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Micro vessel density as an indicator of invasive growth pattern in basal cell carcinoma

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Introduction

Basal cell carcinoma is currently the most common cutaneous cancer of the facial skin. Therefore, there is still a need to find reliable prognostic indicators that correlate with outcome and may detect patients at a high risk of local recurrence. Recent studies have suggested that there is a significant correlation between tumor angiogenesis, expressed as the micro vessel density within and toward the tumor, and tumor aggressiveness (Staibano et al. 1996). The aim of this study was to evaluate the angiogenesis in basal cell carcinomas by measuring the micro vessel density with regard to the local, especially osseous infiltration, and local tumor recurrence in a pilot study.

Material and Methods

The study consits of of 9 basal cell carcinoma patients. All basal cell carcinomas were complete resected. Micro vessels were highlighted by immunhistochemically staining for CD 31, the vascular endothelial growth factor (VEGF) and HIPPEL-LINDAU's proteine in formalin-fixed, paraffin-embedded tissues. The detection was performed using primary and secondary antibodies in accordance to the ABC-method. The interpretation included staining intensity by REMMELE's score of immunreactivity and WEIDNER's micro vessel density measurements. Micro vessel count was performed by light microscopy identifying the individual micro vessels on x200 fields, in areas of the most active neovascularization, previously selected at low power magnification (x40). All immunohistochemical data were compared with the clinical course of the patients.

Results

The immunhistochemical data after staining for CD 31 and VEGF are summarized in Tab. 1 and Tab.2, respectively.

Age	Sex	Recurrence	Staining Intensity	Percent positive Cells	Immunreactive Score
68	male	no	2	2	4
65	male	yes	3	3	9
55	female	no	2	2	4
66	female	no	1	2	2
70	female	yes	1	2	2
73	female	no	1	2	2
76	female	yes	2	2	4
73	female	no	1	1	1
82	female	no	1	2	2

Tab.1 Clinicopathologic and immunhistochemical data of basal cell carcinoma (staining for CD 31)

Age	Sex	Recurrence	Staining Intensity	Percent positive Cells	Immunreactive Score
68	male	no	9	3	3
65	male	yes	12	3	4
55	female	no	2	1	2
66	female	no	4	2	2
70	female	yes	6	2	3
73	female	no	12	3	4
76	female	yes	4	2	2
73	female	no	9	3	3
82	female	no	2	1	2

Tab.2 Clinicopathologic and immunhistochemical data of basal cell carcinoma (staining for VEGF)

In general, CD 31 showed a poorer staining intensity in comparison to VEGF. The angiogenetic factor and mitogene VEGF presented a partial increased number of hot spots as well as intensive staining intensity in HIPPEL-LINDAU proteins in the case of recurrent tumors. On the other hand, CD 31 showed only a poor capillarization in the centre of the tumors. A basal cell carcinoma with a high density of micro vessels (staining for CD 31) is shown in Fig 1. The clinical course confirmed a recurrence. An example of low micro vessel density (staining for CD 31) is illustrated in Fig. 2.

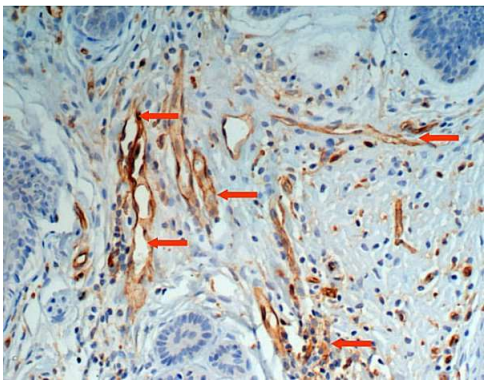

Fig. 1 Basal cell carcinoma: example of an area from a tumor with higher vascularization. Arrows indicate micro vessels (Immunhistochemical staining for CD 31, original magnification x 200)

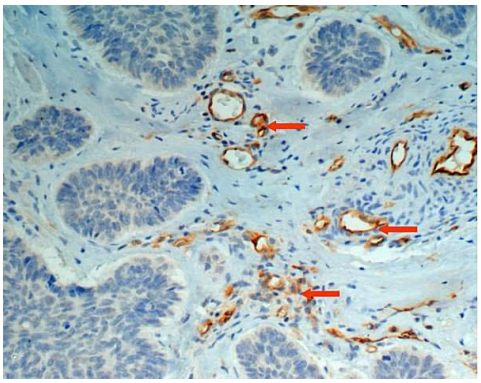

Fig. 2 Basal cell carcinoma: example of an area from a tumor with lower vascularization. Arrows indicate micro vessels (Immunhistochemical staining for CD 31, original magnification x 200)

The clinicopathological data indicated no recurrence. Fig. 3 shows a high vascularization (staining for VEGF), which is in agreement with a recurrent basal cell carcinoma. Additionally, Fig. 4 presents the comparable poor vessel density in a not recurrent carcinoma (staining for VEGF). Our data agree with the results of Bedlow et al.1999.

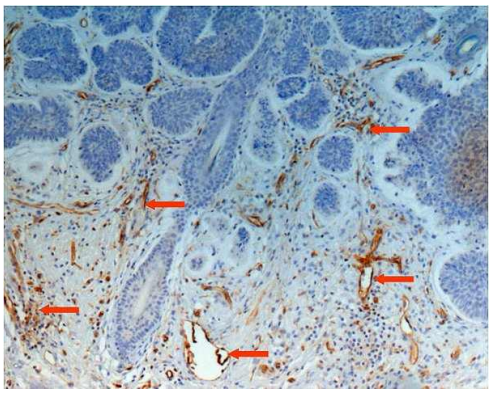

Fig. 3 Basal cell carcinoma: example of an area from a tumor with high vascularization. Arrows indicate micro vessels (Immunhistochemical staining for VEGF, original magnification x 200)

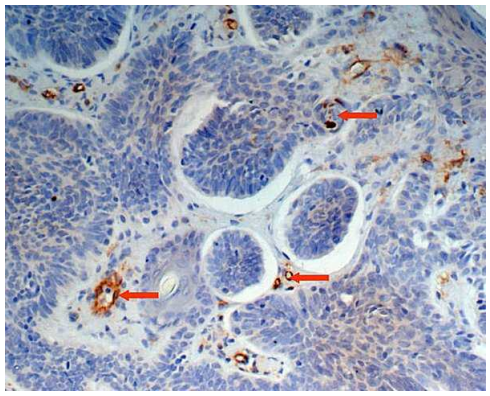

Fig. 4 Basal cell carcinoma: example of an area from a tumor with low vascularization. Arrows indicate micro vessels (Immunhistochemical staining for VEGF, original magnification x 200)

Discussion and Conclusions

Our pilot investigation at a limited number of cases does not show any direct hint on an influence of vascularization on the growth pattern in basal cell carcinoma despite some positive experience in the literature (Staibano et al.1996, Maiolino et al. 2000). Further investigations should include a big number of cases using fresh frozen specimens and looking for proliferation markers. Vascularization per se seems not to be a significant marker for malignancy in basal cell carcinomas.

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CLINICAL MONITORING WITH RESONANCE FREQUENCY ANALYSIS (RFA) OF ASTRA IMPLANTS

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Introduction

A quantitative diagnostical technique capable of assessing implant stability, bone formation and the clinical performance of all implants is supposed to optimise the results and make them more predictable. This study is set up to investigate the healing process of Astra Tech Implants in order to standardise the healing period.

Material and Method

20 patients - 11 females and 9 males - aged 50,5 years on average, were provided with 47 self-tapping Astra Tech Implants. We placed 24 Astra Tech ST Implants sized 4,5 to 5,0 mm in diameter, and 23 Astra Tech Universal Implants sized 3,5 to 4,0 mm in diameter, all 9 to 15 mm in length, according to the two-stage surgical protocol of Astra Tech Dental Implant System. 24 fixtures were placed in the mandible and 23 in the maxilla (tab.1).

Table 1

	9.0mm	11.0mm	13.0mm	15.0mm	
∅ 3.5mm	2	5	11	2	20
∅ 4.0mm			4		4
∅ 4.5mm		5	14	1	20
∅ 5.0mm	1	1	1		3
					47

After implant placement the primary stability was determined by the Resonance frequency analysis (RFA) according to Meredith et al.(1996). Insertion followed under local anesthesia with Ultracain DS and the manufacturer's instructions, with a healing period of 3 months for the mandible as well as the maxilla. After reentry the secondary stability was determined by resonance frequency analysis. All fixtures were immediately provided with a fixed prosthetic supply.

The Resonance frequency analysis makes use of a small L-shaped autoclavable transducer attached by a screw to the Astra Tech Implants perpendicular to the alveolar ridge. Oscillations are produced from the piezo-elements inside the transducer which is connected by wire through the transducer plug-memory to the Ostell-instrument (Integration Diagnostics Ltd, Sävedalen, Sweden). The beam of the transducer is excited over a range of frequencies (from 5 to 15 kHz) and the resonance frequency of the beam is measured and automatically translated into an index called Implant Stability Quotient. The ISQ runs from 1 to 100. The relationship between the ISQ-value and the resonance frequency value is close to linear.

Astra Tech Implants and conical abutments

Ostell Instrument

Results

All implants showed a high initial primary stability (∅ ISQ 67,35). The fixtures placed in the mandible reached a higher primary stability (∅ ISQ 69,46) than fixtures in the maxilla (∅ ISQ 65,25). After 3 months the Astra Tech Implants showed an increase in stability of 2,64 units (∅ ISQ 69,99). Hereby the 24 mandibular fixtures showed a significantly higher increase in stability by 3,60 units (∅ ISQ 73,06) than the 23 implants in the maxilla with 1,83 units (∅ ISQ 67,08). During the healing period of 3 months as well as the time in fuction no implant has failed up to now.

Resonance frequency analysis (RFA)

L-shaped transducer

Transducer perpendicular to the alveolar ridge

The beam of the transducer is excited over a range of frequencies...

...and the resonance frequency of the beam is measured and translated into an ISQ value.

Clinical examples

RFA after implantation

Suture days after insertion

Conical abutment connection

RFA after reentry

Conclusion

The functional loading of Astra Tech Implants after 3 months is a predictable and successful treatment of the mandible as well as of the maxilla. It is a safe surgical procedure for Astra Tech ST-Implants as well as for Astra Tech Uni-Implants. In a subsequent study we are realizing at the moment a reduced healing period of 8 weeks with Astra Tech Implants with ISQ-values of more than 67,00. In the case of increased stability after 8 weeks of healing the implant will be provided immediately with the prosthetic supply. With ISQ-values of less than 67,00 the healing abutment will be left in its place for further 8 weeks in the sense of a progressive loading.

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