ORIGINAL ARTICLE

DIAGNOSTIC ACCURACY OF CONTRAST–ENHANCED HIGH RESOLUTION MAGNETIC RESONANCE IMAGING (MRI) FOR THE DETECTION OF RETINOBLASTOMA

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ABSTRACT

Objective

To determine the diagnostic accuracy of contrast–enhanced high resolution magnetic resonance imaging (MRI) in the detection of retinoblastoma taking histopathology as the gold standard.

Methodology

A total of 50 cases were collected in this comparative cross-sectional study. The sample was taken through non-probability consecutive sampling. The study was conducted at Department of Radiology at Dr. Ziauddin Hospital, Karachi from 2011 to 2013. MRI orbit (Brain), using MRI field strength 1.5-T system head coil combined with one or two small surface coils.

Results

A total of fifty patients were enrolled with mean age 19.2±4.69 months with range (9-34) months. Gender distribution shows, 27 patients (54%) were male while remaining 23 patients (46%) were female. True positive cases were 34 (68%) and false positive cases were 3 (6%). Positive predictive value was 91.89%, negative predictive value 92.31% and the Diagnostic accuracy was found to be 92%.

Conclusion

In conclusion, the results of this study suggest that MR imaging proved to have a high diagnostic accuracy as well as positive predictive value in the detection of retinoblastoma taking histopathology as the gold standard. However, MRI is better in determining the extent of the disease and its complications.

Keywords: Retinoblastoma, Diagnostic Accuracy, MRI, Histopathology.

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1. INTRODUCTION

Retinoblastoma is an intraocular and highly malignant tumor usually present in children[1]. Over ninety five percent of these tumors occur in children age below 5 years[1]. Despite the fact that this type of tumor generally occurs sporadically, however 10% of such tumors show genetic inheritance[2]. This tumor can be unilateral, bilateral, trilateral or quadrilateral. Trilateral retinoblastomas are those which involve midline intracranial tumors whereas quadrilateral retinoblastoma includes 2 midline intracranial tumors[3]. Few of the most common manifestations of retinoblastoma are strabismus (20%), leukocoria (60%), retinal detachment, vitreous hemorrhage and angle closure glaucoma. In addition hyphema, pseudohypopyon, orbital cellulitis, and proptosis are also common[4]

Few of the risk factors that are involved in the poor prognosis and metastasis of this tumor include massive invasion of ocular coats, bilateral eye involvement, vitreous seeds and the involvement of anterior segment. 5 year survival rate is over 90% if the tumor only involves the globe however if it exceeds outside of the globe the mortality is as high as 90%[1, 2]

For the purpose of initial diagnosis determining the extent and staging as well as treatment planning of this tumor the most standardized modality is the Magnetic Resonance Imaging or MRI. Furthermore, MRI is also essentially used in monitoring and follow up of patients post treatment. MRI is also useful in differentiation retinoblastoma from simulating lesions with leukocoria among children[1]. Simulating lesions of retinoblastoma include, coats disease, larval granulomatosis (Toxocaracanis), retinopathy of prematurity, and retinal astrocytichamartoma. Histologically, calcification is present in approximately 95% of the tumor[5]

Computed tomography, ultrasonography and Magnetic resonance imaging are the cornerstone techniques for the imaging of this tumor. However, high resolution contrast enhanced MRI is the modality of choice and has proven to be the most sensitive technique for the assessment of retinoblastoma especially when the tumor has infiltrated the optic nerve or in presence of extraocular extension and intracranial disease[4]. Magnetic resonance imaging has shown high diagnostic accuracy in different setups in detecting retinoblastoma and marked amount of intraocular calcification[6].

Although the diagnostic accuracy of CT scan, as well as the negative predictive value, remains high, however, the disadvantages of CT Scan compared to MRI are reduced soft tissue contrast, iodinated contrast administration and radiation exposure that can be detrimental in this case considering the hereditary pattern of this particular disease as there remains an elevated risk of the development of secondary malignancies. Similarly, ultrasonography has its disadvantages of being ineffective in the direct evaluation of metastasis because of shadowing artifacts from intraocular calcification over the non-calcificextraocular tumor[4, 7].

Retinoblastoma has been reported to be prevalent in 39% of the cases[8]. Primary diagnosis is established through fundoscopy. Survival rates among patients suffering from retinoblastoma vary significantly around the globe with the highest rates exceeding 95% in the developed countries and as low as 30% in Africa. In Asia the survival rate is about 60%, around 80% in Latin America, and 95 to 97% in Europe and North America [9 -11.]

Retinoblastoma RRB is one of the most common intraocular tumors of the childhood with promising prognosis in terms of mortality given the early detection and treatment of the tumor. Therefore, MRI remains the most suitable imaging technique in confirming the diagnosis and staging of the disease as well as the involvement of surrounding structures.

To the best of our knowledge no local data focused on diagnostic accuracy of contrast–enhanced high resolution magnetic resonance imaging 1.5 tesla (MRI 1.5T) by using European Retinoblastoma Imaging Collaboration (ERIC) guidelines therefore the aim of this study was to provide the current

and local statistics of the diagnostic accuracy of this technique for retinoblastoma and making strategy for early detecting and treatment of retinoblastoma to reduce mortality and morbidity in our region.

2. MATERIALS AND METHODS

In this analytical cross sectional study conducted at the Department of Radiology, Dr. Ziauddin Hospital, between 2011 and 2013, a total of 50 study participants suspected of retinoblastoma were enrolled. Participants of both gender and age less than 10 years were included in the study.

Suspicion of retinoblastoma was based on clinical presence of leukocoria, strabismus, vitreous hemorrhage, retinal detachment, angle closure glaucoma, hyphaema, pseudohypopion, iris heterochromia, proptosis and pseudo-orbital cellulitis. These patients were referred from Department of Ophthalmology of the same hospital to the Radiology department for the investigation of retinoblastoma using Magnetic Resonance Imaging (MRI).

1.5-T MRI was performed using head coil combined with one or two small surface coils before enucleation, including spin-echo unenhanced and contrast-enhanced(CE) T1-weighted sequences (slice thickness, 2 mm; pixel size <0.3 x 0.3 mm2).

During T2 weighted Magnetic Resonance Imaging, the retinoblastoma appears to be isointense to hyperintense compared to the vitreous humour. It is employed to detect leptomeningeal enhancement and metastatsis of the parenchyma. Furthermore, it is used to detect the midline tumors which are visible as isointense in comparison to the gray matter using T1 weighted imaging employing prominent enhancement as a result of gadolinium based contrast. Retinoblastoma, being a neuroectodermal cell tumor, has a characteristic finding of Flexner Wintersteiner rosettes made of cells arranged in a circular manner around a well differentiated lumen.

The results of MRI were compared with histopathology as gold standard. Histopathological diagnosis was made through microscopic examination of the specimens. Study participants were enucleated under general anaesthesia by senior eye surgeon (experience more than 5 years) and all surgeries were done by the same eye surgeon. Removal of the intact eyeball was done with at least 10 mm section of optic nerve. Following gross examination of the eyeball specimen, section of the optic nerve margins were done followed by sampling of the main tumour block.

Data was analysed employing SPSS v 21. Sensitivity and Specificity were calculated along with positive and negative predictive values and overall diagnostic accuracy. Age was reported as means and standard deviation while all categorical data were represented as frequencies and percentages.

3. RESULTS AND DISCUSSION

A total of fifty patients were enrolled with mean age 19.2±4.69 months with range (9-34) months. Of total, 27 (54%) were males and 23 (46%) females. MRI based diagnosis of retinoblastoma was made in 37 (74%) of the patients while Histopathological based diagnosis was made in 35 (70%) of the patients. The sensitivity of MRI was found to be 97% while specificity was calculated to be 80%. The overall diagnostic accuracy of the MRI in detecting retinoblastoma was 92%. The comparison of diagnostic results of retinoblastoma based on MRI and histopathology, along with calculation of sensitivity and specificity is shown in table 1.

Table 1
Diagnostic Accuracy of MRI in the Diagnosis of Retinoblastoma Keeping Histopathologyas Gold Standard
n=50

RESULTS OF MRI	RESULTS OF HISTOPATHOLOGY		Total
	POSITIVE	**NEGATIVE**	
MRI(POSITIVE)	True positive(a) 34	False positive (b) 3	a + b 37
MRI(NEGATIVE)	False negative(c) 1	True negative(d) 12	c+ d 13
Total	a + c 35	b + d 15	n 50

Sensitivity = a / (a + c) x 100 = 97.14%

Specificity = d / (d + b) x 100 = 80.00%

Prevalence of retinoblastoma = 70.00%

Positive predictive value = a / (a + b) x 100 = 91.89%

Negative predictive value = d / (d + c) x 100 = 92.31%

Diagnostic Accuracy = 92%

Our study found that the sensitivity of contrast enhanced MRI in detecting retinoblastoma was 97% whereas the specificity was 80%, positive predictive value was around 92% as well as negative predictive value which was also around 92%. The overall Diagnostic accuracy was 92%. In the local setup Computed Tomography (CT) and MRI are known to be reliable diagnostic modality in the diagnosis and staging of retinoblastoma among children superior to both computed tomography and ultrasonography [19].

During the past few decades medical resonance imaging has become extensively useful diagnostic imaging tool helping out clinicians in making optimal choices in terms of treatment planning and post treatment follow up. Despite the cost effective use of ophthalmoscopy and ultrasonography in diagnosis and determination of intraocular diseases, magnetic resonance imaging, although expensive has proven to be the most accurate diagnostic and imaging modality in case of retinoblastoma. When it is the case of such tumors which can become malignant and are related to high mortality rates high sensitivity diagnostic tools are probably the best option even in middle and low income countries like Pakistan. Our study reported a high overall diagnostic accuracy of MRI in case of retinoblastoma.

Regarding retinoblastoma, the data about diagnostic accuracy of MR imaging is scarce. Only two studies carried out by Barkhof et al and Schueler et al demonstrated their results about the MR imaging findings in comparison with his to pathological findings after enucleation[11,17]. Our study

distinguishes it self from these two studies in terms of the higher number of patients. First study analyzed only 18 patients whereas the IInd study analyzed 21 patients. Our findings show promising possibilities for the detection of smaller lesions because of spatial and contrast resolution. Special coils for the examination of the eye which allow imaging with a field of view as small as 60 mm are just becoming available[15.] With these new coils spatial resolution of MRI could be markedly increased. However, a few problems like the presence of motion artifacts, which sometimes occur with long scanning times and low capacity for detecting calcification, are still encountered with this technique[16]

de Jong MC et al [20] also reported in their study that high resolution MRI has the ability of detecting small intraocular seeds and other risk factors of metastasis which are undetectable to the fundoscopy. A meta-analysis carried out by the same author and his associates reported that the conventional MRI has sensitivity of as high 88% (95% CI, 20%–100%) in detecting retinoblastomas[21.]

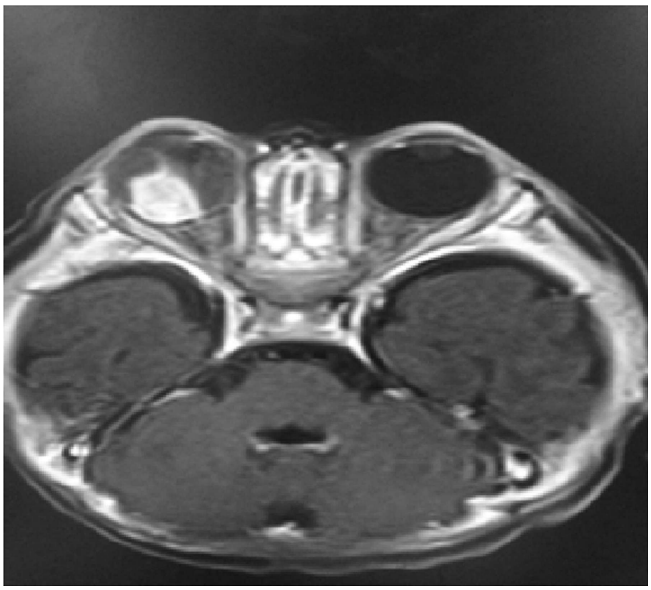

Fig 1: Intraocular mass is seen in the right eye with the involvement of the right optic nerve showing avid contrast enhancement after contrast administration. Incidental finding is retinal detachment and subretinalhemorrhage. Findings match with postoperative findings of Retinoblastoma.

4. CONCLUSION

It is concluded from this study that although Histopathology is the gold standard in diagnosing retinoblastoma but MRI is non-invasive, radiation free, readily available imaging modality that is reasonably good and relatively comparable with the histopathology in diagnosing of retinoblastoma.

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