Role of Ultrasound Biomicroscopy in the Management of Retinoblastoma

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Abstract

Purpose: To determine the role of Ultrasound Biomicroscopy (UBM) in the management of Retinoblastoma cases.

Method: The medical records of 10 eyes of eight patients diagnosed with retinoblastoma from February 2011 to July 2013 were reviewed and data were analysed. Ultrasound biomicroscopic examination was performed for all cases under general anesthesia using Ultrasound biomicroscope (Model DICON P45 UBM Plus Paradigm instruments) with 50 MHz transducer. UBM was used to determine the features of the intraocular tumor and possible extension into anterior retina, ciliary region, and anterior segment.

All cases were enucleated for different reasons, such as poor visual prognosis (six cases) and unilaterality (two cases). Histopathological examinations were performed for all enucleated eyes. UBM findings were compared and correlated with the histopathological features of the enucleated eyes.

Results: UBM documentation was available in 10 eyes of the eight patients which were included in the study. Only 7 eyes were diagnosed on UBM to have extension of the tumor anterior to the ora serrata, and were enucleated. Extension was absent in the other 3 eyes. Histopathological examination confirmed the anterior extension in all the 7 eyes and confirmed the absence of extension in the other 3 eyes. UBM did not yield any false negative or any false positive results.

Conclusion: UBM is an indispensable tool for visualization of the anterior retina, ciliary region, and anterior segment allowing a better staging of the advanced disease process. Primary assessment of the true extent of retinoblastoma is critical for the selection of an optimal management approach. UBM may provide useful diagnostic data governing the indications for enucleation in advanced cases of retinoblastoma.

Key Words: Retinoblastoma – Ultrasound biomicroscopy – Enucleation.

Introduction

THE international classification for intraocular retinoblastoma is a newer staging system, which takes into account what has been learned about the disease in recent decades. It stages the severity of intraocular disease on the basis of the features predictive of eye survival with current management generally based on a combination of chemotherapy and focal therapy [1].

It divides intraocular retinoblastomas into 5 groups, labeled A through E:

Group A: Small tumors (3mm across or less) that are confined to the retina and are not near important structures such as the optic disk (where the optic nerve enters the retina) or the foveola (the center of vision).

Group B: All other tumors (either larger than 3mm or small but close to the optic disk or foveola) that are still confined to the retina.

Group C: Well-defined tumors with small amounts of spread under the retina (subretinal seeding) or into the gelatinous material that fills the eye (vitreous seeding).

Group D: Large or poorly defined tumors with widespread vitreous or subretinal seeding. The retina may have become detached from the back of the eye.

Group E: The tumor is very large, extends near the front of the eye, is bleeding or causing glaucoma (high pressure inside the eye), or has other features that mean there is almost no chance the eye can be saved.

The safe and effective delivery of treatment require that the full extent of the tumor process be identified [2].

In retinoblastoma with peripheral retinal involvement, the assessment of tumour invasion of the posterior chamber remains uncertain in the absence of detectable retinoblastoma cells in the anterior chamber by slit lamp. In these circum-
stances, CT, MRI or conventional ultrasound is of limited value [3].

Current approaches to the primary treatment of retinoblastoma with the new chemotherapeutic agents associated with focal therapy have allowed the preservation of eyes that previously would have been primarily enucleated [2].

Involvement of the anterior retina and ciliary region with tumor is associated with a poor prognosis [1].

The most commonly used imaging technologies, such as indirect ophthalmoscopy, conventional 10MHz ocular ultrasound; CT scan and magnetic resonance imaging do not provide adequate resolution of retinoblastoma anterior to the ora serrata in the ciliary region [2].

Ultrasound biomicroscopy (UBM) has dramatically improved resolution of anterior segment. It yields higher resolution images of the anterior segment and structures hidden from clinical visualization, such as the ciliary body, zonule or posterior chamber. This technique, developed in Canada in the 1990s, uses high-frequency continuous wave transducers (50MHz) incorporated into a B-scan device with an axial and lateral resolution of 50mm and a tissue penetration of 4 to 5mm [4].

UBM has been very useful in the management of adult anterior segment diseases, such as anterior segment tumors, iris tumors, scleral and corneal abnormalities, and glaucoma [5-12].

There are only a few reports documenting the use of UBM in pediatric ocular oncology [2,13,14]. This prompted me to examine the value of UBM in the Primary assessment of the true extent of retinoblastoma which is critical for the selection of an optimal management approach.

**Material and Methods**

A retrospective review of the medical records of 10 eyes of eight patients diagnosed with retinoblastoma from February 2011 – July 2013 was undertaken and data were analyzed.

Approval for this study was obtained from the Research Ethics Board of King Abdul-Aziz University Hospital in Saudi Arabia. Informed consent was obtained from the legal guardian of each patient. The study adhered to the tenets of the Helsinki Declaration.

For each patient, information regarding age, sex, primary or secondary tumour and tumour laterality was retrieved.

All UBM doses were done under general anesthesi at either the staging or a follow-up examination under anesthesia to determine the anterior extent of retinoblastoma using.

Ultrasound biomicroscope (Model DICON P45 UBM Plus Paradigm instruments) with 50 MHz transducer.

**UBM settings**: For measurements, the ultrasound biomicroscope was set at:
- 5.0 X 5.0mm field of view with 90 decibels of gain, and 2.24mm delay.
- The patient in supine position during the examination.
- Using an eye cup filled with 1.5% Methyl cellulose and physiologic saline.

Standard scleral depressor was used to rotate the eye in different positions longitudinal scans were obtained along each meridian circumferentially. Maximal tumour thickness and diameter as well as the presence of abnormal echodensities consistent with retinoblastoma in the posterior or anterior chamber were noted in each case.

Images of the posterior iris, iridocorneal angle, ciliary processes, pars plana, and the anterior retina were obtained for 360º, captured and stored on a hard drive and/or printed. UBM findings were correlated clinically and, when possible, with histopathological studies.

All cases were enucleated for different reasons, such as poor visual prognosis (six cases) and unilaterality (two cases).

Histopathological examinations were performed for all enucleated eyes. Formalin-fixed enucleated eyes were routinely processed, paraffin embedded and serially sectioned. H&E staining was performed on all sections.

Histopathological analysis included, the number of primary tumours, largest tumour diameter, growth pattern, tumour differentiation, presence of calcification, tumour necrosis and precise tumorous involvement of the different ocular structures (Schlemm’s canal, anterior chamber, posterior chamber, ciliary body, vitreous, retina, choroid, sclera and optic nerve). The international classification for intraocular retinoblastoma [1] and TNM [15] was used for grouping each eye at presentation.

**Results**

UBM documentation was available in 10 eyes of the eight patients which were included in the study Table (1). Only 7 eyes were diagnosed on
UBM to have extension of the tumor anterior to the ora serrata, and were enucleated. Extension was absent in the other 3 eyes (Fig. 1). Histopathological examination confirmed the anterior extension in all the 7 eyes (Fig. 2) and confirmed the absence of extension in the other 3 eyes. UBM did not yield any false negative or any false positive results. Table (2).

Table (1): Demographic characteristics of patients evaluated.

<table>
<thead>
<tr>
<th>Total patients</th>
<th>8</th>
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<tbody>
<tr>
<td>Total eyes</td>
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<table>
<thead>
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<th>Female</th>
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<tr>
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<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Female</td>
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<table>
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<th>Mean age (years)</th>
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<th>Unilateral</th>
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<tbody>
<tr>
<td>16 month</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>4.9 years</td>
<td></td>
<td>3</td>
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<table>
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<tr>
<th>Eye</th>
<th>Presence of echodensities consistent with retinoblastoma in the posterior chamber</th>
<th>Absence of echodensities consistent with retinoblastoma in the posterior chamber</th>
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<tr>
<td>Right</td>
<td>Presence of echodensities consistent with retinoblastoma in the posterior chamber</td>
<td>Absence of echodensities consistent with retinoblastoma in the posterior chamber</td>
</tr>
<tr>
<td>Left</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Bilateral</td>
<td>0</td>
<td>3</td>
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</table>

Fig. (1): Correlation between ultrasound biomicroscopy (UBM) findings and pathological findings in an enucleated retinoblastoma case with the absence of invasion of the posterior chamber.

Fig. (2): Correlation between ultrasound biomicroscopy (UBM) findings and pathological findings in an enucleated retinoblastoma case with evidence of the posterior chamber invasion.
Discussion

Determination of the full intraocular extent of the retinoblastoma is critical to the decision for the best therapeutic options. UBM is a very important addition as it overcomes the limitations of the other imaging tools available [16,17].

Retinoblastoma with peripheral retinal involvement may extend into the posterior chamber and ultimately progress into the anterior chamber. Involvement of the anterior segment clearly requires rupture of the anterior hyaloid, an established enucleation criterion according to the international classification of intraocular retinoblastoma (group E). However, the clinical status of the anterior hyaloid cannot be unequivocally determined in the absence of a full evaluation of the posterior chamber. The posterior segment up to the ora serrata can be visualised by fundoscopy or conventional ultrasound, but these modalities appear to be of limited value in the assessment of disease anterior to the ora serrata [3].

For this purpose I examined the value of UBM in the detection of posterior chamber involvement and correlated all cases with Histopathological evaluation.

I identified a significant correlation between UBM findings and Histopathological documentation of posterior chamber invasion by retinoblastoma as shown in (Figs. 1,2).

It is essential to correctly interpret the normal features of UBM in children in order to distinguish them from those relating to retinoblastoma. The ciliary processes are long in children and may be confused with tumours, but their linear aspect can easily be detected by rotation of the UBM device. In a normal situation the vitreous base shows moderate and homogenous reflectivity with UBM, whereas tumour seeding and infiltration of the vitreous base by retinoblastoma show a slightly increased reflectivity of irregular shape and distribution [3].

The UBM reflectivity of the retinoblastoma tumor is very similar to that of the iris, ciliary body, and ciliary processes. Identification of the fine line of higher reflectivity from the retina and the pigment epithelium lining the ciliary body helps to define tumor invasion beyond the retina. The high internal reflectivity of the sclera and the retina is distinct from the overlying and underlying tissues, and is usually easily distinguished from retinoblastoma tumor.

Retinoblastoma seeds are of moderate reflectivity, but are usually irregular in size, shape, and distribution [13].

The size of tumors can be measured from UBM images. This information is useful for follow-up and management of patients. Children suspected to have retinoblastoma with involvement of the ciliary region or anterior, should be treated by enucleation. However, when the involvement of the ciliary region is excluded on UBM, and the International Retinoblastoma Classification is not Group E, a chemotherapy based approach can be safely considered despite a large tumor volume [2].

To safely keep eyes with retinoblastoma, complete visualization of the tumor process is required. Earlier intervention is more likely to allow preservation of eyes, which is especially important for children with one remaining eye. UBM imaging clearly documents anterior disease and contributes to the management of children affected with retinoblastoma, with no evidence of false negative or false positives results in my study as shown in (Table 2). Similar studies by L.M. Vasquez et al., in 2011 and by Alexandre P. Moulin et al., in 2012 had reached a similar conclusion with similar confirmation of the precise role of UBM in the evaluation of anterior extension of the retinoblastoma to the posterior chamber.

Conclusion:

UBM is an indispensable tool for visualization of the anterior retina, ciliary region, and anterior segment allowing a better staging of the advanced disease process. Primary assessment of the true extent of retinoblastoma is critical for the selection of an optimal management approach. UBM may provide useful diagnostic data governing the indications for enucleation in advanced cases of retinoblastoma.

Although my study includes only a limited number of cases, the sensitivity and specificity of UBM in the assessment of anterior extension of retinoblastoma provides useful information for proper therapeutic decision-making.

References


