Correlation of histological tumor vascularization and Doppler sonography in patients with malignant melanoma of the choroid

Abstract • Background: In previous studies Doppler sonography was proven to be useful for diagnostics and follow-up of malignant melanomas of the choroid. • Methods: To evaluate the correlation between Doppler sonographical findings and the histological tumor vascularization, we examined five eyes of five patients with malignant melanoma of the choroid before enucleation with an ATL Ultramark-8 Duplex scanner and compared these results with computerized planimetry of histological tumor vascularization after immunohistochemical staining of vascular endothelium with anti-factor-VIII antibodies. • Results: We found no definite correlation of flow velocities with histological parameters of tumor vascularization. The tendency was for a decrease in maximum flow velocities as histological vascularization increased. • Conclusions: Due to (1) the usual lack of sensitivity parameters of the used Duplex device for the clinical user and (2) the unpredictable branching pattern within a melanoma resulting in an unknown angle of incidence of the Doppler beam, we conclude that the quantitative results of Doppler sonography require cautious interpretation. Nevertheless, presence or absence of Doppler shifts is a valuable parameter for the follow-up of irradiated tumors.

Introduction

Ultrasonographic imaging techniques have reached a high standard in the past few years and are now well established in various fields of medicine. The combination of Doppler sonography with B-scan sonography (duplex sonography) has improved the diagnosis and follow-up of vascular disorders. Recently, duplex technology has been used to evaluate central retinal vessels [3, 5] and tumor vessels within malignant melanomas of the choroid [1, 2, 4, 6, 10, 11]. Previous studies showed that the absence of Doppler shifts in choroidal melanomas after irradiation might indicate tumor regression [1, 2, 4]. However, the value of quantitative evaluation of Duplex sonography in the diagnosis and follow-up of malignant melanomas of the choroid was questionable. To evaluate the correlation between quantitative Duplex sonography and tumor vascularization, we examined five eyes with choroidal malignant melanoma with a Duplex scanner before enucleation and compared the results with the tumor vascularization as determined by computerized planimetry of tumor vessels in histological sections.
Materials and methods

We examined five eyes of five patients with malignant melanoma of the choroid. The diagnosis of uveal melanoma was made by clinical examination and conventional ultrasonography.

For Duplex sonography, an ATL Ultramark-8 Scanner (Advanced Technical Laboratories/Scientific Medical Systems, Bothell, Wash.) with a 7.5-MHz sector probe, 5-MHz Doppler transmission frequency and a 50-Hz wall filter was used. A duplex scanner (Acuson, Mountain View, Calif.) was employed for color studies (7-MHz linear array and 5-MHz sector probe). The tumors were scanned with a large sample volume Doppler beam. 

Flow velocities were determined using a large sample volume Doppler beam. For histological evaluation of tumor vascularization, determination of vessel circumferences was chosen, as this parameter is a valuable measure of the response to conservative treatment such as radiotherapy, hyperthermia, chemotherapy and monoclonal antibodies [4, 9, 10].

For statistical evaluation, flow velocities were correlated with mean vessel circumference, maximum vessel circumference and the total amount of all vessel circumferences per visual field calculated in different tumor areas according to Table 1. Finally, the analysis was limited to the average values calculated over all evaluated tumor areas per section and to the values of area 1 alone, since, due to small sample sizes and the variability of vessel circumferences in other subpopulations, the results could not be statistically evaluated.

Fig. 1 Immunohistochemical staining of vascular endothelial cells within a malignant melanoma of the choroid by anti-factor-VIII antibody detected by alkaline phosphatase - anti-alkaline phosphatase technique: staining of endothelial cells (× 240)

Table 1 Areas of interest for planimetry of tumor vessels

<table>
<thead>
<tr>
<th>Area no.</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Region of interest with marked vascularization</td>
</tr>
<tr>
<td>2</td>
<td>Center of main tumor</td>
</tr>
<tr>
<td>3</td>
<td>Tumor apex</td>
</tr>
<tr>
<td>4</td>
<td>Toward sclera in tumor center</td>
</tr>
</tbody>
</table>

Results

The calculated vessel parameters, flow velocities and other tumor parameters are summarized in Table 2. The correlation of mean flow velocity with mean vessel circumference in areas 1–4, total vessel circumference in areas 1–4, total vessel circumference in area 1 and maximum vessel circumference in areas 1–4 is exemplarily shown in Fig. 2.

Statistical evaluation using Spearman's rank test showed no correlation of histological tumor vascularization with flow velocities within the tumor as determined by duplex sonography. However, all measures of vascularization (except total vessel circumference) had a tendency to decrease with increasing flow velocities.

Discussion

Duplex sonography is an established method for the evaluation of extraocular vascular disorders. The vascularization affecting choroidal malignant melanomas is an important measure of the response to conservative treatment such as radiotherapy, hyperthermia, chemotherapy and monoclonal antibodies [4, 9, 10].