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Research Article

Reliability of Ocular Ultrasonography in Diagnosis and Predicting Prognosis of Retinoblastoma

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Abstract

Background: Retinoblastoma is the most common intra-ocular malignancy in childhood. Early diagnosis is essential for vision preservation and ocular salvage. Ocular ultrasonography is a basic tool in the diagnosis of retinoblastoma. Enhancing ocular ultrasonography utilization for recognition of retinoblastoma spread within the eye may provide more insight for ophthalmologists in remote areas with limited resources.

Objectives: Exploring the role of B-scan ocular ultrasonography in diagnosis of retinoblastoma and identifying ocular invasion and high risk features.

Methods: A retrospective-cross-sectional hospital based study.

Results: B-scan ultrasonography of 62 patients with retinoblastoma showed: the maximum diameter of the masses ranged from 22 mm - 6 mm. Most of the patients presented with a range of (6 - 20) mm of mass diameter. 97% of B-scan examination was done with the gain of 90. Calcification was clearly visible in all retinoblastoma cases except one. Optic nerve involvement appeared in 27%. While 88% of the patients showed anterior segment extension of the retinoblastoma mass.

Conclusion: B-scan ultrasonography is a useful tool in retinoblastoma diagnosis, it could also provide general description of the mass spread within the eye ball and some of the high risk features.

Keywords: *B-Scan Ocular Ultrasonography; Retinoblastoma; Optic Nerve*

Introduction

Being the most common intraocular malignant tumour in childhood, retinoblastoma has been a headache for ophthalmologist and paediatrics oncologists. Early diagnosis is the key for preserving vision and preventing complications that might cause mortality in advanced untreated cases of retinoblastoma. Clinical diagnosis by signs and symptoms should be supported with imaging to confirm diagnosis and predict the course of the disease. Ophthalmologists usually depend on MRI or CT to confirm the diagnosis, but in a low resources setting as in the case of most LMIC, ocular ultrasonography plays a major role in diagnosing ocular conditions including retinoblastoma [1].

B-scan ocular ultrasonography

Ultrasound B-scan of the eye is a practical, non-invasive and relatively cheap tool to visualize the eye ball and diagnose ocular conditions. The eye ball is a fluid-filled organ, its position on the face enhances the accessibility and accuracy of ocular examination

through ultrasonography. B-scan ultrasonography has been the primary tool to diagnose posterior segment conditions especially when the ocular media is not clear for direct visualization of the fundus.

Retinoblastoma is a malignant retinal tumor which originates from the embryonic retinal epithelium of the primary optic vesicle. The retinoblastoma mass grows from the retinal layer and may invades the vitreous. Calcification within the retinoblastoma mass is a pathognomonic feature that can be assessed with B-scan ocular ultrasonography. Calcification is seen in 95% of retinoblastoma cases [2].

Calcifications within the retinoblastoma mass appear as high reflectivity deposits. The shadowing created by them is still preserved with decreased gain of B-scan ultrasonography.

The retinoblastoma mass: without treatment, retinoblastoma mass could enlarge to invade the vitreous and the anterior segment. In advanced stages of the disease the mass could invade the orbit. B-scan ultrasonography is used to visualize the intra-ocular retinoblastoma masses, vitreous seeding and anterior segment in addition to the optic nerve invasion by the tumor [3].

High risk features of retinoblastoma

High risk features of retinoblastoma composes of anatomic and histologic criteria that directly correlates with the possibility of systemic spread of the malignancy and eventually varying morbidity and mortality rates. Almost one quarter of retinoblastoma patients carrying high risk features are subject to systemic spread and hence will need adjuvant therapy whether chemotherapy alone or chemotherapy with radiation. Early recognition of high risk features is essential for proper planning of retinoblastoma therapy. Although the definition of high risk features may vary between different oncology centers but we found general agreement on the following criteria: choroidal invasion, optic nerve infiltration and anterior segment invasion. Precise description of high risk features is provided in the histopathology report. Imaging can help in describing the details of the mass; its size, location and ocular spread [4].

Methods

A cross-sectional study was conducted in 2022 in a tertiary eye center (Mekka Eye Complex-Khartoum Sudan) to describe the reliability of B-scan ultrasonography in the diagnosis of retinoblastoma and the prediction of high risk features presence. 62 patients were included in the study. Retrospectively, data was retrieved from the patients records and filled in data collection forms. Demographic data, clinical presentation, B-scan reports and histopathology reports of each participant were included. Patients with missed relevant data were excluded. Ethical issues and confidentiality were revised by the IRB of SMSB, ophthalmology council which approved the study.

Results

Demographics

Most of the patients were males (61%). The mean age was 3 years, most of the patients' residence was urban areas.

Clinical presentation

More than 50% of the patients presented with leukocoria. Only 4 patients (6.5%) presented with strabismus. 17 patients (27%) already have developed extra-ocular disease (proptosis) on presentation. Only 1 patient was discovered while having routine check-up. 16% of the patients presented with bilateral retinoblastoma.

Ocular B scan ultrasonography

The maximum diameter of the masses ranged from 22 mm - 6 mm. Most of the patients presented with a range of (6 - 20) mm of mass diameter. 97% of B-scan examination was done with the gain of 90. Calcification was clearly visible in all retinoblastoma cases except one.

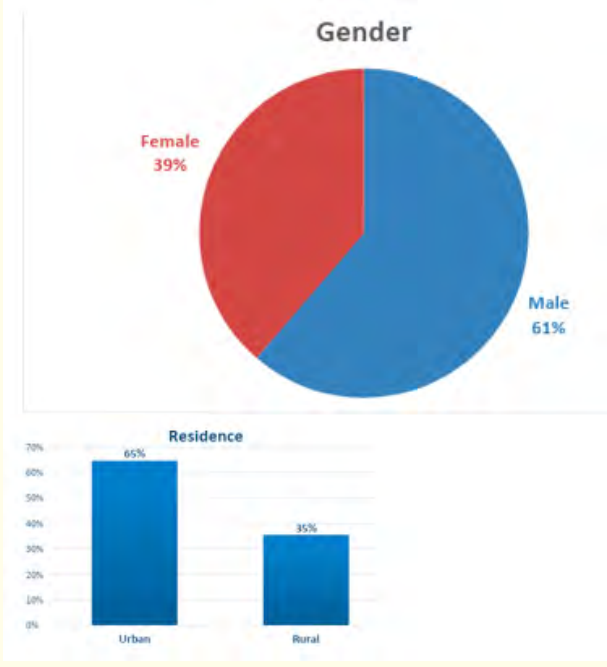

Figure 1

Optic nerve involvement appeared in 17 cases (27%), 17 cases showed optic nerve clear from the mass invasion. In 28 cases (45%) optic nerve was not visible to be evaluated. 88% of the patients showed anterior segment extension of the retinoblastoma mass.

Histopathology results

All of the 62 eyes examined for histopathology showed Rossette cells and calcification within the mass. 61% of the eyes showed optic nerve invasion by the retinoblastoma mass. 73% of the cases showed high risk features.

Cross-tabulation

Pearson-chi-square test showed significant p-value regarding optic nerve involvement and anterior segment extension, supporting the evidence of B-scan reliability as a diagnostic tool for retinoblastoma.

	Yes		No		Not clear	
	N	%	N	%	N	%
Optic nerve involvement 1	17	27.4%	11	17.7%	34	54.8%
Optic nerve involvement 2	38	61.3%	24	38.7%	0	0.0%

Pearson Chi-Square Tests

		Optic nerve involvement 2
Optic nerve involvement 1	Chi-square	11.601
	df	2
	Sig.	.003*,b

Pearson Chi-Square Tests

		Anterior segment extension 2
Anterior segment extension 1	Chi-square	7.037
	df	1
	Sig.	.008*,b

Figure 2

Discussion

Global disparity in retinoblastoma

Approximately 45% of cases are hereditary, which is often bilateral, while 55% are nonhereditary and typically unilateral. In our study, 16% of the patients presented with bilateral retinoblastoma. Incidence of retinoblastoma varies across the world. The highest incidence was reported in India and Africa. The survival rate of retinoblastoma patients falls from 95% among HICs to 30% - 60% among LMIC. This disparity in survival rates reflects the scarcity of specialized health service for such a rare disease like retinoblastoma which doesn't represent a priority for the health care providers in LMICs [1].

Retinoblastoma in B-scan ocular ultrasonography

When using B-scan to explore the posterior segment of the eye in a patient with retinoblastoma, the tumor is seen as an irregular mass with foci of calcifications that are diagnostic for retinoblastoma. Coat's disease which is a differential diagnosis for retinoblastoma is seen through B-scan ultrasonography as exudative retinal detachment when focusing on the sub-retinal space [5].

In our study, B-scan ultrasonography was useful in diagnosing retinoblastoma, assessing the maximum diameter of the mass, in addition to predicting high risk features. As we live in Sudan, in a middle of a conflict and a major humanitarian crisis, limitation of imaging modalities like CT scans and MRI enhances the role of ocular ultrasonography in diagnosis ocular conditions. B-scan can be maximally utilized in different ophthalmic centers in countries with limited resources or ongoing unstable conditions.

Optic nerve infiltration by retinoblastoma cells

Optic nerve involvement leads to central nervous system infiltration with the malignancy.

It's a major risk factor for disease spread and further complication. On ocular imaging, optic nerve infiltration is an indicator of advanced disease and recognized before enucleation may lead the ophthalmologists and oncologists to consider adjuvant chemotherapy session in advance of surgery to limit tumor cells seeding that is expected to occur intra-operatively. MRI examination of the optic nerve is mainly used to identify optic nerve infiltration. Histopathology examination of the enucleated eye would provide details of optic nerve infiltration whether prelaminar, laminar, post-laminar, to the transection line or a combination of all that [6].

B-scan ultrasonography can predict optic nerve infiltration which appears as a solid mass upon the optic nerve head and an enlarged retro-laminar optic nerve shadow [7].

In our study 27% showed signs of optic nerve involvement, 45% of the B-scan images did not clarify the optic nerve head to be assessed for infiltration, following enucleation and histopathology, 61% of the eyes found to have optic nerve infiltration with retinoblastoma cells.

Anterior segment extension of retinoblastoma mass

Diffuse retinoblastoma may infiltrate the anterior segment by invading the aqueous humor. Retinoblastoma cell within an inferior peripheral intra-retinal mass could infiltrate the ciliary body, vitreous base and the anterior chamber of the eye. Ultrasound bio-microscopy (UBM) [7].

High frequency ocular ultrasound can detect anterior segment extension of retinoblastoma [5,8].

High risk features of retinoblastoma

The importance of high risk features definition and identification is due to the direct relation between high risk features and metastasis in retinoblastoma patients. High risk features are mainly identified by the histopathological examination of the enucleated eye. The

children oncology group defined them as: massive choroidal invasion ≥ 3 mm in maximum diameter. The global survey on 2022 included other definitions of high risk features such as: anterior chamber seeds, optic nerve invasion, scleral invasion, iris invasion and ciliary infiltration [4]. The variation of high risk features definition among oncology centers around the world is reflected on the variation in treatment protocols [5].

In our study, B-scan visualization of anterior segment extension and optic nerve involvement showed significant p-values (0.008 and 0.003 respectively). This will add to the value of ocular ultrasonography as a diagnostic tool for retinoblastoma in settings with limited resources and for ophthalmologists practicing in remote areas where other modalities of imaging such as CT or MRI may not be available.

Conclusion

Retinoblastoma is an aggressive malignancy that threats vision and even life if not treated. Beside clinical diagnosis, imaging modalities are essential in confirming the diagnosis of retinoblastoma as tissue biopsy for histopathology will not be available before enucleation of the eye. B-scan ocular ultrasonography is a non-invasive, cheap and practical tool for diagnosis of retinal pathologies including retinoblastoma. Our study showed that B-scan can provide more details of retinoblastoma mass regarding its size, location, extension and ocular invasion in addition to some high risk features.

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