Diagnostic accuracy of ultrasound in differentiating retinoblastoma from persistent hyperplastic primary vitreous (PHPV) in pediatric leukocoria patients with MRI as gold standard

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Aims and objectives

Retinoblastoma is the most common paediatric intraocular tumour. It usually presents as leukocoria and strabismus in children between 1-5 years of age. Around 47-58 percent of leukocoria cases in children are due to retinoblastoma, making it the leading cause of white pupillary reflex[1].

Though retinoblastoma is a life-threatening disease, it is curable with early diagnosis and appropriate treatment. Establishing the best management of retinoblastoma and differentiating it from other causes of leukocoria is imperative for preservation of visual function. Persistent Hyperplastic Primary Vitreous (PHPV) is the second most common cause of leukocoria[1, 2]making it an important differential to rule out.

PHPV is a congenital disorder occurring due to abnormal persistence of foetal intraocular vessels in the anterior or posterior segments of the eye. Primary vitreous forms around the 7th week of gestation and starts involuting during the 20th week and almost always disappears at the time of birth. Failure of regression of primary vitreous results in PHPV and associated complications like vitreal haemorrhage, vitreal and retinal detachments[3].

While histopathology remains the gold standard for diagnosis and evaluation of high risk features of retinoblastoma, imaging studies are the non-invasive means of establishing diagnosis and planning treatment for patients presenting with leukocoria[4].

MRI is the investigation of choice when evaluating patients with suspected retinoblastoma; it is indicated in evaluation of all ocular tumours. The tumour mass usually appears hyperintense to vitreous on T1 and hypointense to vitreous on T2 weighted sequences and shows significant post-contrast enhancement. Details provided by MRI can also be useful in mapping a treatment plan. However, calcifications and lesions less than 2mm have been inconsistently detected on MRI[5]. MRI can also be used for the diagnosis of PHPV where a hyperintense retrolental membrane, tubular hyaloids vessels, retinal detachment and microphthalmia provide clues for diagnosis[6,7]. If a triangular retrolental vascular mass with a central stalk of hyaloid artery remnant connected to the optic disc is seen in the vitreous, PHPV should be the top most differential. The overall shape of PHPV has been likened to a martini glass[3]. The closest differential of PHPV is retinal detachment but, in the latter, there is a hyperintense band extending from optic disc to ora-serrata rather than to posterior surface of lens[3].

Ultrasound is the ideal imaging modality for ophthalmological pathologies due to the superficial and fluid filled nature of the eye. It provides painless, radiation free imaging that does not require general anaesthesia. Ultrasound is a diagnostic aid when there is

restriction of fundoscopic examination due to cataracts and hyphema[4]. Retinoblastoma is visualized as an echogenic soft-tissue mass that contains calcification[5]. Approximately 95 percent tumours show histological evidence of calcification. It is the main feature that differentiates retinoblastoma from other causes of leukocoria[4]. Calcification is also important in differentiating retinoblastoma from other tumours in children and ultrasound has been shown to identify 92-95 percent of calcifications that are present histologically[8,9]. Colour Doppler can be used to determine the vascularity of the tumour. It is useful in distinguishing retinoblastoma from PHPV which shows characteristic retrolental membrane that may have persistent patent hyaloid artery and may also have features of retinal detachment along with vitreous hemorrhage[10].Tumor seeding and optic nerve involvement have also been reported to have been detected by ultrasound[11].

In a case report, it was seen that ultrasound can be used in detecting PHPV in antenatal scans as well. Two cases were reported in which bilateral PHPV was diagnosed in foetuses in early third trimester. The ultrasound findings were comparable to post-natal scans with retinal detachments and echogenic membranes extending from posterior part of lens to the posterior pole of eyeball[12].

This study aims to determine the diagnostic accuracy of ultrasound in differentiating retinoblastoma from PHPV taking MRI as gold standard in order to explore the possibility of utilizing ultrasound as a cost-effective screening tool in children presenting with leukocoria.

Images for this section:

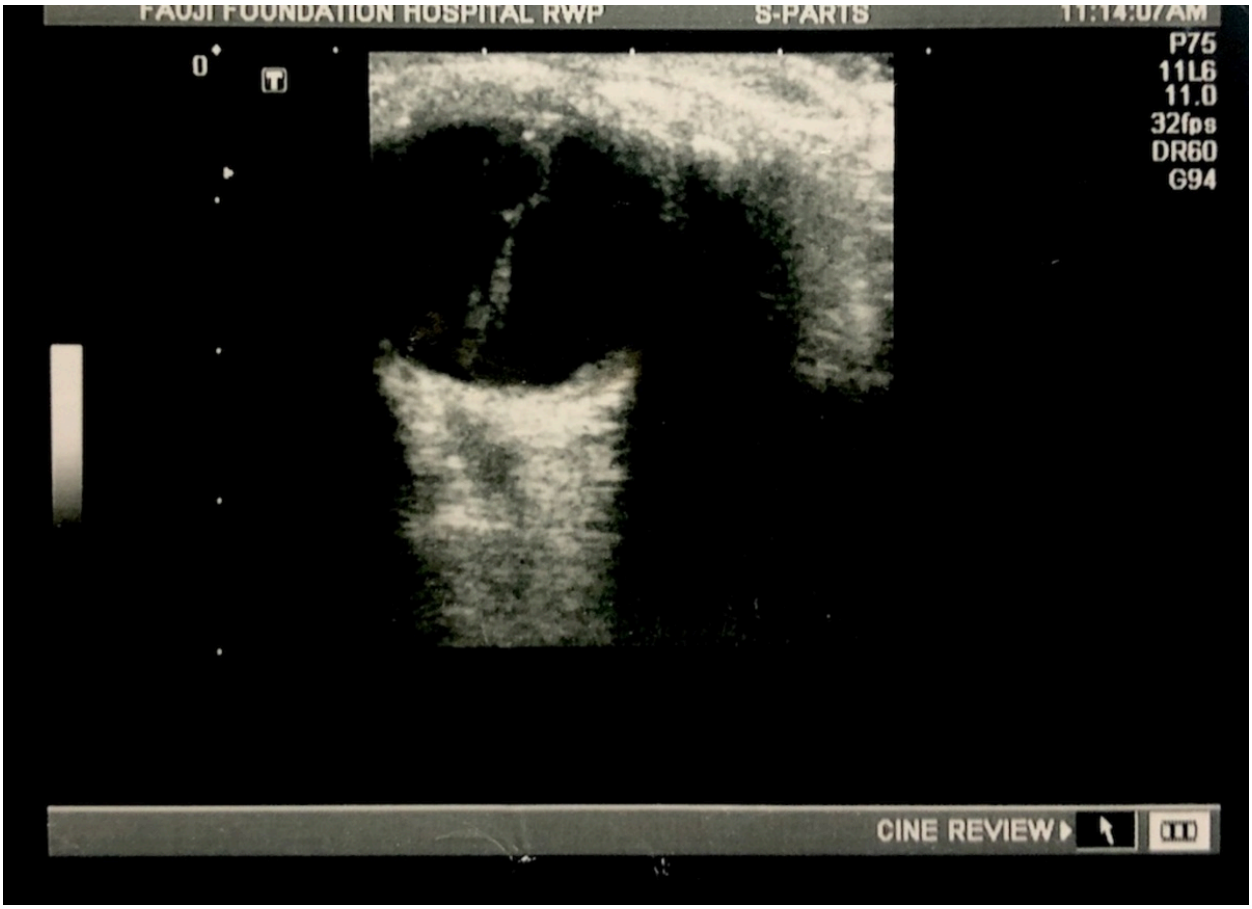

Fig. 1: Persistent Hyperplastic Primary Vitreous on Ultrasound

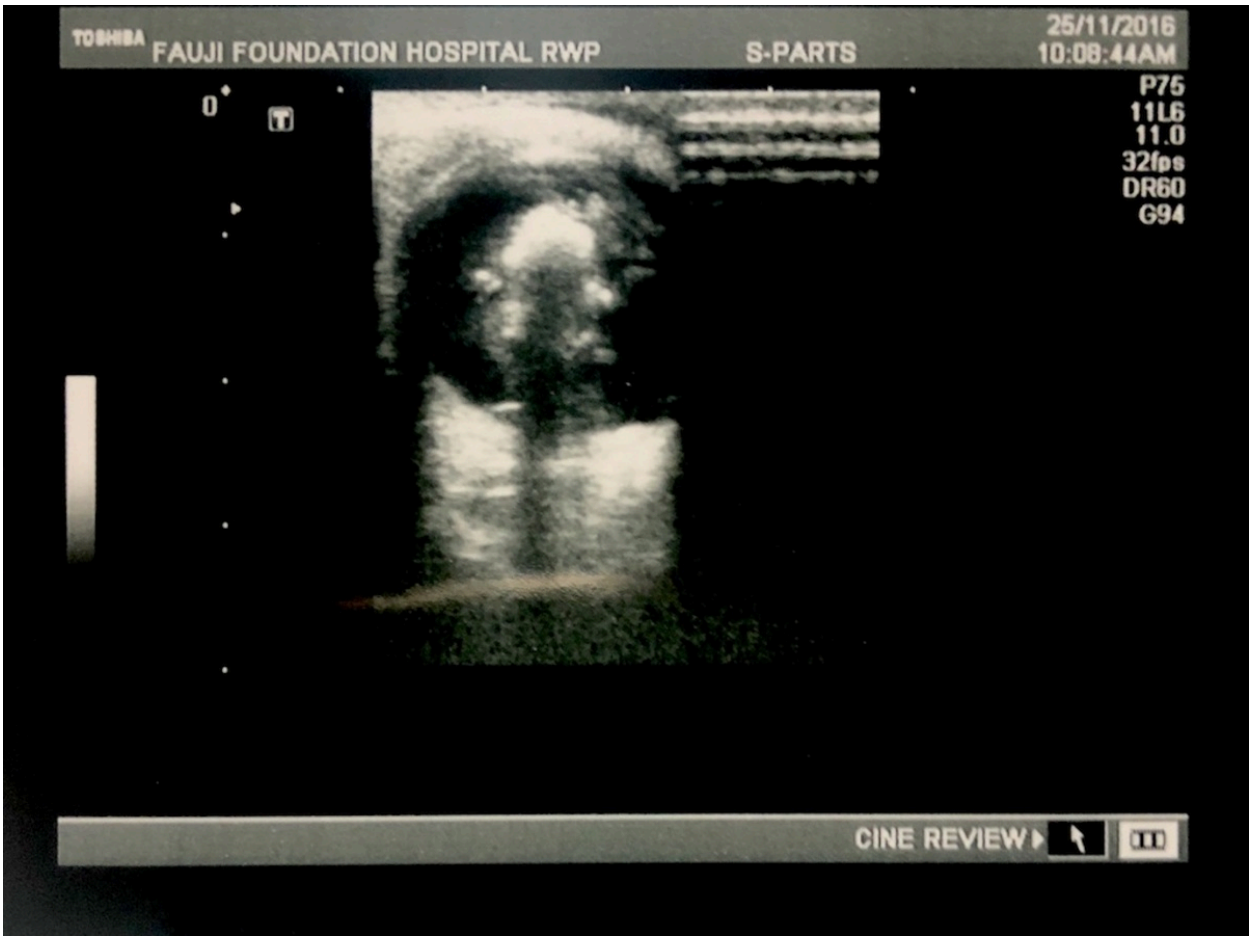

Fig. 2: Retinoblastoma on Ultrasound

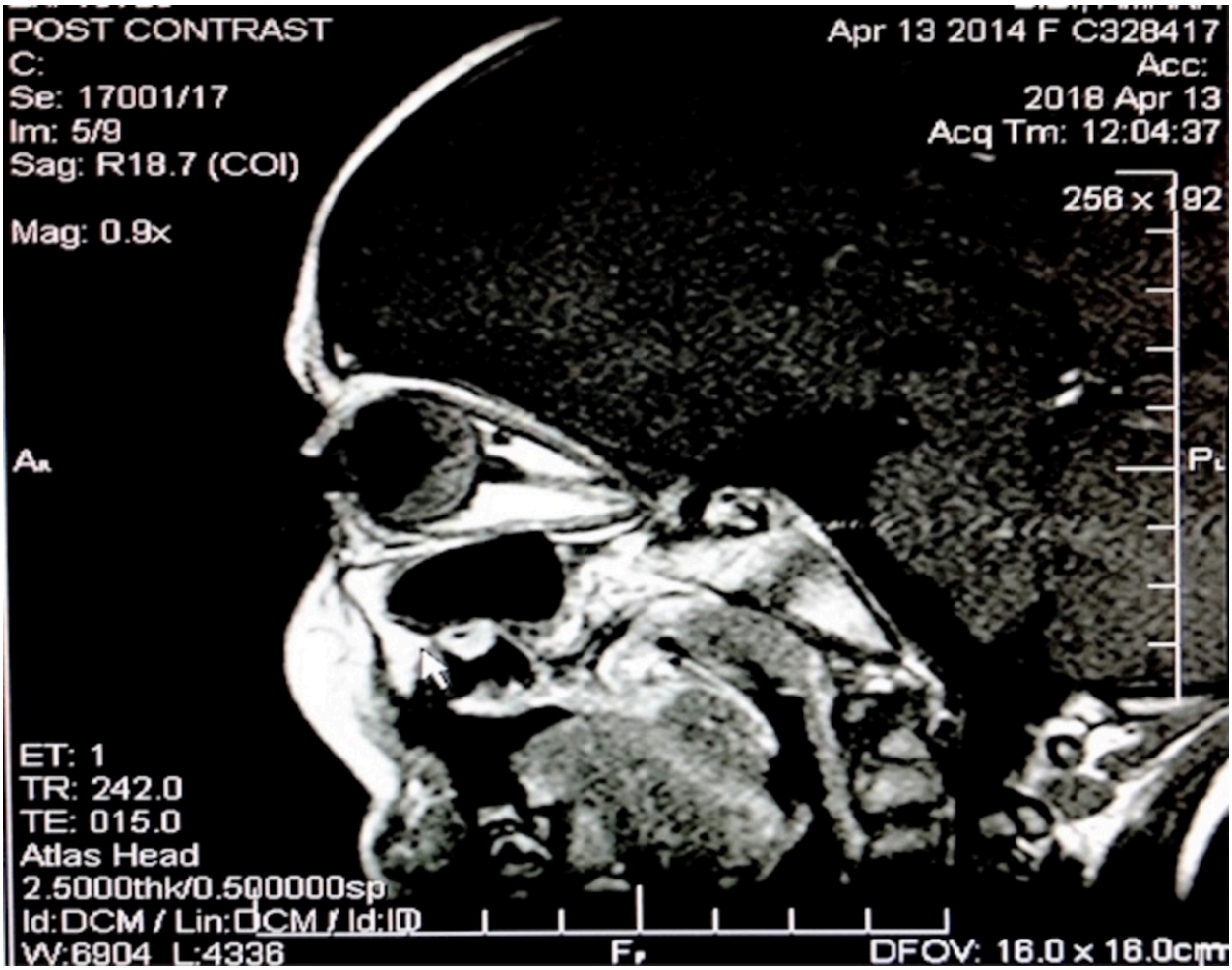

Fig. 3: Retinoblastoma on MRI

Methods and materials

Patient Population:

This study was conducted at Radiology Department of Foundation University Medical College / Fauji Foundation Hospital, Rawalpindi, Pakistan from January 2016 to September 2018. A total of 56 suspected retinoblastoma patients, 31 males and 25 females, within the age bracket of one month to ten years (mean age 3.11), presenting with leukocoria referred to the hospital by paediatric ophthalmologists were randomly selected. Previously diagnosed patients of retinoblastoma coming for follow up scans were not included.

Data Acquisition:

MRI was done on 1.5 tesla Toshiba Vintage Titan machine. T1, T2, FLAIR, T1 FATSAT, post contrast T1 and post contrast T1 FATSAT sequences were done. Images were taken in axial, sagittal and coronal planes. Ultrasound was performed on Toshiba Aplio 500 machineusing high frequency probe of 14 megahertz. To avoid observer bias, ultrasounds and MRI scans were reported by different radiologists. Patients were given general anaesthesia prior to MRI as per guidelines[13].
The basis of diagnosis for retinoblastoma on ultrasound was orbital mass with or without calcification and PHPV was diagnosed by the presence of retrolental membrane.

Data Analysis:

The data was recorded and analysed using SPSS version 21.0.

2 X 2 tables were constructed for the ultrasound and MRI findings for characteristic features of each disease i.e. retrolental membrane for PHPV, orbital mass with or without calcification for retinoblastoma. The True Positives (TP), False Positives (FP), True Negatives (TN), False Negatives (FN), sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and diagnostic accuracy were calculated for the ultrasound diagnosis of PHPV and retinoblastoma compared to MRI diagnosis, which was kept as the gold standard.

Results

When comparing the findings of ultrasound and MRI, diagnosis of PHPV by ultrasound is comparable to that of MRI. Ultrasound was unable to detect only 1 case where retrolental membrane was visualized on MRI as shown in Table 01.

Ultrasound was able to detect 31 cases of orbital mass while the number of cases detected by MRI was 39 as shown in Table 02.

Ultrasound out performed MRI in detection of calcification as seen in Table 03 where 24 cases picked by ultrasound were not detected by MRI.

When comparing the final diagnosis of ultrasound with that made by MRI for differentiating retinoblastoma from PHPV the Sensitivity was = 97.14%, Specificity = 100.0%, PPV = 100.0%, NPV = 95.45% and Diagnostic Accuracy = 98.21% based on the results shown in Table 04.

Table 01. Ultrasound & MRI findings in detecting retrolental membrane

			MRI membrane		Total
			positive	negative	
Ultrasound membrane	positive		19	2	21
	negative		1	34	35
Total			20	36	56

Table 02. Ultrasound & MRI findings in detecting orbital mass

			MRI Mass Findings		Total
			positive	negative	
Ultrasound Mass Findings	positive		31	3	34
	negative		8	14	22
Total			39	17	56

Table 03. Ultrasound & MRI findings in detecting calcification

	MRI Calcification	Total

			positive	negative	
Ultrasound Calcification	positive		9	24	33
	negative		1	22	23
Total			10	46	56

Table 04. Ultrasound & MRI findings in detecting Retinoblastoma & PHPV

			MRI Findings		Total
			Retinoblastoma	PHPV	
Ultrasound Findings	Retinoblastoma		34 (97.1%)	0 (0.0%)	34
	PHPV		1 (2.9%)	21 (100.0%)	22
Total			35	21	56

Conclusion

Ultrasound findings were comparable to that of MRI in patients of retinoblastoma and PHPV. Ultrasound is a highly sensitive diagnostic tool for differentiating between the two diseases in paediatric leukocoria patients. It can be used as a screening tool in resource poor settings having limited sophisticated imaging modalities for early diagnosis and management.

Personal information

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