additionally, the patient denied experiencing any abnormal sensation in the lower right lip.

History of past illness

There was no significant medical history related to this illness.

Personal and family history

The patient had no family history of hereditary diseases or malignant tumors.

Physical examination

The patient's general health was satisfactory, and no anomalies were detected on the skin of the face or the rest of the body. The patient's facial features were symmetrical, with no apparent swelling. No significant buccolingual bulge was observed in the right mandible, nor was there any palpable ping-pong-like sensation. The right mandibular molars exhibited second-degree loosening and discomfort upon percussion. Slight redness and swelling were noticed on the buccal side of the right lower posterior tooth's gingiva, with no sinus, pus discharge, or bleeding.The patient reported symmetrical sensory acuity in both upper and lower lips.

Laboratory examinations

The results of routine blood tests were as follows: Mean Platelet Volume (MPV):8.7 fL (reference value:9.0–13.0 fL); Platelet Distribution Width (PDW):8.8 fL (reference value:9.0–17.0 fL).

Imaging examinations

CBCT revealed a hypodense image measuring approximately 4.7 cm*2.3 cm*1.6 cm in the body of the right mandible. A white bone line surrounding the lesion was observed, along with thinning of the cortical bone. The lesion affected the apex of the lower right second molar with evident root resorption. The apical lesion of the lower right first molar seemed isolated, while the lower right third molar was located outside the mass and buried within the bone. The affected area of the inferior alveolar nerve canal was locally dilated without displacement (Figure 1).

FINAL DIAGNOSIS

After comprehensive assessment of the clinical presentation, blood test results, imaging findings, and pathological examination, the patient was diagnosed with a solitary intraosseous neurofibroma of the right mandible.

TREATMENT

On September 7, 2022, we performed complete tumor resection, along with partial removal of the right inferior alveolar nerve and extraction of the lower right third molar. During surgery, the tumor appeared as a grayish-white solid and the main trunk of the inferior alveolar nerve was not visible. Microscopic examination revealed spindle-shaped fibroblasts and fibroblast-like cell proliferation, with a slight increase in nuclear size. The nuclei were short and spindle-shaped, the cytoplasm showed rich red staining, and axons were locally visible (Figure 2). Immunohistochemistry results showed positive staining for S100, CD34, and H3K27me3(Figure 2) and negative staining for SMA, NF, and EMA (Supplemental Figure 1).

OUTCOME AND FOLLOW-UP

Nine months after the surgery, there were no signs of tumor recurrence. However, the patient developed numbness in the lower right lip, which had not improved at the time of writing this report.

DISCUSSION

Solitary neurofibromas are slow-growing benign tumors that are not encapsulated. In cases where patients do not exhibit other manifestations of neurofibromatosis, such as axillary freckling, iris hamartomas, or skeletal dysplasia, they are diagnosed with isolated neurofibromas. Neurofibromas of the oral cavity primarily originate from the mucosa. Bone involvement in neurofibromatosis is typically attributed to subperiosteal neurofibromas, which can cause bone erosion[4]. Solitary intraosseous neurofibromas are rare because the bone marrow space lacks nerve sheaths or myelinated nerves[5]. We have compiled the results from 38 studies on the subject, published since the discovery

of solitary intraosseous mandibular neurofibromas (Table 1). The posterior part of the mandible is the most common location, with a higher incidence in females. The average age of presentation is 27.5 years[6]. The length and thickness of the inferior alveolar nerve bundles may contribute to the comparatively high frequency of this illness in the mandible[7].

In the early stages, solitary intraosseous neurofibromas may not cause any symptoms; however, as the lesions grow, they can lead to expansion of the mandibular cortex. This expansion may occur with or without destruction and can result in pain, anesthesia, or paresthesia[8]. Further invasion of surrounding tissues may lead to abnormalities that alter mouth opening. However, the clinical symptoms lack specificity. This is the third reported case of a solitary intraosseous neurofibroma in the mandible with tooth root resorption. Therefore, the early diagnosis of solitary intraosseous neurofibromas without obvious symptoms is difficult. In contrast to mandibular cystic lesions, which often manifest as local swelling, loose teeth, and discomfort during biting, our patient presented with local numbness of the gums in the posterior mandibular region. Our initial neglect led to a diagnostic bias. Performing pulp vitality tests on the teeth involved in the lesion can also help identify neurofibromas. It should be noted that the clinical manifestations of non-chief complaint diseases in the adjacent teeth may affect judgments regarding the nature of the tumor, highlighting the need for improved accuracy in the clinical judgment of the chief complaint.

The imaging characteristics of solitary intraosseous neurofibromas typically show low-density unicystic or multicystic images with clear or unclear borders that lack specificity. However, these images may be similar to those of the mandibular nerve canal. We have compiled a list of mandibular diseases that can easily be mistaken for solitary intraosseous neurofibromas (Table 2). The radiological appearance of this patient closely resembled periapical cysts, unicystic ameloblastoma (UA), and

odontogenic keratocysts. Periapical cysts are inflammatory odontogenic cysts and are generally the most common type of jaw cysts. They are associated with the apex of non-vital teeth[9]. Radiographically, periapical cysts show well-defined unilocular radiolucency with sclerotic borders in close proximity to the adjacent teeth[10]. Unicystic ameloblastoma is a variant of ameloblastoma that presents as a cyst and shares clinical and radiological characteristics with odontogenic cysts. They appear as well-defined unilocular radiolucencies that often surround the crown of an impacted tooth[11]. In the present case, the impacted tooth crown was located outside the lesion. Compared to ameloblastomas, odontogenic keratocysts exhibit less prominent buccolingual expansion and less frequent and severe adjacent tooth root resorption. The presence of pasty fluid in odontogenic keratocysts can lead to areas of attenuation within the cystic cavity, resulting in uneven internal density on CT[12]. George *et al.*[13] and Larsson *et al.*[14] observed radiographic evidence of calcification in solitary intraosseous neurofibromas and proposed that this might be the result of high collagen content rather than genuine calcification. Odontogenic lesions in the mandible originate above the mandibular canal. Neural and vascular lesions mostly arise within the mandibular canal, whereas lesions centered below the mandibular canal are usually of non-odontogenic origin[15]. Therefore, it is crucial to carefully analyze the correlation between lesions and the inferior alveolar nerve canal. If the lesion involves the inferior alveolar nerve canal, it is essential to consider that the swelling may have a neural origin.

Histologically, solitary neurofibromas originate from the nerves and are composed of Schwann cells, perineural cells, endoneural fibroblasts, and intermediate cells[16,17]. They have well-defined boundaries with the surrounding connective tissue, distinguishing them from the multiple neurofibromas observed in cases of neurofibromatosis[3]. It is crucial to perform S-100 and CD34 immunostaining on biopsy samples. In neurofibromas, tumor cells are loosely arranged and fragile, often with wavy or snake-shaped nuclei, and S-100 protein-positive cells are less common than in

schwannomas[18]. The final pathological diagnosis should be based on the presence of CD34, which is located in the cell membrane and cytoplasm. CD34 positivity is observed in neurofibromas but not in schwannomas[19].

Surgical resection is currently the primary treatment for solitary intramedullary intraosseous neurofibromas. However, there have been no reports of adjuvant therapy, and the local recurrence rate of neurofibromas is higher than that of schwannomas, possibly because of the lack of an envelope[20]. This makes complete tumor removal more challenging, and the affected nerve is sacrificed during radical resection of neurofibromas[8]. While neurofibromas may progress to neurofibromatosis or undergo malignant transformation as the primary disease[21,22], the likelihood of solitary neurofibromas becoming malignant is quite low compared to that of neurofibromatosis[23]. The possible development of this disease emphasizes the importance of regular monitoring for patients with early neurofibroma symptoms. Our patient showed no signs of recurrence or progression to neurofibromatosis nine months after surgery. In the future, we will continue to monitor these patients.

CONCLUSION

In this report, we detail the case of a 37-year-old female with tooth root resorption and local sensory abnormalities in the right mandible, indicative of a solitary intraosseous neurofibroma. While pathological examination remains the primary diagnostic method for intraosseous neurofibroma, clinicians must carefully examine the patient's symptoms and observe the relationship between the lesion and inferior alveolar nerve canal. An accurate distinction between cystic lesions and neurogenic tumors in the mandible is crucial for early diagnosis and appropriate treatment. Following surgical intervention, patients with solitary neurofibromas of the mandible should undergo long-term follow-up due to the potential for local recurrence and malignant transformation of these tumors.

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