Expression of Basic Fibroblast Growth Factor in Human Ameloblastoma

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Abstract **Objective** To study the expression of basic fibroblast growth factor(bFGF) in human ameloblastoma (AB). **Methods** Expression of bFGF was detected in 61 cases of AB (including 36 cases of primary AB, 19 of recurrent AB, 6 of malignant AB), 11 cases of odontogenic keratocyst (OKC), and 4 cases of oral normal mucosa. Standard immunohistochemical techniques were used. **Results** The expression of bFGF in AB was higher than that in OKC and normal oral mucosa, and the difference was significant in statistics ($P<0.05$). The expression rate of bFGF increased gradually in primary, recurrent, and malignant AB ($P<0.05$). The positive staining were mainly found in cytoplasm, and partly in the nuclei of cells. **Conclusion** The expression of bFGF is closely related to tumor invasive biological characteristics in AB, and it may be an important factor in angiogenesis.

Key Words ameloblastoma; odontogenic keratocyst; basic fibroblast growth factor

Ameloblastoma is the most popular tumor among the maxilla, and is formed by the co-inducement of odontogenic epidermis and extra-interstitial tissue. Its main biological character is invasive development and recurrent after operation [1]. Its recurrent and invasive behaviors are associated with many factors [2], of which basic fibroblast growth factor is one. At present, the study about bFGF in odontogenic disease, and the relationship between bFGF and clinical biological behavior of AB is still not clear, so we study the expression of bFGF in AB and its clinical significance.

Material

The Material samples come from the stocked wax sample in pathological department of stomatological institute and the first affiliated hospital of china medical university. There are 61 cases of AB (36 cased of primary AB, 19 cases of recurrent AB, 6 cases of malignant AB), 11 cases of odontogenic keratocyst, and 4 cases of oral normal mucosa. All samples are processed with fixation in 10% formalin, routine buried in paraffin, successive section was made in 4 m thickness.

All cases have complete clinical information and follow-up. The follow-up time is 3~30 years.

Reagent and method

using S-P immuno-chemical staining. bFGF multi-antibody (Ba0259), SABC reagent box (SA1020) are purchased from Wuhan biological limited company. DAB chromogenic reagent (DAB0031), purchased from FuJian MaiXin biological limited company, is the product of Maxim . SABC staining is directed by the handle book, and we routinely set positive control, with PBS as negative control.

Result judgement

The improved score system was taken to half-quantify bFGF expression. (1) Score according to chromogenic degree of cell: 0 point is no color; 1 point is yellowish; 2 point is brown yellow. (2) Score according to the ratio of chromogenic tumor cell in total tumor cell: 1 point is below 25%, 2 point is 25%~75%, and 3 point is over 75%. Integral for each case = (1) × (2), and according to the integral: (−), integral is 0 point; (+), integral is 1~4 point; (++), integral is more than 4 point.

Statistical method

Adopting SPSS 11.5 statistic software, using Kruskal-Will method and chi-square test to analysis

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bFGF expression.

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There is weakly positive expression of bFGF in shallow acanthoid layer cytoplasm of oral normal mucosa; the expression site of bFGF in OKC usually also lies in shallow acanthoid layer; the positive expression in AB lies in external layer of tumor focus and in the asteroid cytoplasm; 13 cases have AB positive expression in nuclei, but the expression in the keratocyst and granular cytoplasm is weakly positive or negative. Around AB tumor there is positive expression in endovascular cell and inflammation cytoplasm; for interstitial tissue there are 9 cases positive expression in fibroblast. Expression of bFGF in the three lesions is present in Table 1.

Tab.1 Expression of bFGF in normal oral mucosa, OKC, and AB

group	n	expression of bFGF		total
		(+)	(++)	n(%)
normal mucosa	4	2	0	2(50.0)
OKC	11	5	3	8(72.7)
AB	61	14	38	52(85.2)[1), 3)]
primary	36	10	18	28(77.8)[1), 3)]
recurrent	19	4	14	18(94.7)[2), 4), 5)]
malignant	6	0	6	6(100.0)[2), 4), 5)]

notes;compared with normal mucosa : 1) P <0.05,
2) P<0.01;compared with OKC: 3)P<0.05, 4) P<0.01;
5) compared with primary AB: P<0.05

AB is analyzed separately according to clinical biological behavior. comparisons made between the three groups present to be P<0.05. Following with recurrence and neoplasm of AB, the positive expression rate and degree are also increased. The differences between the three group´s were obviously statistical significance.

Rapid proliferation, local invasion and metastasis of tumor are all related with angiogenesis in tumor, so angiogenesis is an important factor to estimate prognosis of tumor. AB and OKC are the lesion of the most invasively developed and recurred easily in maxilla, and like many tumors, they are also a vaso−dependent lesion[3].

As reported, acid FGF (aFGF) and bFGF exist in plasma with dose-dependent character among the cultured AB and promote the development of AB. bFGF mainly exists in basement membrane and few exists in epithelium. But our experiment indicates that bFGF widely exists in external area of AB and asteroid cytoplasm. The expression rate hit 85.2% in which 13 cases of AB have nuclear positive expression, which is similar with So´s study [4]. Our study also suggests that bFGF not only exists in AB and OKC epithelium, but also have expression in interstitial fibrocyte, endovascular cell, inflammation cell (mononuclear cell, lymphocyte, plasmic cell) around AB. Cam[5] found in rat dental embryo that bFGF is strongly expressed in asteroid layer and dental interstitial cell, but aFGF staining is defect, which proves that extra cell matrix can act as deposited pool for growth factor, especially bFGF.

bFGF is associated with development of many kinds of tumors and angiogenesis of tumor[6,7]. It is strongly expressed in abnormal proliferation of oral epithelium and squamous carcinoma, but weakly expressed in epithelium basement membrane. The development of odontogenic tumor is complex process which involved repeated signal transfer of odontogenic epithelium and extra embryo interstitial tissue. Someone supposes that bFGF which combined with tissue matrix and base membrane is a stockage factor. The release of stockage factor may be a way for rapid promotes growth factor to stimulate vessel genesis in the process of angiogenesis.

In this experiment bFGF is weakly expressed in normal mucous, and its expressed in OKT increased, but is mainly still weak. In AB its expression is obviously increased concomitant with recurrence and malignant of AB, and bFGF expression trend is mainly moderate to high degree. This proves bFGF is tightly associated with biological behavior of AB, which is never reported in previous studies. The positive expression of bFGF in AB and partial fibroblast nuclear may prove that bFGF is related with nuclear activity in the stage of tissue differentiation and leads to activation of multiple transfer factors in nuclei, then promotes occurrence and development of AB.

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