Abstract

Introduction
Lipomas are common benign soft tissue neoplasms composed of mature white adipocytes. They are the most common soft tissue mesenchymal neoplasms. However, they are relatively uncommon in the oral and maxillofacial regions. Their overall incidence in the oral cavity is thought to be between 1% and 4% of all benign oral lesions. Specific anatomic locations within the oral and maxillofacial region include the parotid region, buccal mucosa, lips, submandibular region, tongue, palate, floor-of-mouth and vestibule. Infrequent locations of orofacial lipomas include the maxillary bones, especially the mandible. Among lipomas, different subtypes can be described: simple lipoma, lipoma with chondro-osseous metaplasia, chordoid lipoma, fibrolipoma, infiltrating lipoma, angiolipoma, myolipoma of soft tissue, angiomyolipoma, spindle cell/pleomorphic lipoma (SCL/PM), myxolipoma, angiomyxolipoma, dendritic myxofibrolipoma, sialolipoma, congenital lipoma, hibernoma and atypical lipomatous tumor (ALT).

Case Report
We report an unusual large-sized lipomatous tumor located on the left side of floor-of-mouth, one of the rarest sites of intraoral lipoma. The final diagnosis of the lesion was fibrolipoma. The unusual characteristics of this case report were the large-sized dimensions of the neoplasm, which were 3 cm along the main diameter, and the histological subtype which is not common among the lipomas of the floor-of-mouth and of the oral cavity in general.

Conclusion
A histological examination after removal of lipomas is imperative to exclude liposarcomatous degeneration. A detailed revising of the subtypes classification of the benign lipomatous tumours of the oral cavity is provided in this paper.

Introduction
Lipomas are common benign soft tissue neoplasms composed of mature white adipocytes. They are the most common soft tissue mesenchymal neoplasms. They primarily affect the region of the trunk, shoulders, neck and axilla, with 15 to 20% of the cases involving the head and neck region. However, they are relatively uncommon in the oral and maxillofacial regions. The overall incidence in the oral cavity is thought to be between 1% and 4% of all benign oral lesions. Lipomas are more common in males than females, although several authors believe that there is not sex predominance. Oral tumours generally occur in adult patients between the ages of 40 and 60 years, similar to other benign soft tissue lipomas. Lipomas are usually described as long-standing soft nodular asymptomatic swellings covered by normal mucosa. The first description of oral lipomas was provided by Roux in 1848 in a review of alveolar masses. He referred to it as a “yellow epulis”.

Lipomatous benign tumoural tissue is very similar to normal adipose tissue; however lipoma metabolism differs, as it has been shown that the fat tissue of lipoma is not used for energy production during starvation periods as occurs with normal adipose tissue. Specific anatomic locations within the oral and maxillofacial region include the parotid region, buccal mucosa, lips, submandibular region, tongue, palate, floor-of-mouth and vestibule. Infrequent locations of orofacial lipomas include the maxillary bones, especially the mandible.

Site predilection is most likely associated with the availability of adipose tissue, which is high in the buccal mucosa due to the proximity of the buccal fat pad and very low in the palate. The tumours are described as circumscribed, encapsulated, and firm to rubbery with a tan, yellow greasy cut surface. They appear as a single or lobulated long-standing painless lesion with either a sessile or a pedunculated base. A characteristic feature is a change in consistency and form of the lesion during contraction of involved muscle. The mean tumour size according to the literature is 2.2 centimetres.

Oral lipoma is diagnosed more frequently at a mean age of 50 to 62 years. The duration of lipomas ranges from 2 to 84 months, with a mean of 30.4 months.

No consensus exists regarding the pathogenesis of oral lipomas. Currently, heredity, fatty degeneration, hormonal basis, trauma, infection, infarction, metaplasia of muscle cells, lipoblastic embryonic cell nest in origin and chronic irritation are probable representative theories to elucidate...
Case report

Histological subtypes

**Simple lipoma**

Simple lipoma is composed of lobules of mature adipose tissue with variably sized adipocytes which appear as fat cells with peripherally located, flattened nuclei. The cytoplasm is clear and contains fine sudanophilic granules. In some cases, single or multiple vacuoles are present. The cells are separated into lobules by thin septae of connective tissue, and the whole tumour is thinly encapsulated. In some cases the capsule is absent. A small number of capillary vessels supply the tumour.

**Lipoma with chondro-osseous metaplasia - Osteolipoma**

Cartilaginous or osseous metaplasia in lipoma is characterised by mature, benign cartilage or bone formation within the neoplastic fatty tissue. The pathogenesis is poorly understood but is most likely associated with endochondral ossification by pluripotent mesenchymal cells within the fat. Osteolipoma is a very rare histological variant accounting for less than 1% of cases. It appears as a mass physically similar to lipoma with bone-hard nodes in the centre. Histological examination shows lipomatous proliferation of mature non-atypical adipocytes with metaplastic ossification foci in the centre. Trabeculae of vital lamellated bone of varying sizes and shapes are scattered among adipocytes. It has been described in the parotid region, the tongue as well as the hard and soft palates.

The pathogenesis of osteolipoma remains unclear. Two principal theories have been formulated. These tumours may originate directly from multipotent cells, which differentiate into lipoblasts, chondroblasts, osteoblasts or fibroblasts, characterising a “mesenchymoma”. Alternatively, osteolipoma has been suggested to arise after repetitive trauma, metabolic changes, or possibly ischaemia, thereby leading to metaplasia of pre-existing elements within the lipoma and the development into osteoblasts. Furthermore, huge lipomas showing fast enlargement may have cystic degeneration and necrosis. Consequently, necrotic tissue may ossify mimicking osteolipoma. Only 16 lipoma cases with chondro-osseous metaplasia have been reported in the literature from 1960 to 2012.

**Chondrolipoma**

Chondrolipoma is a benign lipoma variant that can simulate liposarcoma and myxoid chondrosarcoma. This lipoma variant typically occurs in slightly younger adults with a female predominance. Histologically, chondroid lipomas may be confused with liposarcomas and chondrosarcomas due to the scattered nests of lipoblast-like cells and myxochondroid matrix. However, these components are typically single, well-circumscribed lobules, and a mature fatty component is always identified.

**Fibrolipoma**

Fibrolipoma is characterised by the presence of lobules of mature adipose tissue of different sizes separated by fibrous connective tissue septae of various widths.

Figure 1: A large-sized, painless, long-standing swelling was reported by the patient on the left side of the floor-of-mouth. It appeared as a soft, pinkish-yellow, nodular lesion covered by normal mucosa. Submucosal increasing of vascularity can be observed.

Figure 2: Occlusal and lateral views via MRI examination. A large ovoidal highly obvious lesion was observed in the left sublingual region (T2). It appears as a well-encapsulated, homogeneous mass of neoplastic tissue with the absence of continuity with the most important adjacent structures. A presumptive diagnosis of lipoma was formulated.
Fibrolipoma is an uncommon variant of the benign tumours of adipose tissue. This tumour has been reported to be more frequent in the cheek, and it shows a slight predominance in females. Histological features of fibrolipoma are similar to those of simple lipoma. Additionally, in this tumour, broad bands of dense connective tissue are interspersed between fat cells. Simple lipoma and fibrolipoma are both usually well circumscribed and thinly encapsulated, which are features that can assist in their differential diagnosis with herniated adipose tissue and fibrous polyp with fat entrapment, respectively. They often exhibit capillary vessels in the overlying mucosa.

**Infiltrating lipoma**
Infiltrating lipoma is also known as intramuscular lipoma (when it arises within skeletal muscle) or intermuscular lipoma (when it arises between skeletal muscles). It is characterised by the presence of fat cells, which are separated by a scant fibrous stroma containing small numbers of blood vessels and by strands and groups of striated muscle fibres. The tumour is semi-firm and rubbery, with poorly defined margins. It is usually situated in the deeper tissues (tongue muscles). The infiltrating lipoma is not encapsulated, and complete excision is difficult due to the diffuse muscular infiltration. The ability of this lipomatous subtype to infiltrate adjacent muscles and to recur locally may lead to a false clinical diagnosis, such as liposarcoma. A useful diagnostic marker in the differential diagnosis between benign and malignant adipose tissue tumours is the immunohistochemical detection of aP2 protein, which is expressed in lipoblasts.

**Angiolipoma**
Angiolipoma typically consists of mature adipocytes and thin-walled capillary-sized vessels, which often contain fibrin thrombi. Angiolipomas are relatively common and usually appear in the late teens or early twenties. They are more common in males than in females. Angiolipoma has been reported in the mucolabial fold, the buccal mucosa, and other sites of the head and neck. Although often painful and found in multiple other locations, the oral tumours described in the literature were painless and solitary. However, in the case of histological observation of abundant vascularity, careful examination should be performed to exclude angiosarcoma and Kaposi’s sarcoma.

**Myolipoma of soft tissue**
Myolipoma is composed of fascicles of bland smooth muscle traversing mature fat within a relatively well-circumscribed or encapsulated lesion. Prominent thick-walled vessels, as seen in angiomyolipoma, are absent.

**Angiomyolipoma**
Angiomyolipoma is composed of varying proportions of vascular cells, immature smooth muscle cells and fat cells. Angiomyolipomas are typically found in the kidney but have also been commonly found in the liver and less commonly in the ovary, fallopian tube, spermatic cord, colon and palate.

**Spindle cell lipoma/Pleomorphic lipoma**
Spindle cell lipoma is characterised by an admixture of mature fat and bland spindled cells, bundles of ropey collagen, and scattered mast cells. Pleomorphic lipoma also contains multinucleated giant cells. These cells may have radially arranged nuclei in a “floret-like” pattern. Spindle cell lipoma and pleomorphic lipoma represent the two extremes of a morphological continuum. SCL/PL typically presents in older men with a median age of 55 years. It was originally described by Enzinger and Harvey (1975). It is more common in the cheek and tongue, but one case located on the alveolar mucosa has been reported.

Macroscopically, the tumour resembles a simple lipoma except for grey-white gelatinous foci representing the areas of spindle cell formation. The microscopic features of SCL/PL range from tumours predominantly composed of mature fat cells, with a moderate amount of myxoid material and widely scattered spindle cells, to cellular...
lesions containing numerous spindle cells, thick bundles of collagen and a small number of mature fat cells. Intraoral spindle cell lipomas do not tend to recur, but the behaviour of intraoral spindle cell lipoma with pleomorphic features is currently poorly understood. Two cell types exist in these lesions: spindle-shaped mesenchymal cells with features of fibroblast and differentiated fat cells in almost equal proportions. Adipocytes often lie in a myxoid interstitial matrix, separated by thick bands of rope-like birefringent collagen. Mast cells, lymphocytes, multinucleated giant cells and blood vessels are present. The spindle cells are usually of uniform size, shape and staining intensity. They are characterised by a pale staining vesicular, oval or compressed nuclei, with sparse, poorly defined, eosinophilic cytoplasm, and they sometimes demonstrate nuclear palisading. It has been suggested that spindle cells are fibroblast rather than pre-adipocytes or immature mesenchymal cells. Another possible origin involves CD34-positive dendritic interstitial cells. The differential diagnosis must be made with simple lipoma, fibrosarcoma, schwannoma, leiomyoma, myxolipoma, myxoid neurofibroma, nodular fascitis, fibrolipoma and myxoid solitary fibrous tumours. Variants include fat-dominated tumours with scant spindle cells and those with a prominent spindle cell component with only few, if any, fat cells. The matrix can be extensively myxoid (spindle cell lipoma with myxoid changes). Further histological findings in spindle cell lipoma include sinusoidal changes and hemangiopericito-like changes.

**Myxolipoma**

Myxolipoma is a lipoma admixed with abundant mucoid substances, and it is considered to be a lipoma with a high degree of myxoid change. The mucoid substances are positively stained with alcian blue and are digested by hyaluronidase\(^ {15} \). Only 14 cases of this variant involving the oral regions have been reported in the literature, with patient ages ranging from 30 to 70 years. The incidence rate in the tongue, the buccal mucosa and the lower lip was almost equivalent. Myxolipoma must be distinguished from benign and malignant lipomatous tumours with abundant myxoid substances, such as chondroid lipoma, spindle cell lipoma with myxoid changes and myxoid liposarcoma.

**Angiomyxolipoma**

Angiomyxolipoma is a rare tumour characterised by a proliferation of adipose tissue associated with a myxoid stroma and multiple vascular channels. Only one case has been reported in the literature involving the oral cavity\(^ {16} \). Histologically, the tumour appears as a combination of mature adipocytes and bland spindle cells scattered within a myxoid stromal background containing abundant small to medium-sized vascular channels.

**Dendritic myxofibrolipoma**

Dendritic myxofibrolipoma is a newly described benign soft tissue tumour that could be easily mistaken for sarcoma. It represents a combined feature of solitary fibrous tumour and spindle cell lipoma\(^ {17} \). It is more common in middle-aged and elderly men. It is characterised by an admixture of mature adipocytes and spindle and stellate cells, and abundant myxoid stroma with prominent collagenisation. A case involving the lower lip has been reported in the literature. The lesion consisted of loosely arranged spindly or stellate cells in a grossly oedematous stroma. The stroma was richly vascular with thin-walled vessels, mainly mucinous, and was focally collagenous. Additionally, dendritic myxofibrolipoma is characterised by the dendritic nature of spindle cells, a proliferation of plexiform capillaries, and an abundance of keloidal-type collagen.

**Minor salivary gland lipoma (sialolipoma)**

Minor salivary gland lipoma is intraglandular lipoma-containing atrophic salivary gland acini and dilated ducts\(^ {3} \). It has been proposed that lipomas growing close to salivary glands can induce marked changes in their acini and ducts. In the diagnosis of sialolipoma in the context of minor salivary gland, the amount of adipose tissue and glandular tissue should be equal in proportion and limited peripherally by a fibrous capsule\(^ {10} \).

**Congenital lipoma**

Congenital lipoma of the oral cavity is considered very rare\(^ {3} \). Although lipoma is considered a neoplasm in adults, in children, it is classified as either a neoplasm or a malformation, such as in orofaciiodigital syndrome.
Hibernoma

Hibernoma is a rare, benign, encapsulated, and richly vascularised proportion of brown fat cells admixed with white adipose tissue. Lobular, myxoid, lipoma-like, spindle cell-like variants have been described. No case reports involving the oral cavity have yet been described.

Atypical lipomatous tumour

ALT is a locally aggressive mesenchymal neoplasm composed either entirely or partially of mature adipocytic proliferation showing significant variation in cell size and at least focal nuclear atypia in both adipocytes and stromal cells. The presence of scattered hyperchromatic, often multinucleated, stromal cells and a varying number of monovacuolated or multivacuolated lipoblasts may contribute to the morphological diagnosis. Use of the term “atypical lipomatous tumour” is determined principally via clinical evaluation of tumour location and resectability. Some researchers, however, define this entity as “well-differentiated liposarcoma”.

Case report

A.C., a 57-year-old female patient, was referred to our hospital due to an unusual swelling on the left side of the floor-of-mouth. The lesion was located in the submucosal tissues, its macroscopic appearance was nodular, elevated, and pinkish-yellow in colour, and no symptoms of pain were reported by the patient (Figure 1). The pathological anamnesis revealed that the lesion was present for at least two years and increased in volume very slowly during this time. A differential diagnosis was imperative with ranula, sialolithiasis of the Warthon duct, intraoral dermoid cyst and sublingual neoplasm. Ranula was excluded as the lesion was not blue in colour and it was not cystic-like upon palpation. Furthermore, it was painless and did not increase in volume during mealtime. No traumatic injury in the region was reported. An occlusal X-ray did not reveal the presence of any calculus or radiopaque neoformation. Sialolithiasis was thus excluded. Magnetic resonance analysis was performed to visualise the lesion consistency, vascularity and anatomical relations with adjacent structures, such as the sublingual gland, the tongue muscle, the Warthon duct, the lingual nerve, the milo-jodean muscle, the tongue muscle and the internal surface of the mandible. The result was the presence of a neoplasm dislocated among the soft tissues of the floor-of-mouth, that was well-encapsulated and highly captured the contrast liquid (Figure 2). The morphological characteristics, the presence of a capsule, and the absence of continuity with the adjacent structures, which appeared to be compressed and dislocated in the sublingual region, prompted us and the radiologist to formulate a presumptive diagnosis of intraoral lipomatous neoplasm.

We decided to perform a surgical excision of the lesion. After a superficial cold-blade incision upon the most declivous pole of the lesion, the tumour was removed via dissection using Meztenbaum scissors and carefully avoiding important anatomic structures, such as the lingual nerve, the milo-jodean muscle, the tongue muscle and medium-calibre arteries (Figure 3). After the surgical intervention, which was performed under local anaesthesia (truncular lingual block), the patient did not report complications, with the exception of a temporary lingual dysesthesia due to the wound healing and compression, which resolved after 4 months. The sample was preserved in paraffin and sent to the Unit of Pathologic Anatomy; it was 3 cm long along the main diameter (Figure 4). The histopathologic analysis revealed the presence of a lipomatous neoplasm composed of mature adipose tissue subdivided into lobules by the presence of an important number of dense connective tissue bundles (Figure 5). A final diagnosis of fibrolipoma of the floor-of-mouth was proposed, and there was no recurrence after 1 year following the excision. An ultrasound examination confirmed the presence of a fully restored architecture of the sublingual region.

Figure 5: a) Histologic examination of the lesion stained with haematoxylin-eosin (x10): it is possible to observe the presence of mature adipose tissue and the presence of a large number of dense connective bundles subdividing the lesion into various lobules; b) an enlarged (x50) view of the lesion with the presence of lobulated fat and interspersed rope-like bundles of fibrous tissue; c) (x100) the two main histological components of the lesion were the presence of non-atypical and uniform adipocytes and the presence of oriented homogeneous collagen fibres; d) (x200) in this image, it is possible to observe the morphologic features of mature adipocytes: polygonal cells with a mono-vacuolated clear cytoplasm. No cellular atypia was found. Thus, a final diagnosis of fibrolipoma was made.
Discussion

We report an unusual large-sized lipomatous tumour located on the left side of the floor-of-mouth, a rare site for intraoral lipoma. The final diagnosis of the lesion was fibrolipoma.

The unusual characteristics of this case report were the large-sized dimensions of the neoplasm, which were 3 cm along the main diameter and the histological subtype, which is not common among lipomas of the floor-of-mouth or oral cavity in general.

Lipomas are benign soft tissue neoplasms composed of mature white adipocytes.

They are relatively uncommon in the oral and maxillofacial region. Their overall incidence in the oral cavity is thought to be between 1% and 4% of all benign oral lesions.

Among lipomas, different subtypes can be described as follows: simple lipoma, lipoma with chondro-osseous metaplasia, chondroid lipoma, fibrolipoma, infiltrating lipoma, angiolipoma, myxolipoma of soft tissue, angiomylipoma, spindle cell/pleomorphic lipoma, myxilllipoma, angiomylipoma, angiomylipoma, myxofibrolipoma, sialolipoma, congenital lipoma, hibernoma and atypical lipomatous tumour.

Lipomas in buccal mucosa occur more often in males. Simple lipoma is the most common histological pattern found, followed by spindle cell lipoma and then fibrolipoma.

Lipomas of the lips tend to occur more often on the lower lip than on the upper lip and a male predominance is associated with this disease. Spindle cell lipomas and their variants are the most common subtype.

In the submandibular region, there is a right-sided predominance. Simple lipoma and spindle cell lipoma occur equally in this region. Chondroid lipoma is occasionally reported.

Lipomas of the tongue occur in approximately equal numbers in males and females. The simple lipoma is the most frequent subtype; sometimes, lipomas with cartilaginous metaplasia or poorly delineated within the tongue muscle (intramuscular lipoma) are reported.

Spindle cell lipoma is the second variant.

Lipomas of the palate can be registered in the hard and soft palates. Simple lipoma and spindle cell lipoma can be equally found in the palate.

Finally, lipomas of the floor-of-mouth show a male predominance. Simple lipoma and spindle cell lipoma are the most common variants.

Intraosseous lipomas are unusual despite the large amount of fatty marrow in adults, and are considered to be rare benign primary tumours of the bones. Only 15 cases of intraosseous mandibular lipoma have been documented since 1948. They are usually described as located adjacent to the apices of vital teeth via radiolucency. Differential diagnosis must be posed with odontogenic keratocyst, odontogenic myxoma, early benign cemento-osseous lesions and central giant cell granuloma.

The aetiology of intraosseous lipomas remains unclear; however it is widely accepted that the intraosseous lipoma is a true benign tumour of the medullary adipose tissue.

Intraosseous mandibular lipomas mainly arise in the posterior region of the mandible.

Histologically, simple lipoma, fibrolipoma and angiolipoma are reported in the literature as the most common variants.

The occurrence of multiple lipomas is associated with Cowden's syndrome or multiple hamartoma syndrome. In conclusion, simple lipomas are the most common subtype overall described in the literature.

However, site-specific in the parotid and lip, the spindle cell subtype is predominant. There are an equal number of classic and spindle cell lipomas including the submandibular region, palate and vestibule.

The microscopic subtypes have no clinical significance with respect to the behaviour of tumours. Infiltrating lipomas are an exception, as the absence of a capsule and their ability to infiltrate the surrounding skeletal muscles represent a high-risk factor for recurrence. Depending upon the site, lipoma can also be categorised into superficial, deep and perioveal.

Although rare, the malignant transformation of oral lipomas into liposarcomas has been reported. Intramuscular location seems to be a risk factor for malignancy. Immunohistochemical detection of aP2, a protein expressed by lipoblasts, could assist in differential diagnosis.

Conclusion

A histological examination after removal of lipomas is imperative to exclude liposarcomatous degeneration, to detect the absence of a capsule, which requires a constant follow-up due to a high probability of recurrence.

Furthermore, the small number of studies regarding lipomatous tumours of the oral cavity suggests the necessity of more attention on the soft tissue tumours that could affect the oral cavity. Thus, a possible expansion of the subtype classification and description of topographic issues may be revised in the future.

References


