

Diagnostic accuracy of C.T scan in retinoblastoma

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Abstract:

Objective: To determine the diagnostic accuracy of computed tomography in evaluation of retinoblastoma keeping histopathology as gold standard.

Study design: Cross-sectional validation study

Duration of study setting: The study was conducted at Radiology department of Postgraduate Medical Institute (PGMI) Hayatabad Medical Complex Peshawar from January 2011 to May 2011 and Civil Hospital Dow Medical College Karachi from October 2011 – April 2012 and

Patients and Methods: In this cross sectional validation study a total of 54 numbers of cases presenting with proptosis were enrolled. These patients referred to the Radiology Department at Civil Hospital Karachi and PGMI of Hayatabad Medical Complex for C.T scan. Patients under 05 years of age of both genders having proptosis were included in the study. Diagnosed and follow-up cases for retinoblastoma, patients above 05 years of age, patients with thyrotoxicosis and simulating lesions like coats disease were all excluded from the study. All CTs were reported by the expert and senior radiologist of the department. CT results assess for the presence of intraocular mass with calcification and extent of the disease with and without involvement of optic nerve. All observations were properly recorded and the biopsies performed by experts and results were followed. Data was entered and analyzed using SPSS version 15.0 software. The study outcome was determined in terms of diagnostic accuracy of CT in retinoblastoma keeping histopathology as gold standard.

Results: A total of 54 patients were enrolled. The mean age of patients was 3.6 + 1.2 years. Male gender was predominant while 24.0% patients were females. According to analysis CT had 91.4% sensitivity and 71.3% specificity while the positive and negative predictive values were 97.7% and 20.0% respectively.

Conclusion: Based on our study findings it is concluded that CT imaging has a high sensitivity and a reasonable specificity in the detection of calcification and assessment of Retinoblastoma at earlier stage which is confirmed by histopathology. CT has a sensitivity and specificity of 91.4% and 71.3% in detecting retinoblastoma in the current study so it is better not to do histopathology and treated on the basis of C.T report.

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Introduction:

Retinoblastoma is the most common intraocular malignancy of infancy and childhood, with an incidence of 1/15000 to 1/20000 live births¹. Approximately 60% of retinoblastoma are unilateral and most of these forms are non hereditary (median age at diagnosis is two

years). In 40% of the cases retinoblastoma is bilateral (the median age at diagnosis is one year). All hereditary forms are bilateral and multifocal unilateral lesions are usually hereditary¹. Retinoblastoma causes 5% of childhood blindness and 1% childhood cancer deaths².

Presentation of retinoblastoma varies, Most of the patients present with proptosis leukocoria, also known as amaurotic cat's eye reflex and strabismus.² Proptosis is the commonest mode of presentation in Asian countries^{3, 4}. In Pakistan 60% of cases are diagnosed after the age of 5 years. Late diagnosis affects the stage of the disease and hence the prognosis. In Pakistan incidence of retinoblastoma is 4/100000 in children under the age of 5 and slightly decreases to 2.4/100000 at 10 years age.⁴

The prevalence of retinoblastoma in proptosis among pediatric age group is 38% on computed tomography and retinoblastoma being the commonest cause of proptosis^{5,6}. Proptosis is defined as an abnormal protrusion of the eyeball. It is referred as non-endocrine-mediated globe protrusion while exophthalmus is used in protrusion secondary to endocrinopathies⁷. However exophthalmous is used for conditions related to the eye and proptosis can be used for protrusion of any organ. The rate of onset of proptosis provides a clue to diagnosis.

Calcification can be detected by computed tomography with high degree of accuracy in approximately 90% of cases. Further advantages of CT are its easy enhancement capability, its potential for detecting the presence of calcified lesions and short acquisition time in seconds of orbital CT studies compared with MRI in minutes reduces decreases motion artifacts⁴.

Once Retinoblastoma diagnosed the Computed tomography is helpful to demonstrate the precise extension of the orbital lesion, the involvement of adjacent paranasal sinuses and nasal cavity. The evidence of bony erosion and intracranial extension helps in pre treatment evaluation and post treatment follow-up⁸.

CT shows an intraocular mass with higher density than the vitreous body and calcification in 90% of cases. The sensitivity and specificity of CT in retinoblastoma is 96% and 91% respectively^{5,8}. Intralesional calcium deposition is considered a key element for differentiating retinoblastoma from simulating lesions. On enhanced

CT with 1.5 mm sections non-visualization of central retinal vessels reliably show the optic nerve involvement with retinoblastoma.

The purpose of this study is to assess on C.T scan the presence of high density intra orbital mass with calcification and the extent of the disease and to determine the diagnostic accuracy of computed tomography in the diagnosis of retinoblastoma at an initial stage as to improve the quality of vision and survival rate.

Patients and Method:

In this study patients referred from eye and pediatric wards / OPD with H/O proptosis to The Postgraduate Medical Institute (PGMI) Hayatabad Medical Complex Peshawar and Radiology Department of Civil Hospital Karachi for C.T scanning. Inclusion criteria were Paediatric age groups (0-05 years) of both genders with H/O proptosis. Exclusion criteria were Patients above 05 years of age, thyrotoxicosis and simulating lesions like coats disease etc. Bias and confounders were controlled by excluding diagnosed and follow-up cases of retinoblastoma by thoroughly reviewing patient history or attendant past history of this disease. Only new cases of proptosis were enrolled to check frequency of retinoblastoma, as proptosis can not be determined on period of birth hospital is different. Written informed consent from the patient's attendant was obtained. Explanation was given regarding the nature of the procedure, time consumed and risks to the patient. Diagnosis of retinoblastoma on computed tomography include all of the following, An intraocular high density mass, calcification and extensions in to surrounding structures, Non visualization of central retinal vessels shows optic nerve involvement considered.

The standard protocol for orbital CT scan axial and coronal sections was carried out by using Toshiba Activion 16 Slice CT Scanner at Civil Hospital Karachi .and X-Vision Toshiba Helical CT Scanner available in HMC Peshawar. Unenhanced CT scans of the orbits were obtained in all 54 patients. Contiguous 1.5-mm-thick sections parallel to the canthomeatal line through the orbits were obtained. An experienced Radi-

ologist examined the CT scans to evaluate the presence of hyperattenuating intraocular areas consistent with calcifications. Histologic examination were performed in all cases and results followed. The data was analyzed with the help of statistical rogramme SPSS, version 15. Mean + standard deviation was computed for age. Categorical variables like gender and histopathology results were calculated in frequencies and percentages. The diagnostic accuracy of computed tomography in retinoblastoma was evaluated in terms of sensitivity, specificity, positive predictive value and negative predictive value using histopathology as gold standard.

Results:

In this study a total of 54 patients were enrolled. The mean age of patients was 3.6 + 1.2 years. Majority of the patient 31.5% and 25.9% were between 2 to 3 and 3 to 4 years of age. While around 20.0% of the study patients were below 2 years of age. As depicted in (Table 1)

In the current study male gender was predominant with 41 in numbers (76.0%) proportion while 13 (24.0%) patients were females. (Table 2)

Out of 54 cases, 38 cases (70.3%) were unilateral while 16 (29.6%) cases were bilateral.

As per CT scan, out of the total 54 study cases, 44 cases (81.5%) had calcification and positive diagnosis of retinoblastoma while 10 cases (18.5%) had negative results. As shown in

Table 1: Age of study patients (n = 54)

Age in years	No of patients	%age
0 – 1	06	11.1%
1 – 2	05	9.3%
2 – 3	17	31.5%
3 – 4	14	25.9%
4 - 5	12	22.2%
Mean age	3.6 + 1.3	

Table 2: Gender of study patients (n = 54)

Gender	No of patients	%age
Male	41	75.9%
Female	13	24.1%

(Table 3). Fungating mass with Optic nerve involvement in 30 cases (55.5%) noted and adjacent maxillary and ethamoidal sinuses in 18 (33.3%) cases (table 4).

Similarly, the results of histopathology were analyzed. This shows that, 94.4% patients had positive findings of retinoblastoma while only 5.5% had negative findings (Table 5)

The distribution of true positive, false positive, true negative and false negative cases was measured. In the current study out of the total 54 cases, 79.6% were true positive cases, 1.8% was false positive, 14.8% were false negative and 3.7% were true negative cases (Table 6). The diagnostic accuracy of the CT was calculated using histopathology as gold standard. In our study CT had 91.4% sensitivity and 71.3% specificity. While the positive and negative predictive values were 97.7% and 20.0% respectively (Table 7).

Discussion:

Computed tomography is still the method of choice for detecting intraocular calcification and investigating orbital pathologies.^{9,10} However currently MR imaging is not considered as sensitive as C.T in detecting intraocular calcification. Although MRI is usually specific enough to differentiate Retinoblastoma from other simulating lesions¹¹

The diagnostic accuracy of the CT was calculated using histopathology as gold standard. In current study CT had 91.4% sensitivity and 71.3% specificity. While the positive and negative predictive values were 97.7% and 20.0% respectively. Our results validate the previous findings reported by many investigators where they found out sensitivity of CT scan in detecting calcifications in retinoblastoma between (81% to 96%)¹²⁻¹⁶. A study conducted by Radhakrishnan V et al found out that PET/CT had a sensitivity and specificity of 40.0% and 100.0% respectively¹⁷.

If the accuracy is high then we could save the patient's time and money and above all from the

Table 3: CT calcification result in the diagnosis of retinoblastoma in the study (n=108)

	No of patients	%age
Positive	44	81.5%
Negative	10	18.5%

Table 4: C.T Findings of Retinoblastoma in the study (n=54)

Findings	No. Of patients	%age
Calcification	44	81.5%
Optic Nerve involvement	30	55.5%
Sinuses Involvement	18	33.3%

Table 5: Histopathology result in the study patients (n = 54)

	No of patients	%age
Positive	51	94.4%
Negative	3	5.5%

Table 6: Distribution of true positive, false positive, false negative and true negative cases in the C.T study (n=54)

	No of patients	%age
True positive (TP)	43	79.6%
False positive (FP)	01	1.8%
False negative (FN)	08	14.8%
True negative (TN)	02	3.7%

Table 7: Diagnostic accuracy of CT in retinoblastoma keeping histopathology as gold standard (n=54)

	Percentage
Sensitivity	91.4
Specificity	71.3
PPV	97.7
NPV	20.0

invasive procedure of biopsy. It was thought that our study would help in increasing diagnostic information especially in our setup as there were no previous study done here.

In the current study a total of 54 patients coming to the radiology department with proptosis for CT. The average age of study patients was 3.6 + 1.2 years. One third of study patients 31.5% were between 2 and 3 years with another one fourth 25.9% were between 3 and 4 years. Similar mean age of their patients (3.6 years) was found in the study of Radhakrishnan V in India¹⁷.

In a recent retrospective study "On clinical presentation of retinoblastoma from Argentina" revealed an average age of their patients to be

2 years with high unilateral age 2.5 years compared to 13.3 months in the bilateral disease¹⁸. Another study from Turkey, also found out the median age of 2 years of patients with retinoblastoma¹⁹. Intrabulbar calcified mass in children younger under 3 years, is most likely a retinoblastoma^{20,21}. Retinoblastoma is rare in older patients²².

In our study majority of the cases were male 76.0% compared to female gender. Compared to the study conducted on the role of PET/CT in staging and evaluation of treatment response in locally advanced retinoblastoma in which the male gender was dominant with (60.0%) proportion¹⁷. The role of PET/CT in pediatric cancers like retinoblastoma remains investigational.²³

Calcification is the most important differentiating feature of retinoblastoma. Variable diagnostic strengths of CT have been reported, however, few investigators have shown that CT detection of calcifications in retinoblastoma has a sensitivity of 81 to 96% with high specificity²⁴. CT is supposed to be the best imaging modality for the detection of intraocular calcifications^{24,26}.

Contrast C.T helps to detect optic nerve invasion in retinoblastoma produces. There is distortion of the anastomotic vascular network in the anterior optic nerve region. Non-visualization of the central retinal vessels is a reliable indicator of the optic nerve invasion that is considered by Jacquemin and Karcioğlu²⁷.

CT and MRI represent the primary modalities for visual-pathway imaging in children. However, CT is still the method of choice for the detection of intraocular calcium and investigating orbital pathologies^{28,29}. As compared to MRI, CT scan revealed calcification in 99% cases and was a confirmatory evidence of Retinoblastoma³⁰.

CT has a sensitivity and specificity of 91.4% and 71.3% in detecting retinoblastoma in the current study. However, for generalizability and confirmation of our findings further research on this topic is mandated. CT should be continued as



Figure 1: Unenhanced C.T scan, axial view, showing an area of intraorbital coarse calcification

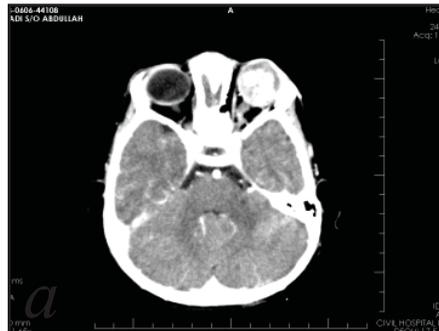


Figure 2: Axial and coronal contrast C.T showed intraorbital high density mass with specks of coarse calcification, optic nerve appears thickened



a first choice of imaging technique in suspected cases of retinoblastoma in our local settings. In a study from Pakistan it was reported that since July 1999 to 30th September 2002, newly diagnosed 70 retinoblastoma cases were registered. Of the total 70 cases, 65 (92.8%) were diagnosed before the patients were 5 years of age out of which 20 (30.7%) were diagnosed before one year of age in less than 5 years group.

MRI may be beneficial in estimating the degree of differentiation of retinoblastomas but is not as specific as computerized tomography because of its lack of sensitivity in detecting calcium.

The current study was one of the attempts done in the local setting and at a national level. We succeeded in enrolling a large sample of under 5 years of populations with suspected retinoblastoma. We believe that keeping in mind the financial constraints, less health facilities and services in the developing countries like Pakistan; CT has an important role and may be continued as the first choice for the assessment of ocular lesions and calcifications.

The results of the study were to be shared with other health professionals so that they clinically diagnose retinoblastoma in proptosis at an early stage using the information given by study or knowledge in their mind. The current study results were significant as compared to previous studies and the need of invasive procedure would be reduced and we would give suggestions to all pediatric ophthalmologists to refer the patients with proptosis for computed tomography as screening test.

Conclusion:

Based on our study findings it is concluded that CT imaging has a high sensitivity and a reasonable specificity in the detection of retinoblastoma. Presence of calcification is the indicator of retinoblastoma in young patients 05 years of age. C.T imaging has substantial role in the diagnosis of retinoblastoma. As early diagnosis and treatment of Retinoblastoma greatly improve the patients survival rate and quality of vision.

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At present, MR imaging with its superior contrast resolution is generally recommended as an additional diagnostic method to CT scan in cases of suspected retinoblastoma. 16, 19â€”23 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.Â We performed MRI scans in 21 cases of retinoblastoma with a newly developed 5 cm surface coil and fast spin echo sequences. 13 This high resolution MR imaging of the eye is well tolerated without adverse effects in examination of intraocular masses in adults.Â Nevertheless, MR imaging with the new surface coil shows a higher accuracy than other available imaging techniques. 27. Download figure.