Original article

Ultrasound diagnosis in vasoproliferative tumours of the ocular fundus

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ABSTRACT

Objective: The aim of this work is to describe the ultrasound features in vasoproliferative tumors of the ocular fundus (VPTOF).

Methods: The medical records corresponding to eight patients were retrospectively studied. Clinical data from the complete ophthalmologic examination and ultrasonographic findings were analyzed.

Results: Nodular masses affecting either the retina or both the retina and the choroid were found. The surface contour of the tumor was regular in 5, and irregular in 3 cases. In terms of dimensions (mm/SD), the average major base was 7.14/2.56; the minor base was 6.74/2.48 and the height was 2.38/1.26. Internal structure was always solid and irregular, and reflectivity was mostly medium–high in 6 eyes. Angle kappa was not present in any case. No vascularity signs were detected.

Conclusion: According to the results it is suggested that when a differential diagnosis of VPTOF is carried out, not only should ophthalmoscopic signs be studied, but an ultrasound examination should also be done.

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Diagnóstico ecográfico de los tumores vasoproliferativos del fondo de ojo

RESUMEN

Objetivo: Describir las características ecográficas en los tumores vasoproliferativos del fondo de ojo (TVPFO).

Métodos: Se estudiaron retrospectivamente las historias clínicas correspondientes a 8 pacientes afectados de TVPFO. Se analizaron los datos correspondientes a la exploración oftalmológica completa y a la exploración ecográfica.

Resultados: Se encontraron masas nodulares afectando a la retina o bien a la retina y la coroides. La superficie tumoral era regular en 5 casos e irregular en los 3 restantes. La media de las dimensiones fue (mm/DE): base mayor, 7,14/2,56; base menor, 6,74/2,48 y altura 2,38/1.26.


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Introduction

Ocular fundus vasoproliferative tumors (OFVPT) are benign chorioretinal lesions of undetermined etiology. Isolated cases or short series of this entity have been published under different denominations: angioma-like masses, \(^1\) presumably acquired retinal hemangioma, \(^2\) hemangioma-like masses, \(^3\) massive retinal glyosis, \(^4\) all of which probably describe the same ocular disease. In 1995 Shields et al. \(^5\) published a long series and for the first time applied the term “ocular fundus vasoproliferative tumors”.

In most cases, OFVPT affect healthy individuals between 40 and 60, regardless of sex. Generally, OFVPT are nodular tumors exhibiting uneven surface in ocular fundus exploration and a high degree of vascularization which is easily detectable in ophthalmoscopy and exhibiting reddish-yellowish colors which vary from one case to another. OFVPT are generally located anterior to the equator and predominantly in the lower temporal quadrant. \(^6\) In general, OFVPT are associated to exudative and hemorrhagic changes or epiretinal growths which end up affecting the macular area giving rise to its main symptom which is diminished visual acuity.

OFVPT has been described as associated with other ocular diseases such as uveitis (pars planitis, toxoplasmosis and histoplasmosis), cup-shaped cell retinopathy, pigment retinopathy, retinopathy of prematurity and Coats disease. \(^5\) However, in most cases (about 75%) no associations with other diseases have been found. \(^7\)

In pathologic anatomy study, the said tumors have been classified as benign lesions characterized by reactive gylal proliferations with variable degrees of glysis and vascular proliferation. In addition, literature reports thin capillary networks and dilated and hyalinized vessels, some occluded, as well as exudates, macrophages and foreign body-like giant cells. \(^5,8,9\) Accordingly, the histopathology of these tumors does not truly indicate a vasoproliferative tumor. For this reason, the term reactive retinal glyosis has been suggested. \(^3\)

Even though the natural course of OFVPT is not predictable, various treatments have been proposed. Some authors suggest radiotherapy \(^10\) while other interventions such as laser photocoagulation, cryotherapy, \(^11\) photodynamic therapy (PDT), \(^12,13\) intraocular injection of antiangiogenic agents \(^14\) and surgical resection \(^9\) have been also tried with various degrees of success.

Although OFVPT are non-malign lesions because no metastatic potential or malign proliferation has been described, it is very important to carry out an adequate differential diagnostic. On the one hand, tumor entities involved in the posterior segment of the eye, such as malignant melanoma or choroidal metastasis, must be excluded. On the other hand, the possibility of benign entities such as choroidal hemangioma must also be considered. Accordingly, ophthalmoscopy is a crucial technique when performed by an ocular oncology expert. Echography has been utilized as a supplementary technique in the majority of published cases. However, no in-depth studies have been performed to date to analyze its actual contribution to diagnosis and differential diagnostic of these tumors.

Subjects, material and methods

Eight eyes of 8 patients (4 female and 4 male) with OFVPT who were referred to the Ocular Oncology Unit of the Santiago de Compostela hospital complex were retrospectively studied. The patients included in this study were consecutively selected between January 1999 and February 2009.

In all cases, anamnnesis was performed together with a comprehensive ophthalmologcal exploration including visual acuity, intraocular pressure, anterior segment study and ocular fundus ophthalmoscopy with photographic documentation and fluorescein angiography in all cases. The ecographic study was performed with the \(1^3-\)ABD system (10 MHz probe for posterior segment echography and 8 MHz probe for standardized echography, Innovative Imaging Inc., CA, USA). The probes were utilized directly over the ocular globe after the administration of 2 drops of topical anesthesia.

The ecographic findings considered for this study matched the first exploration carried out in each patient before follow-up or application of treatment. The relevant ecographic parameters were studied by means of quantitative and kinetic topographic echography, which was always carried out by the same physician (Antonio Piñeiro-Ces). In order to avoid losing kinetic echography information, the findings derived from this echography were recorded on video and immediately reported by the explorer. The relevant ecographic parameters were those utilized for the diagnostic and follow-up of other intraocular tumors such as choroidal melanoma. Accordingly, the following parameters were considered: mass morphology, superficial contour, dimensions, location, existence of associated retinal detachment, kappa angle, choroidal cup and vitreous gel condition (posterior hyaloids detachment or inflammatory infiltration and/or hemorrhage). The exact location of the tumor was obtained by means of longitudinal, transversal and axial B ecographies. On the other hand, in all cases an exhaustive study of the integrity of the tumoral base was carried out as well as an estimation of its size by means of standardized echography A and B. \(^15\) Mode A echography was carried out with probe A and the vector associated to echography in mode B. The internal structure, reflectiveness and presence of Kappa angle were studied.
Table 1 – Clinical findings of ocular fundus vasoproliferative tumors.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Eye</th>
<th>BCVA</th>
<th>Ocular disease associated to uveitis</th>
<th>Reference diagnostic</th>
<th>Macular involvement</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>22</td>
<td>R</td>
<td>FC</td>
<td>Retinopathy of prematurity</td>
<td>AM</td>
<td>CME + E</td>
<td>125I</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>67</td>
<td>R</td>
<td>0.5</td>
<td>Retinopathy of prematurity</td>
<td>AM</td>
<td>E</td>
<td>Observation</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>52</td>
<td>L</td>
<td>1.0</td>
<td>Coats disease</td>
<td>AM</td>
<td>–</td>
<td>Observation</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>56</td>
<td>R</td>
<td>0.05</td>
<td>Coats disease</td>
<td>CM</td>
<td>CME + E</td>
<td>Observation</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>43</td>
<td>L</td>
<td>0.05</td>
<td>Magnus myopia</td>
<td>AM</td>
<td>E</td>
<td>Observation</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>21</td>
<td>L</td>
<td>0.05</td>
<td>Magnus myopia</td>
<td>H</td>
<td>E</td>
<td>Observation</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>43</td>
<td>R</td>
<td>1.0</td>
<td>Retina detachment</td>
<td>AM</td>
<td>–</td>
<td>Observation</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>65</td>
<td>R</td>
<td>0.15</td>
<td>Retina detachment</td>
<td>H</td>
<td>E</td>
<td>Observation</td>
</tr>
</tbody>
</table>

BCVA: best corrected visual acuity; FC: finger counting; R: right; E: exudation; CME: cystoid macular edema; H: hemangioma; L: left; 125I: brachytherapy with I; F: female; AM: atypical melanoma; CM: choroidal metastasis; M: male.

in a detailed quantitative echography. The reflectiveness of each mass was included in one of the following categories: low, medium or high, depending on the height of peaks compared with the initial echogram peak. The quantitative echo technique was performed utilizing the tissue sensitivity setting. Finally, internal vascularity signs were analyzed utilizing kinetic echography techniques.

Results

The clinical records of 4 females and 4 males were retrospectively studied. The subject ages were comprised between 21 and 67 (mean: 46.12). Five of these patients exhibited OFVPT in the right eye and 3 in the left eye. The best corrected visual acuity in the affected eye ranged between finger counting and 1.0. The follow-up of these patients ranged between 6 and 85 months.

All cases had been referred to the Ocular Oncology Unit of the Santiago de Compostela hospital complex with the following reference diagnostics: atypical choroidal melanoma (5 cases), choroidal hemangioma (2 cases), and choroidal metastatic carcinoma (one case). The final diagnostic of all the patients was carried out utilizing a combination of ophthalmoscopy and echography, without any case requiring biopsy for diagnostic confirmation.

It was decided to treat case 1 with brachytherapy with 125I in an attempt to improve the macular changes experienced by the patient (Table 1). The remainder of patients were assessed regularly. To date, no enucleation was necessary.

In addition, 5 of the 8 patients had ocular disease histories: retinopathy of prematurity (one case), uveitis (one case), Coats disease (one case) and myopia magnus (one case) (Table 1).

Fig. 1 – Retinographies corresponding to cases 1–4 (identified in the upper left corner). It can be seen how OFVPT are nodular lesions with irregular contour and yellowish-reddish coloring.
The ocular fundus and fluorescein angiography findings were highly vascularized yellowish-pinkish masses in the lower quadrants, visible at the tumor surface (Fig. 1).

Changes in the adjacent retina and macula (lipidic exudation, edema and hemorrhage) were also detected (Fig. 1 and Table 1). Fluorescein angiography did not exhibit sufficient quality in any of the cases and therefore the visibility of angiographic signs largely depended on the inflammatory infiltration and/or hemorrhage in the vitreous gel. In general, we found a loss of contrast derived from the tumoral vessels during the arterial-venous phase and in later phases of the test (images not shown).

In the echographic study, isolated nodular masses were found affecting the retina or the retina and underlying choroids. The location thereof was anterior to the equator and the inferior-temporal quadrants in all cases except in case 7 that exhibited inferior-nasal location. Flat retina detachment was found in the 3 patients and complete hyaloids detachment in 6 cases. The superficial contour of the mass was smooth in 5 cases and irregular in the remaining 3. The average size of the masses was of \( (mm/SD) \): main base, 7.14/2.56; smaller base, 6.74/2.48; and height 2.38/1.26 (Fig. 2).

In addition, a quantitative echography revealed increased reflectiveness in the vitreous gel in cases exhibiting inflammatory and/or exudative activity (3 patients). In all cases, the internal structure of the tumors was solid and irregular, although hypoechochogenic areas were not found in any case. Reflectiveness was low in 2 patients and medium–high in 6 patients. Kappa angle was not found in any patients and internal vascularity signs were not detected with kinetic echography (Table 2 and Fig. 2).

### Discussion

According to the published OFVPT cases, the greater part of patients described in this study had a tumor localized in the inferior-temporal quadrant, with one exception that was located in the inferior-nasal quadrant. To date, no suggestions have been made to explain the preference of the tumors for this location.

Associated signs were detected in all patients (retinal edema, lipidic exudates, retinal hemorrhages) giving rise to the visual acuity reduction (which ranged between finger counting and 0.15). However, 2 patients exhibited a visual acuity of 1.0. Obviously, these 2 cases did not exhibit macular involvement.

In the case of the uveal melanoma, the tumor could exhibit a mushroom-shape morphology after the invasion of Bruch’s membrane. However, nearly 80% of uveal melanomas are characterized by solid nodular morphology. In this study, mushroom shaped morphology cases were not found as all the tumors were nodular solid masses. This could be related to the fact that these are benign lesions lacking the ability to invade the overlying layers. The mass contour, analyzed by B mode echography, was irregular in 3 cases, which is exceptional in uveal melanoma except cases responding to brachytherapy or proton beam radiation. In general, the OFVPT dimensions were small in comparison with other types of intraocular tumors such as choroidal melanoma,
Fig. 2 - Mode B echograms are shown with associated mode A of the affected patients in the series. The first number shown in the upper left corner corresponds to the case number, followed by the affected eye. Subsequently, the meridian in which the tumor was located is indicated with a clock. All the echograms were made in longitudinal sections over the indicated meridian with a gain of 90 dB. The large arrows indicate the OFVPT in each case and the smaller arrows show the associated exudative retina detachments. It can be seen that in some cases the vitreous gel reflectiveness is diffusely enhanced (for example, case 4).

retinoblastoma and even benign tumors such as hemangioma. In a revision, Damato\textsuperscript{7} reported mean OFVPT sizes measured with echography ranging between 1.0 mm and 5.0 mm with a mean of 3.0 mm. Heimann et al.\textsuperscript{6} reported a tumoral thickness ranging between 1.0 and 5.6 mm (mean 2.8 mm) in a series of 22 cases corresponding to 21 patients. According to the choroidal melanoma classification followed by COMS (COMS report 4),\textsuperscript{16} the OFVPT dimensions found in our study are small in what concerns their base (mean large base of 7.14 mm, SD: 2.56; mean small base of 6.74 mm, SD: 2.48). Accordingly, OFVPT would grow following a spherical pattern. Metastatic carcinoma in the choroid is of lower height and generally exhibits uneven contours.\textsuperscript{17} The authors consider that all these findings should be taken into account for the differential diagnostic.

Although undoubtedly the intraocular melanoma is in the uveal layer, it is important to note that it is not clear which other layers affected by the OFVPT in the ecographic images obtained in this study. Our findings indicate choroidal involvement in 3 cases and retinochoroidal involvement in the remaining 5. Published papers about the pathological study of these tumors do not clarify in which global layers the tumor is assumed to begin its growth.

The internal structure was uneven in all cases, and this finding could be related to the highly heterogeneous tissue structure that is characteristic of these lesions. Similar irregular structures have been described in choroidal metastasis produced by the lack of histological regulation. Other tumors such as nevus, choroidal melanoma and hemangioma exhibit a highly regular echographic internal structure. It is well-known that uveal melanoma has a characteristic histological order with highly compacted small malignant cells.\textsuperscript{15} In addition, choroidal hemangioma is characterized by benign vascular proliferation which also gives rise to an ecographically smooth structure. Surprisingly, in our series we did not identify hypoecogenic areas despite the tumors having a highly uneven structure. However, even though this structure is generally very even, hypoecogenic areas were described in uveal melanoma in relation to spontaneous necrosis after treatment with radiation\textsuperscript{15} and in cases ciliary body melanoma cases.\textsuperscript{18} Variable internal reflectiveness was observed, with 2 cases in which reflectiveness was predominantly low and the rest was between medium and high. This finding was already published by Heimann et al.\textsuperscript{6} and Damato\textsuperscript{7} and we believe it could also be related to the irregular histological characteristics of the tumor.
The kappa angle is a quantitative echography sign which is present in most choroidal melanomas.\textsuperscript{19} It is related to the echographic attenuation attributable to the histological regulation of melanoma. In our OFVPT series the kappa angle was not identified in any of the cases.

Choroidal excavation has been described for uveal melanoma\textsuperscript{20} and it is believed it is linked to the homogeneous infiltration carried out by the tumor in the underlying healthy choroids. However, it has also been described in other lesions and it is not considered pathognomonic of uveal melanoma.\textsuperscript{21} In this study, no choroidal excavations have been identified in any of the cases, although there also are other tumor lesions such as choroidal hemangioma which did not exhibit it either.

Exudative retinal detachment is frequent in the diagnostic of choroidal melanoma as a consequence of the tumoral activity (growth and/or related to inflammation) and these retina detachments are located close to the tumor or even in lower quadrants without an identifiable spatial relationship with the tumor. In our series we detected retina detachment in 3 cases and in these patients the detachment was flat and was found below the mass. We believe that this finding was related to the cases in which the tumor began growing from within the retina itself.

The study of the vitreous revealed a full detachment of the posterior vitreous in 6 cases. The vitreous gel reflectiveness was increased in the patients and, in these cases, these findings were correlated with inflammatory and/or exudative activity of the tumor or the hemorrhages detected in the ocular fundus exploration.

The internal vascular flow (internal vascularity) is an echographic sign that can be observed in almost all uveal melanomas.\textsuperscript{22} In order to identify this sign it is necessary to utilize an echograph with an analog screen to observe it in real-time. It can be identified in mode A as well as in mode B, and it is characterized by fast movement of dots on the tumoral base. This sign is clearly related to the vascular tree of the melanoma and has not been described for other vascular tumors such as the choroidal hemangioma. In relation with this fact, we did not detect this sign in any of the cases studied in our series. We believe that this finding has the same cause proposed for choroidal hemangioma as both are vascularized tumors and probably the spaces are filled in with non-circulating blood and for this reason the internal vascularity sign fails to appear.

In summary, even though OFVPT share echographic signs with other intraocular tumors, the authors propose the following profile to assist in the final diagnostic: nodular and solid morphology, low height, tendency towards uneven/irregular surface contour, uneven internal structure, variable reflectiveness and absence of kappa angle, absence of choroidal excavation and lack of internal vascularity signs. Accordingly, an adequate OFVPT diagnostic must be carried out taking into account not only ophthalmoscopical but also echographic signs.

Conflict of interests

None of the authors have declared any conflict of interests.

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