AGGRESSIVE JUVENILE MANDIBULAR FIBROMATOSIS

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ABSTRACT
Aggressive juvenile fibromatosis of the jawbones is a rare tumor presenting as infiltrative mass with unpredictable evolution. We report herein a 17-year-old student with a 6-month history of radiologically proven resorption of a part of the mandible, lingual displacement of tooth 34 and malocclusion. Alveolar ridge resorption and three dark-brown foci in the bone were seen after the tooth was extracted. Histological study showed the tumor tissue to have a bundle-like structure; immunohistochemically it was positive for vimentin, smooth muscle actin, β-catenin, Ki-67 (5%), and negative for desmin and cytokeratin 34βE12. The golden standard in the diagnostics of desmoid fibromatoses is the nuclear or membrane expression of β-catenin, which is found in 90% of the cases. Differential diagnosis include mandibular fibroma, well-differentiated fibrosarcoma, fibrosing histiocytoma, and infiltration from adjacent soft-tissue tumor. Aggressive juvenile fibromatosis should be managed by radical excision. Local recurrences are not rare, but metastases do not develop. In rare cases this type of fibromatosis has been known to regress spontaneously. Aggressive fibromatosis is a diagnostic challenge, since it remains in the grey zone between benign and malignant lesions of the oral cavity.

Keywords: aggressive juvenile fibromatosis, mandible, histopathology

INTRODUCTION
Fibromatoses represent a group of non-metastasizing locally aggressive tumors with borderline malignancy. Being categorised as the “grey zone” between benign and malignant tumors they present a challenge for clinicians and pathologists. Fibromatoses develop before 40 years of age (childhood and juvenile age prevail) in any part of the body. Their prevalence in the total population is extremely low – 0.2-0.5 per 100000 newly found cases per year¹, and the oral cavity is the place of origin of only 3-10%.² Aggressive juvenile fibromatosis of the mandible is not reported widely in the literature.

Fibromatoses are divided into two broad categories: superficial and deep.³,⁴ The superficial fibromatoses (palmar and plantar) are usually small (< 5 cm) slow-growing lesions. Surrounding tissues are rarely involved in their development. Deep fibromatoses (desmoids) are fast growing lesions, which frequently reach significant size, if their localization allows so, e.g. in the intra-abdominal type of desmoid. They are referred to as aggressive fibromatoses for their infiltrative pattern of growth, but also because of their high recurrence rate (as frequently as 70%).

The fibromatoses of the head and neck belong to the group of extra-abdominal fibromatoses (60% of the cases). Only deep fibrotic proliferations occur in the oral cavity: they are sporadic, familial adenomatous polyposis associated and multicentric. They present as variously sized masses, localized centrally in the jawbones or the soft tissues. Because soft tissue and intraosseous aggressive fibromatoses of the head and neck are histologically indistinguishable and because of their mutual infiltration, they are usually termed desmoid fibromatosis.⁴,⁵

We present herein a case of rare aggressive mandibular fibromatosis.

CASE REPORT
B.P.M, a 17-year-old female student. History of the illness: Complaints of intensifying pain in the left mandibular corpus and mobile 1st premolar for 6 months. The patient received orthodontic treatment for maxillary prognathism with braces 4-5 years previously. A recurrence of the tumor...
occurred 1 year ago. The patient saw her dental general practitioner with these complaints and was prescribed radiographic study and referred to an oral surgeon for consultation. **Objective findings:** Intraorally: malocclusion with open bite in the front and to the left with distal position of the mandible. First lower premolar is III degree mobile and displaced lingually, and second premolar is inclined mesially (Fig. 1). The gingiva surrounding the premolar is bluish with soft consistence. A circular bone loss with depth of the pockets 10 mm was found by probing. The X-ray shows bone erosion around tooth 34 and resorption of the tooth root (Fig. 2). Complete alveolar ridge resorption, smoothly delineated and three dark-brown foci in the bone were seen after the tooth was extracted. Extraorally – without alterations.

**Clinical diagnosis:** Granuloma eosinophilicum. Differential diagnosis: Osteoblastoclastoma.

**Biopsy (B 34072/12):** The material obtained by curettage from the tissue around the first left mandibular premolar (1.5 cm³, fixed with 10% buffered neutral formalin) was processed routinely (H-E staining) and immunohistochemically (vimentin, smooth-muscle actin, desmin, high-molecular cytokeratin, estrogen receptor and Ki-67).

A diffuse proliferative process with infiltrative growth was found subepithelially on microscopy. Its main mass comprised spindle-like elongated mesenchymal cells with fibroblast/myofibroblast characteristics (Fig. 3). Their nuclei were ovoid,

**Figure 1.** The first mandibular premolar is mobile and displaced lingually, and the second premolar is inclined mesially.

**Figure 2.** Bone erosion around tooth 34.

**Figure 3.** Spindle-like cells, structured in whirl-like bundles (HE, magn. 10 x 20). Inset: Giant multinuclear cell, type osteoclast (HE, magn. 10 x 100).

**Figure 4.** Anti-β-catenin (x100).
relatively uniform, with visible nucleoli. The nucleo-cytoplasmic index was low, within normal limits. Single mitotic figures were visible, but no atypical mitoses were present. These cells formed interweaving, relatively large and long bundles. Single giant multinucleous osteoclast-type cells were found (Fig. 3a). There was a lot of elongated blood vessels in the stroma, but these were poorly collagenized. Perivasal hemosiderin granules were scarce. No myxoid alterations and necrosis were found. The lining mucous epithelial layer was mechanically eroded, with no infiltration.

The spindle-like cells expressed vimentin (++); smooth muscle actin (++); β-catenin (+) (Fig. 4); desmin (-); cytokeratin 34βE12 (-); estrogen receptor (+); Ki-67 (MIB -1) (+) in approximately 5% of the nuclei.

Pathomorphological diagnosis: Aggressive juvenile mandibular fibromatosis.

The patient’s condition is followed up by an oral surgeon. After 1 year of follow-up no recurrence occurred and the bone alterations in the jaw were stabilized (Fig. 5).

DISCUSSION

The etiology of fibromatoses is not completely elucidated and is probably quite diverse: mutations in the adenomatous polyposis coli-gene in chromosome 5q22, sporadic cases with mutation in the β-catenin-gene or the occurrence of scar on the spot, have been described.

The fibromatosis is an infiltrative tumor that is difficult to excise, possessing high recurrence potential. It is recommended that it is excised at least 2-3 cm within normal tissue.1,2 Radiotherapy, chemotherapy or endocrine therapy should be included in the treatment of surgically unresectable fibromatoses, even though they might be benign.7 Radiotherapy is given in high doses (> 50 Gy), and yet 20-36% of the patients have recurrences.2

Anti-estrogen hormonal therapy for aggressive fibromatosis is based on its prevalence in women in fertile age (up to 80%) and its faster growth during pregnancy. Immunohistochemically, as has been shown by our study, the tumor cells are positive for estrogen receptors (especially in Gardner syndrome). This finding may be related to the report of stabilization and even regression of the process by tamoxifen therapy.8 Beneficial effect has been reported in using NSAIDs as well.3,8 Chemotherapy is used in cases of impossible or unsuccessful surgical and radiological approaches.

Myofibroblastic immunophenotype is supposed in fibromatosis: vimentin (+), actin (+), variable desmine. The golden standard in the diagnosis of desmoid fibromatoses is β-catenin – a genetic immunohistochemical marker. Its nuclear and membrane expression are observed in more than 90% of the cases of fibromatosis, associated with Gardner syndrome and in sporadic fibromatoses. The proliferative nuclear index is usually lower than the one presented in this case (5% - a predictor of recurrence).

The differential diagnosis clinically includes eosinophilic granuloma (but without fever), osteoblastoma and well differentiated fibrosarcoma.1,3,4,7 Clinically it is quite similar to fibromatosis in location, age range5,9 and infiltrative presentations. The morphological study has to eliminate the first two options. The fibrosarcoma presents with a higher mitotic index and signs of cellular atypism.
and frequent necroses. In malignant fibrous histiocytoma the atypical cells are histiocytes, some giant multinucleous (but not osteoclast-type) cells. The ossifying mandibular fibroma is indisputably a benign tumor without infiltration. The inflammatory myofibroblast tumor is characterized by intratumor inflammatory lymphoid proliferations and the myofibroblasts are reactive. The nodular (pseudosarcomatous) fascitis possesses myxoid regions and significant intratumor haemorrhages, differing from the perivascular ones in fibromatosis.

Fibromatoses recur in the first few years. Ogunsalu and Barclay\(^1\) propose staging of histologically verified clinically aggressive fibromatoses on 4 levels: A – recurrence after aggressive surgical treatment; B – no recurrence after aggressive surgical treatment; C – no recurrence after non-aggressive surgical treatment; D – tumor regression without definitive surgical treatment.

**CONCLUSION**

Aggressive fibromatosis of the jawbones is extremely rare. Clinically, the tumor tends to present as malignant – it erodes the bone, infiltrates the surrounding tissues, and recurs. The microscope finding is also not always conclusive. Crucial for the diagnosis is the immunohistochemical expression of β-Catenin. The good collaboration between the clinician and the pathologist helps in differentiating this lesion with borderline malignancy from the many other types of fibroblastic processes – reactive and neoplastic, and specifically from the well-differentiated fibrosarcoma.

**REFERENCES**


**АГРЕССИВНЫЙ ЮВЕНИЛЬНЫЙ ФИБРОМАТОЗ НИЖНЕЙ ЧЕЛОВЕК**

Г. Иванов, Д. Атанасов, Б. Анаев

**РЕЗЮМЕ**

Агрессивный ювенильный фиброматоз костей человека — это редко встречающаяся опухоль — инфильтрационная масса с непредсказуемым ростом и эволюцией. Представлен случай 17-летней девушки с рентгенологическим „расплыванием” участка мандibuлы давностью 6 мес., с смещением 34-ого зуба в лингвальную сторону и с нарушением окклюзии. При его экстракции установлена полная резорбция альвеолярного гребня и три темно-коричневых гнезд в кости. Гистологически опухолевая ткань имеет нонное строение; иммуногистохимически: Vimentin (+), SMA (+), β-catenin (+), Ki-67 (5%), Desmin (-), Cytokeratin 34bE12 (-). Золотой стандарт для диагностики десмоидных фиброматозов представляют ядерная или мембранная экспрессия β-catenin, которые встречаются в 90% случаев. Диагностически-диагностически обсуждаются фиброма нижней челюсти, высоко-дифференцированная фибросаркома, фиброзирующая гистоциитома, инфильтрация с соседней тканью мягкой ткани. Агрессивный ювенильный фиброматоз подлежит широкой экспертизе. Локальные реакции не являются редкостью, но метастазы не реализуются. В редких случаях формируется регрессирует спонтанно. Агрессивный фиброматоз представляет диагностический вызов, так как остается в серой зоне между бенIGNными и малыми опухолями в ротовой полости.