ORIGINAL PAPER

Histopathological aspects of benign mesenchymal tumors located in "high risk areas" of the tongue

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Abstract

Although a series of premalignant or potentially malignant lesions are described in the tongue, there are many other lesions whose potential of degeneration can be determined by a prolonged action of irritant or carcinogenic factors. Even if they are practically considered to be harmless, benign formations of mesenchymal origin with lingual location represent in the same time a neoplastic lesion under the influence of local and general factors, for a variable period of time. When these structures are located in major risk areas from the oral cavity and in particular, those directly related to the tongue, special attention should be paid to their development. In this study (conducted on a total of 16 cases of benign mesenchymal malignancies), we planned a histopathological evaluation of surgical excision samples obtained from interventions on lingual neoplasias, and harvested from areas with the highest risk for lingual cancer development (pelvilingual groove, the base of the tongue and the insertion of the anterior pillar) in order to assess the histopathological aspects in different types of lesions and the possible presence of degenerative changes.

***Keywords*:** fibromatosis, hemangioma, lymphangioma, lipoma, rhabdomyoma, histopathology.

Introduction

Hemangioma is a malformation composed of seemingly disorganized masses of vessels covered by epithelium, full of blood and connected to a main vascular source. They may occur as isolated entities in the oral cavity or as multiple ones, associated with other hemangiomas located in different regions [1].

Lymphangioma is histologically and etiologically similar with the hemangioma, except that the abnormal vessels are filled with a clear liquid, rich in protein, with fewer lymphocytes and no red blood cells. It may present as a solitary formation or associated with hemangiomas or other vascular abnormalities with vessels anastomosing with those of the lymphangioma. Some opinions suggest that the lingual lipoma draws its origin from the remains of adipose tissue located in close proximity to the lingual septum and which, at a later time during the process of lipomatous proliferation, would migrate along muscle fascia to reach its final destination beneath the mucosa [1].

According to some authors, the genesis of the lingual lipoma must be sought in the development of the immature mesenchymal elements towards the adipose series. However, the neoformation is composed of mature fatty cells, which are metabolically different from normal fatty cells, even though they share the same histology [2].

The origin of the *rhabdomyoma* is in the striate muscle of the tongue and is more common than the leiomyoma. It is considered to be rather a development anomaly than a neoplasm [2]. It is located on the back of the tongue as a sessile, rounded, painless, well-defined nodule, which rarely ulcerates. It generally affects males starting from the fifth decade of life, but fetal rhabdomyoma is also described in the literature.

Material and Methods

The material investigated in this study was human material from the Oral and Maxillofacial Surgery Clinic of the Emergency County Hospital of Craiova, sent to the Pathology Department of the same hospital for histopathological examination. The material came from patients between 3 and 89-year-old who shared the same clinical diagnosis of lingual tumor. They were submitted to either diagnostic biopsy, or therapeutic and diagnostic excision or partial resection of the tongue were performed. When appropriate, surgery was accompanied by extensive lymphadenectomy.

The study included 183 cases selected in a period of 10 years, between 1999 and 2000.

The histopathological analysis of the 183 cases with the clinical diagnosis of lingual tumor revealed that that in 167 cases (91.2%) the lesions were tumoral, and in 16 cases the lesions were non-tumoral: specific or non-specific inflammatory type in five cases and pre-neoplastic in 11 cases.

Given the wide variety and complexity of tumor aspects encountered as well as their variable prognosis, the selected cases were reviewed, sorted and classified according to several criteria. In this regard, the macroscopic, microscopic, histogenetic and evolutionary aspects were of great use to us.

Taking into account the morphology and the evolutionary aspect, in the first phase, the 167 tumors analyzed were divided into benign and malignant ones. Thus, we found 38 cases of benign tumors and 129 cases of malignant ones. Subsequently, for each of the two major categories of tumors – benign and malignant – we used the histogenetic criterion that allowed the classification of cases analyzed according to the structure of origin of the neoplasia.

From the histogenetic point of view, we found that benign tumors were of epithelial, mesenchymal or uncertain origin, while malignant tumors were all of epithelial origin. It can be noted that benign lingual tumors showed various histogenetic aspects. Tumoral aspects encountered in our study were extremely variable, even within each histogenetic group. Thus, we encountered the following tumors:

- epithelial: papillomas, condylomas, adenomas;
- mesenchymal: desmoid lingual fibromatosis, hemangioma, lymphangioma, lipoma, rhabdomyoma;
- tumors with uncertain histogenesis: granular cell tumor (Abrikosov's tumor).

Some tumors showed more than one type of lesion. For example, in the case of benign mesenchymal tumors, hemangiomas studied were of capillary, cavernous and pyogenic granuloma type. For each category of tumors encountered, we analyzed and described both common and specific histopathological aspects. Also, if the case, we described the accompanying (reactive) aspects of structures adjacent to the tumor.

For the histopathological study of selected cases, we used the classical technique for paraffin inclusion, followed by the classical Hematoxylin–Eosin staining technique and van Gieson's trichrome stain, and when it was required, we also used special stains (Gömöri's silver impregnation).

Results

We encountered 16 cases with benign mesenchymal tumors, representing 42.10% of all benign tumors of the tongue and 9.58% of all tumors with this location. They were diagnosed in patients aged between 3 and 68 years.

It can be noted that unlike benign epithelial tumors, the mesenchymal ones were present at younger ages, from the first decade of life, when in fact we observed the highest incidence of this group of tumors. Thus, in the first decades of life we found four cases, representing one quarter of all benign mesenchymal tumors studied. It was followed in order of frequency by decades III to VI of life, with three cases each. For the remaining age groups we found 1–2 cases each, and there were no cases in the decades of VIII and IX of life (Table 1).

Most tumors in this group belonged to male patients, in whom a total of 14 of the 16 benign tumors of mesenchymal origin were diagnosed (Table 2).

Table 1 – ***Distribution of benign mesenchymal tumors according to age groups***

Age group [years]	0–9	10–19	20–29	30–39	40–49	50–59	60–69
No. of cases	4	1	3	2	2	3	1
Percentage	25	6.25	18.75	12.50	12.50	18.75	6.25

Table 2 – ***Distribution of benign mesenchymal tumors according to the patient's gender***

Gender	Males	Females
No. of cases	14	2
Percentage	87.50	12.50

The histopathological study of the 16 cases with benign mesenchymal tumors allowed the observation of a great variety of forms and aspects even within the same type of tumor. Taking into consideration both the histogenetic and microscopic criteria, the benign mesenchymal tumors analyzed were classified into one of the following categories: desmoid-type lingual fibromatosis, hemangioma, lymphangioma, lipoma and rhabdomyoma.

We encountered two cases with **lingual fibromatosis**. One of them belonged to a 58-year-old male and the other case was diagnosed in a male child, 8-year-old. These cases accounted for 12.50% of benign mesenchymal tumors of the tongue, 5.26% of benign tumors of the tongue and only 1.19% of all lingual neoplasms (Table 3).

Table 3 – ***Histopathological distribution of benign mesenchymal tumors of the tongue***

Tumor type	Fibromatosis	Hemangioma	Lymphangioma	Lipoma	Rhabdomyoma
No. of cases	2	8	2	3	1
Percentage	12.50	50	12.50	18.75	6.25

Fibromatosis of the adult was characterized microscopically by a proliferation of thin and elongated spindle cells, resembling fibroblasts. Their nuclei were small, pale, with prominent nucleoli. Cytoplasm was well represented, with well-defined limits. Neoplastic cells were arranged in imprecisely delimited bands, separated by a collagen stroma and sometimes-myxoid (Figure 1). In some areas of tumor, collagen was more abundant and surrounded individual tumor cells. Tumor stroma also contained a small amount of mostly lymphocytic, inflammatory infiltrate. The periphery of the tumour showed areas where the proliferation of neo-

plastic tissue infiltrated the skeletal muscle. We noticed the existence of residual skeletal muscle fibers embedded in the tumor tissue (Figure 2).

The microscopic appearance raised the problem of differential diagnosis with fibrosarcoma and exuberant reactive fibroblastic proliferation. The uniform appearance of the proliferation, the mature appearance of neoplastic cells as well as the low mitotic activity, excluded the diagnosis of fibrosarcoma. In the case of reactive fibroblastic proliferation, the proliferation shows a variable pattern, with constant association of micro-hemorrhages or hemosiderin deposits.

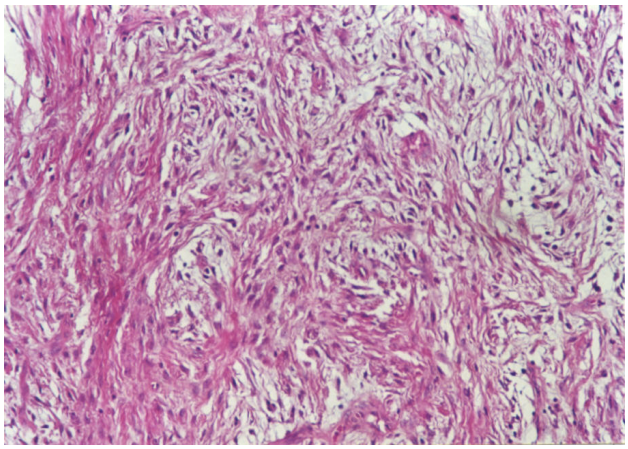

Figure 1 – ***Adult-type lingual fibromatosis (HE stain, ob. 10×).***

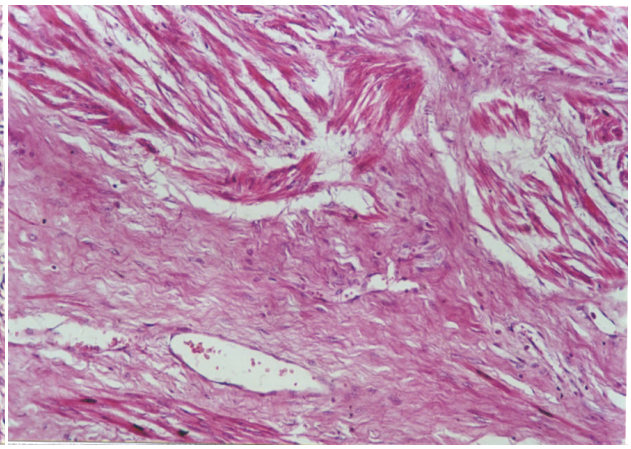

Figure 2 – ***Adult-type lingual fibromatosis (HE stain, ob. 10×).***

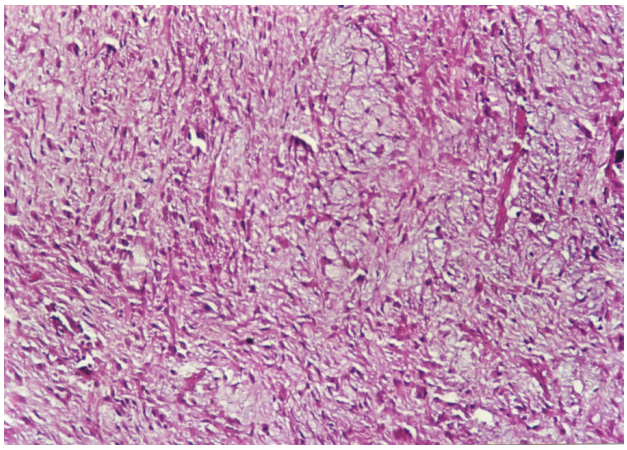

Figure 3 – ***Infantile lingual fibromatosis (HE stain, ob. 10×).***

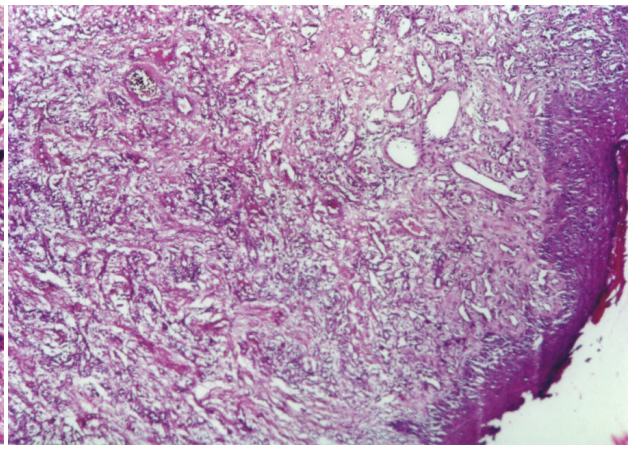

Figure 4 – ***Capillary hemangioma (HE stain, ob. 10×).***

In terms of microscopic appearance, fibromatosis of the child was also composed of a spindle cell proliferation similar to young fibroblasts, arranged as bundles, sometimes less obvious (Figure 3). Neoplastic cells had an elongated shape and smaller size than fibroblasts. On serial sections from different areas of the tumor, the collagen-type tumor stroma was variably represented. Paucicellular areas rich in collagen fibers were seen along with bundles of tumor cells, sometimes crossing each other, separated by several collagen fibers. The margins of the tumor were imprecisely defined, extending diffusely into adjacent tissues.

We encountered eight cases with **lingual hemangioma**, accounting for half of the benign mesenchymal tumors, 21% of all benign tumors of the tongue and 4.7% of all lingual neoplasms. They were the most common benign mesenchymal malignancies of the tongue encountered in our study. Tumors belonged to patients whose age varied widely, from 11 to 48-year-old. However, the highest incidence was seen in the fifth decade of life. More than half of the tumors were seen in men (six cases). Four out of eight cases with hemangioma were capillary hemangiomas, one was cavernous hemangioma and three cases were granulation tissue type hemangiomas. The four *capillary type hemangiomas* were made up of vascular spaces with narrow walls and small lumen. They were lined by swollen, cuboid, sometimes elongated endothelial cells. Vascular lumina generally had a round to oval shape and were either dilated containing blood, or collabated and empty (Figure 4).

In one case, there were diagnostic difficulties due to difficulties in identifying the vascular lumina because of the hypercellular aspect of the tumor. Swollen endothelial cells showed a compact proliferation in which tumor vessels were difficult to reveal (Figure 5). In this case, the Gömöri's stain highlighted the presence of reticulin fibers arranged around vascular lumina (Figure 6).

In two of the four cases with capillary type hemangiomas, tumors showed diffuse interstitial fibrosis

around obvious vascular lumina. Thus, tumors as a whole, showed an angiofibroma appearance (Figure 7). In the other three tumors, suprajacent epithelium was ulcerated and their stoma showed an abundant inflammatory infiltrate composed of lymphocytes, plasma cells and neutrophils (Figure 8).

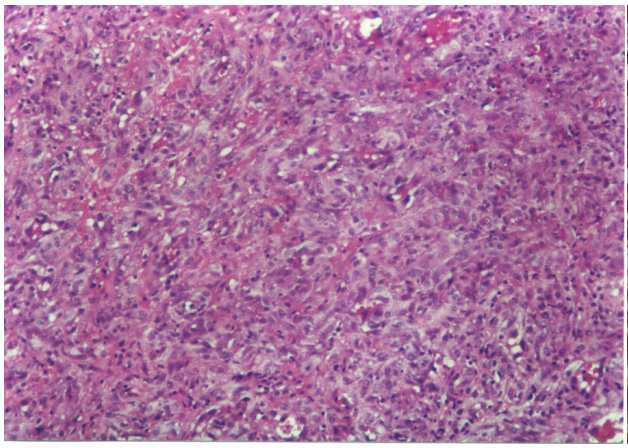

Figure 5 – ***Highly cellular capillary hemangioma (HE stain, ob. 6×).***

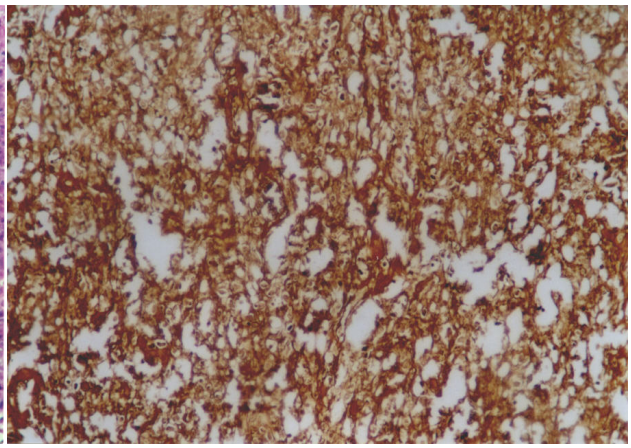

Figure 6 – ***Capillary hemangioma (Gömöri's stain, ob. 6×).***

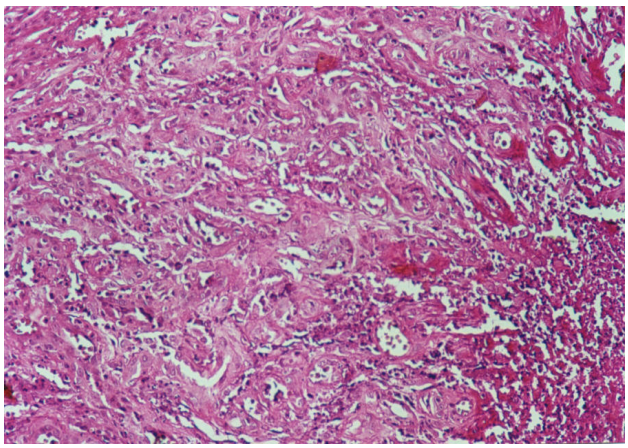

Figure 7 – ***Capillary hemangioma with fibrous stroma (HE stain, ob. 6×).***

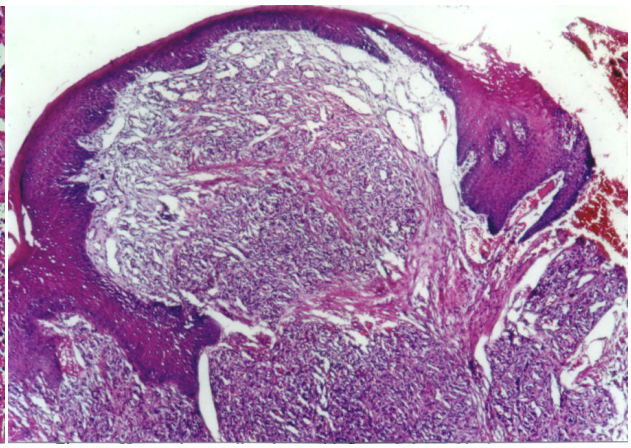

Figure 8 – ***Ulcerated and inflamed capillary hemangioma (HE stain, ob. 6×).***

In the case of the cavernous hemangioma, the tumor was composed of large and irregular vascular spaces, dilated and filled with blood. Vascular lumina were lined by flattened endothelia and their walls were thickened due to adventitial fibrosis (Figure 9). Tumor vessels showed a rough lobular arrangement or were diffusely arranged. The fibro-collagen tumor stroma showed non-specific inflammatory infiltrates, sometimes with areas of calcification.

The three cases of type granulation tissue type granulomas, highly cellular hemangiomas, with a lobular arrangement in a fibro-myxoid stroma (Figure 10). Tumor lobuli were composed of large vessels sometimes have thicker walls with muscle-type differentiations, surrounded by capillary-type cell clusters. In two of the three cases, the lesions had an abundant inflammatory infiltrate of acute and chronic type, with diffuse arrangement (Figure 11). The covering epithelium of the tumor was atrophic or sometimes even ulcerated, and the epithelium adjacent to the tumor showed acanthosis and hyperkeratosis (Figure 11).

There were two cases of **lymphangioma**. They accounted for 12.50% of benign tumors with mesenchymal origin, 5.26% of benign tumors of the tongue and 1.19% of all tumors of the tongue, for the period discussed. Tumors were diagnosed in patients between the first and fifth decades of life and both were seen in males.

The microscopic appearance in both cases corresponded to the cavernous-type lymphangioma. They were composed of the large lymphatic spaces, lined by flattened endothelial cells, similar to normal ones (Figures 12 and 13).

Sometimes, a few underdeveloped muscle fibers were seen in the walls of large vessels. The lumina of lymphatic spaces were filled with a homogeneous, eosinophilic liquid, which sometimes contained a few lymphocytes and even red blood cells. Tumor stroma was of fibro-collagen type, with discrete inflammatory infiltrates consisting of lymphocytes. In both tumors, at the periphery of the tumor and sometimes even between tumor lymphatics, atrophy and degeneration of skeletal muscle fibers were seen. We also observed changes in the suprajacent flattened epithelium of the tumor. At this level, we noticed areas with papillomatosis and acanthosis, whereas the suprajacent epithelium was apparently normal or even atrophic (Figure 14).

The diagnosis of lymphangioma was relatively easy to establish. However, due to secondary associated

hemorrhages, one of the tumors had to be differentiated from a cavernous hemangioma. In this case, the presence of stromal infiltrates with lymphocytes and irregularly shaped vascular lumina lined by cells with nuclei located at large distances to each other, allowed the diagnosis of lymphangioma.

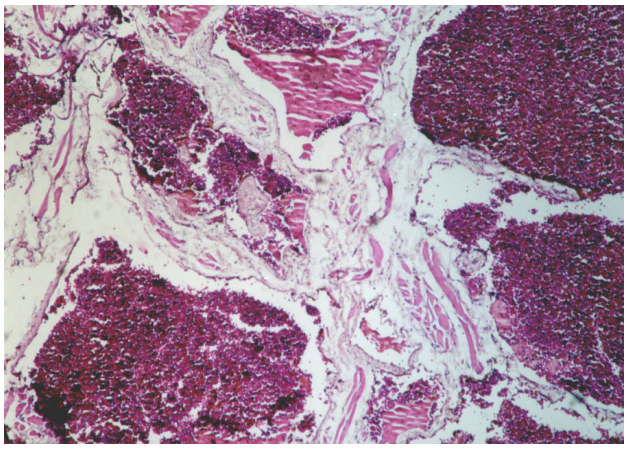

Figure 9 – ***Cavernous hemangioma (HE stain, ob. 6×).***

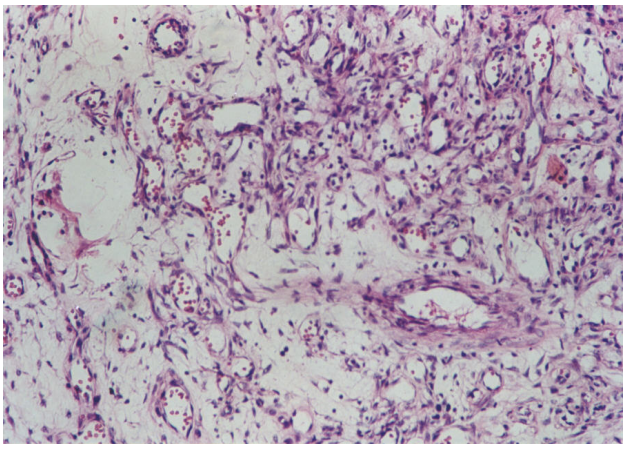

Figure 10 – ***Granulation tissue-type hemangioma (HE stain, ob. 10×).***

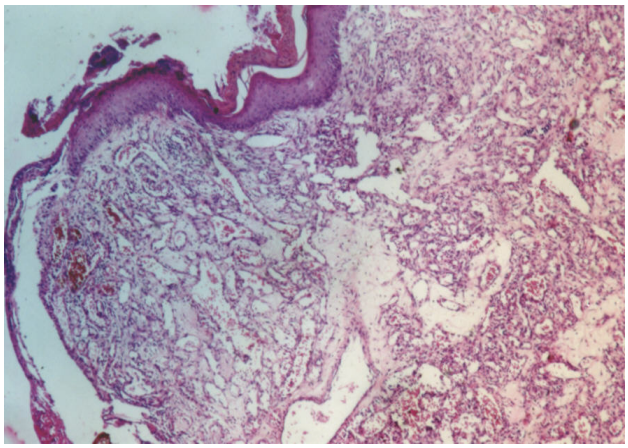

Figure 11 – ***Granulation tissue-type hemangioma with areas of acanthosis and keratinisation as well as atrophy of the covering epithelium (HE stain, ob. 6×).***

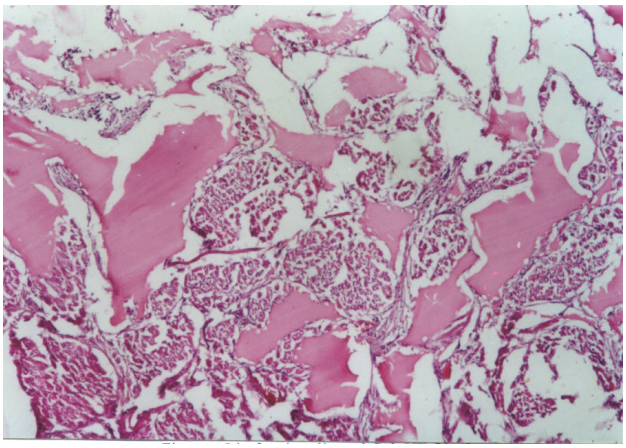

Figure 12 – ***Lingual lymphangioma (HE stain, ob. 6×).***

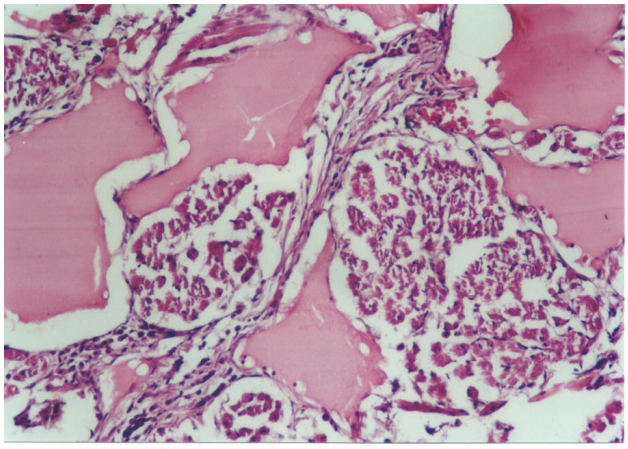

Figure 13 – ***Lingual lymphangioma (HE stain, ob. 6×).***

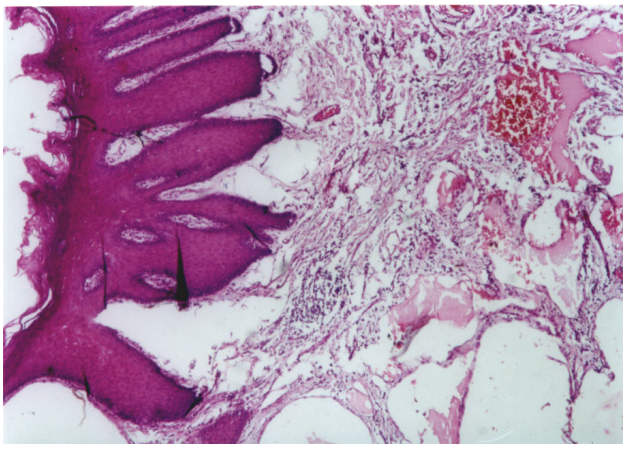

Figure 14 – ***Lingual lymphangioma – papillomatosis and acanthosis of the covering epithelium (HE stain, ob. 6×).***

Lingual lipomas were seen in three cases, representing 18.75% of benign mesenchymal tumors, 7.89% of lingual benign tumors and 1.79% of all the studied neoplasms.

One of the cases belonged to a 22-year-old person, the other two were diagnosed in patients in the seventh decade of life. All three patients were males.

Microscopically, tumors were composed of generally globular and large cells, similar to mature fatty cells. Neoplastic cells had a clear cytoplasm and peripheral

nuclei, often difficult to identify (Figure 15). They were arranged in a lobular pattern, separated by thin fibrous septa containing capillary-type blood vessels. Skeletal muscle fibers adjacent to or interspersed between tumor lobules were atrophic or showed minimal degenerative lesions (Figure 16).

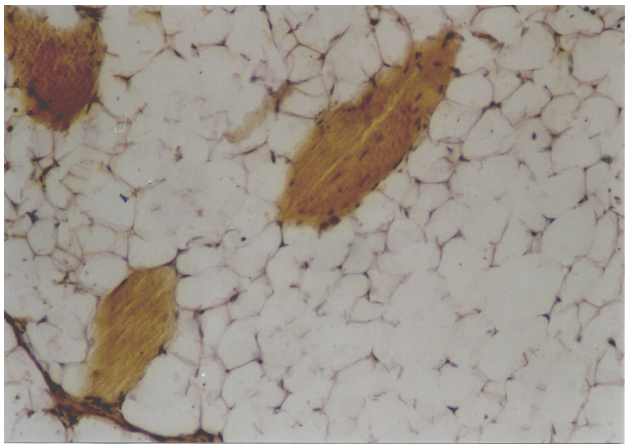

Figure 15 – ***Lingual lipoma (van Gieson stain, ob. 6×).***

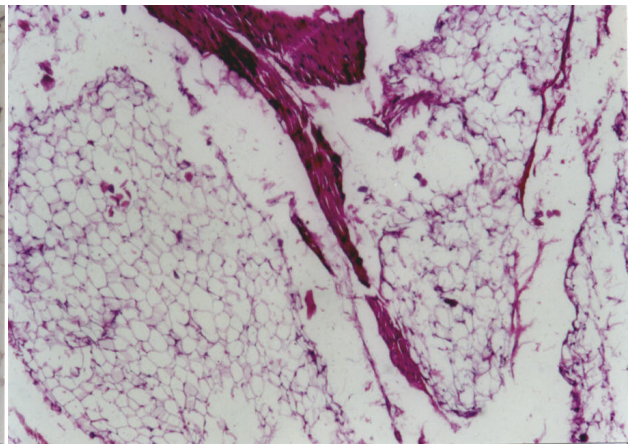

Figure 16 – ***Lingual lipoma (HE stain, ob. 6×).***

There was only one case of rhabdomyoma. The tumor belonged to an 8-year-old male patient. Its location was at the base of the tongue. Similar data from the literature indicates the presence of such tumors at much younger ages, between 0 and 3-year-old, with a propensity for males. The microscopic appearance indicated a fetal type rhabdomyoma. The cellularity and the appearance of neoplastic cells varied on different sections at different levels of the tumor mass. It was composed of primitive non-differentiated oval-shaped or spindle cells together with skeletal muscle fibers with different degrees of differentiation in a well represented myxoid matrix (Figure 17). Neoplastic cells resembled the skeletal muscle tissue, which is visible in the second and third months of intrauterine life. Areas in which tumor cells were arranged as bundles were seen, separated by a myxoid stroma, along with areas where the myxoid stroma surrounded individual cells. Cross striations were rare and more obvious in the periphery of the tumor (Figure 18).

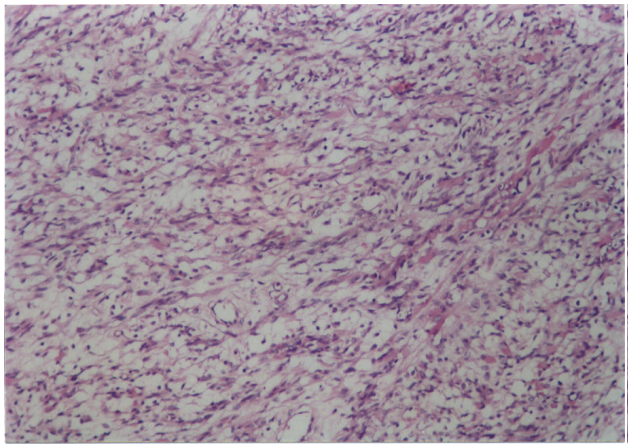

Figure 17 – ***Lingual rhabdomyoma (HE stain, ob. 6×).***

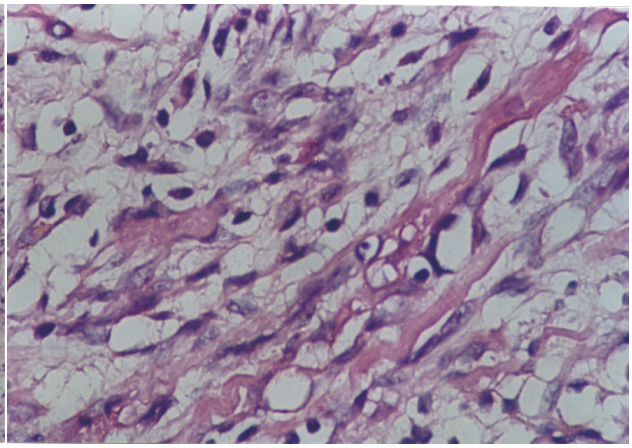

Figure 18 – ***Lingual rhabdomyoma (HE stain, ob. 20×).***

The appearance of the tumor imposed its differentiation from an embryonary rhabdomyosarcoma, but unlike the latter, the tumor diagnosed in our study showed a discrete cell pleomorphism and rare mitoses.

Discussion

Lingual fibromatosis is a form of extra-abdominal desmoid and is considered a tumor with intermediate behavior due to rapid proliferation, infiltration of adjacent structures and high rate of relapse [3]. Age of onset of desmoid tumors is between puberty and 40-year-old, with a maximum incidence between 25–35 years. Its incidence according to gender indicates an equal impairment or, as other statistics show, a propensity for males. In a study on 367 cases, seven tumors developed in the head [4].

Infantile desmoids fibromatosis is considered the equivalent of the adult extra-abdominal desmoid in childhood. It usually develops in the skeletal muscles of the head and neck where one of the most common locations is the tongue. Children aged between 0 and 5-year-old were found to be most affected, especially in the first two years of life [4, 7]. In our study, the tumor diagnosed as infantile fibromatosis belonged to an 8-year-old male child.

Hemangiomas are defined as benign non-reactive processes in which there are a growing number of vessels. In this context, it is difficult to classify these lesions as neoplasms, hamartomas or malformations.

They are considered the most common soft tissue tumors and are usually located in the head and neck [7, 8]. In a study on 540 cases [5], 370 cases were either hemangiomas of the skin or of mucous membranes, of which 80 cases were located in different structures of the mouth. A group of researchers reported the hemangiomas of the mouth to the overall incidence of hemangiomas and concluded that tumors of the oral mucosa represented 14% of the cases [7]. The same author indicates the most commonly injured areas of the oral mucosa as sites of predilection for hemangiomas in the adult: lip mucosa (63% of cases), oral mucosa (14% of cases) and the lateral margins of the lingual mucosa (14% of cases).

A special place is occupied by granulation tissue type hemangiomas or pyogenic granulomas that may occur anywhere on the skin and mucous membranes, but over 60% of cases develop on mucous membranes. In a study on 279 cases [5], 20 cases of granulation tissue type hemangiomas had lingual localization. In our study, the granulation tissue type hemangiomas had a relatively high incidence, accounting for 37.3% of all varieties of lingual hemangiomas encountered.

As the case of hemangiomas, it is difficult to assess whether lymphangiomas are true neoplasms, hamartomas, lymphangiectasies or malformations. They are rare compared with hemangiomas. Thus, in a study performed over a period of 15 years on 768 benign childhood tumors, only 48 cases were lymphangiomas. In another statistic [6] on 65 cases of lymphangioma, 35 of them were located in the head, of which eight had lingual development. This finding is consistent with our data, lymphangiomas accounting for only 1.19% of tongue cancers diagnosed over a 10-year period.

Data in the literature on the incidence of these tumors by age groups indicate that approximately 50–60% of them are present from birth and 90% of them show up at the end of the second year of life. As to gender distribution of tumors, there was a slight predominance in males [9]. The two cases encountered were diagnosed in male patients, aged 5 and 31 years respectively.

The literature recorded the presence of lipoma in the mouth, with the following locations as preferential ones: tongue, floor of mouth, buccal mucosa, gums, muco-buccal or labial grooves. It is considered that such tumors develop more frequently in adult males [2, 7, 10–12].

The histogenesis of the rhabdomyoma is controversial. Its various forms are regarded as either hamartomas or true neoplasms. In the case of the lingual location, the lesion is regarded as neoplastic in nature, with its origins in the muscles developed from the third and fourth branchial arches. Lingual rhabdomyomas are rare tumors that mainly affect people over 40-year-old, with a higher incidence in males [13–18].

Conclusions

The microscopic appearance of adult fibromatosis raised the problem of differential diagnosis with fibrosarcoma and fibroblastic exuberant reactive proliferation, with the uniform appearance of the proliferation as well as the mature appearance of neoplastic cells and the low mitotic activity differentiating it from the latter ones.

Half of capillary hemangiomas resembled angiofibromas, showing diffuse interstitial fibrosis, as well as fibrosis around the obvious vascular lumina. In three quarters of all cases, suprajacent epithelium was ulcerated and the stoma of the lesion showed an abundant inflammatory infiltrate.

In cavernous type hemangiomas, tumor vessels showed a rough lobular or diffuse arrangement, while the diffuse type fibro-collagen stroma presented non-specific inflammatory infiltrates and occasional areas of calcification.

In granulation tissue, type hemangiomas the lesions showed an abundant inflammatory infiltrate of acute and chronic type with a diffuse pattern; the covering epithelium was atrophic, sometimes ulcerated, and the epithelium adjacent to the tumor showed acanthosis and hyperkeratosis.

Lymphangiomas showed skeletal muscle atrophy and degeneration in the periphery of the tumor and sometimes even between tumor lymphatic vessels. In the flattened epithelium covering the tumor we noticed areas showing acanthosis and papillomatosis, while the epithelium adjacent to the tumor was apparently normal or even atropic.

Skeletal muscle fibers adjacent to or interspersed with the lobules of the lipomas were atrophic or showed minimal degenerative lesions.

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