ORIGINAL ARTICLE

DIAGNOSIS OF RETINOBLASTOMA IN CHILDREN

Safia Izhar[1], Shazia Kadri[1], Samia Perwaiz Khan[2]
[1]Department of Radiology, [2]Department of Pharmacology, Jinnah Medical & Dental College, Karachi

ABSTRACT

Background: The purpose of this study is to assess radiological features (CT and Ultrasound) of retinoblastoma in clinically susceptible patients.

Methods: This study has been conducted at Jinnah Medical College and Hospital from January 2016 to January 2017. 39 children with clinical diagnosis of retinoblastoma referred from Layton Rahmatulla Benevolent Trust (LRBT) Eye hospital and by other eye clinics to Jinnah Medical College and Hospital Karachi. Ultrasound and CT scan of orbit of all children under the age 5 years was performed to see local tumor extent and associated intracranial primitive neuroectodermal tumor (trilateral retinoblastoma).

Results: Out of 39 children with clinically suspected to have retinoblastoma, of these 32 were male and 7 were female children. Mean age of patients was 2.5 years. Out of 39, only 25 children had unilateral and 14 had bilateral intraocular tumor on ultrasound and CT scan. It appeared as a heterogenous mass with areas of calcification and retro- orbital extension, was better seen on CT images. Ultrasound of orbits showed calcification in only 29 children out of 39. Only 3 children found to have trilateral retinoblastoma. Ultrasound was found to bediagnostic but CT showed better results for imagining and diagnosis of retinoblastoma (unilateral, bilateral).

Conclusion: This study shows that CT scan, is more accurate for the assessment of tumor size, localization and retro-orbital and intracranial extension of the retinoblastoma rather than other modalities. Thus CT scan, found to be affective in diagnosis, planning treatment and determining the prognosis of this disease.

Key words: Retinoblastoma, Leukocoria, CT scan, Doppler Ultrasound.

Corresponding Author:
Samia Perwaiz Khan
Department of Pharmacology,
Jinnah Medical & Dental College,
Karachi.
Email: samiaphk@gmail.com

INTRODUCTION

Retinoblastoma is the most common pediatric intraocular malignancy, having a frequency of 1:17,000-34,000 live births[1]. The tumor usually arises from the inner retinal layers and extends as a fleshy nodular mass into the vitreous cavity. Commonly RB-1 gene mutations (chromosomal location 13q14) result in retinoblastoma[2], origin in sites of the same eye. In the diseased eye, loose cohesive cells and nodules of tumor may be invaded into the vitreous or into the adjacent retinal surface or the anterior chamber. The extraocular extension is usually along the optic nerve, and into the subarachnoid space. Secondary disorders of bone marrow, liver, and lymph nodes may also be present. The majority of cases are of the sporadic or familial (mode of inheritance is an autosomal dominant trait)[3,4].

Retinoblastoma may be either sporadic or familial (due to a genetic mutation). It may be unilateral or bilateral. Unilateral tumors (60-70% of cases) are usually caused by a germline mutation in approximately 15% of cases, whereas 85% are sporadic[5,6]. Bilateral (30-40% of cases) mostly have caused due to genetic

mutation[5,6]. This mutation is inherited in an autosomal dominant with 90% penetrance, the child of a retinoblastoma survivor who has 50% chance of inheriting a mutation, and if they do these children have 90% chance of developing a retinoblastoma. It occurs in infancy from one to two years of age, median age of diagnosis is 18-24 months[5,6]. Children with familial condition, have increased risk of developing trilateral retinoblastoma (bilateral retinoblastomas and pineoblastoma) and osteosarcoma, may occur early (median age of diagnosis 12 months)[6].

Inherited forms are more commonly bilateral, and tend to occur at a younger age[5,6]. Most of the children affected by retinoblastoma are diagnosed before the five years of age.

The most prominent and common sign of a retinoblastoma is the absence of the normal red reflex that occurs when a light is shone into the child's eyes. It is called leukocoria or loss of red-eye reflex. This red color results from the reflection of light from the abundant, retinal blood vessels. In the eye with retinoblastoma, instead of red, the pupil looks white in the reflection. Leukocoria is scattered, visible only at certain angles and under certain light conditions. This sign resembles the flash photography. This sign is seen in 6 of every 10 patients with retinoblastoma. Strabismus also the most common symptoms of retinoblastoma, it can become constant, resulting in further deterioration of the vision. Squint is another common symptom of this disease. While performing ophthalmic examination, it is to be noted that eyes should be the same size, and move together when the child looks at an object. While child is focusing on something, the line of sight from each eye should not cross with that of the other. These signs are often overlooked and requires ophthalmological consultation for ocular fundoscopic examination. Other signs may include iris rubeosis, hypopyon, hyphema, buphthalmia, orbital cellulitis, and exophthalmia. Although some pediatric patients with retinoblastoma may have no symptoms.

Systemic symptoms with retinoblastomas may include bone pain due to metastasis or concurrent osteosarcomas. Screening in case of familial history or dysmorphic syndrome with a 13q14 deletion[7] may lead to diagnosis of retinoblastoma. Ocular Doppler ultrasound identifies a mass more echogenic than the vitreous, with fine calcification and increased vascularity. Retinal detachment may also be observed in exophytic forms in ultrasonography. Computed tomography (CT) typically shows an intraocular mass with greater density than the vitreous body, calcified in 90% of cases and moderately enhanced after iodine contrast agent injection. It may show extensions into the optic nerve, anterior chamber or orbital fat. Magnetic resonance imaging (MRI) is the imaging modality of choice to assess the local extension. The mass has a signal equivalent to or a slightly more intense than that of the vitreous, with a relatively low-intensity signal on T2-weighted.

Although it is better appreciated on CT/MRI[8]. Ophthalmic examination of the fundus under is performed under general anesthesia for diagnosis. This lesion appears as a white tumor with angiomatous dilatation of the vessels.

METHODS

This study has been conducted at Jinnah Medical College and Hospital from January 2016 to January 2017. Thirty-nine children with clinical diagnosis of retinoblastoma were referred from Layton Rahmatulla Benevolent Trust (LRBT) Eye hospital and some other centers to Jinnah Medical College and Hospital Karachi. Ultrasound and CT scan orbit of all children under the age of 5 years was performed for pretreatment assessment not only for diagnostic confirmation but also to see local tumor extent and associated intracranial primitive neuroectodermal tumor.

RESULTS

There were 39 children with clinically suspected Retinoblastoma. Mean age of patients was 2.5 years in which 32 were male and 7 were female children. Out of these 39 cases, 25 children had unilateral and 14 had bilateral intraocular tumor on ultrasound and CT scan (Table 1). It appears as a heterogenous mass with areas of calcification and retro orbital extension which better appreciated on CT image (Figure 1). B-Scan Ultrasound showed calcification in 29 children.

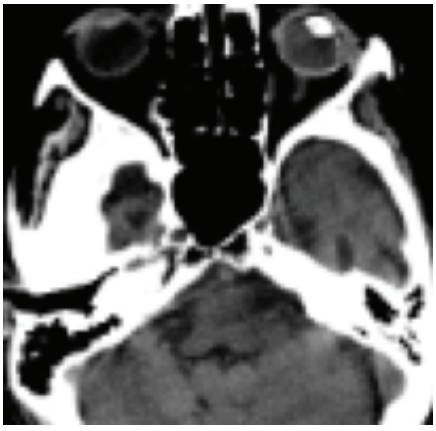

Figure 1: CT-Scan showing retinoblastoma of left globe.

Table 1: Comparison of children with retinoblastoma, on basis of gender and unilateral vs bilateral tumors.

Total No. children with Retinoblastoma (n=39)	CT/ Ultrasound N=39	N=39 ratio	Percentage
Male : Female	-	32: 7	83%: 17%
Unilateral: Bilateral Intraocular tumor	CT -Scan	25: 14	65%: 35% = 100%
Calcifications	Ultrasound	29	74%

DISCUSSION

Diagnosis of retinoblastoma by fundoscopy through clear optical media is the simplest and most convenient method[9]. When refractive media is clear, the presence of large calcified areas is also easily detected by fundoscopy. These frequently appear as bizarre shapes, and echo comes from the interior of the human eye[1]. The accuracy of ultrasound for this condition is only 80% [2]. CT and MRI are the imaging technology ocular lesions[9-12]; however CT is most commonly used for detecting intraocular calcium and investigating orbital pathologies[13,14].

This study has shown that CT scan is essential in the assessment of patients with clinically diagnosed retinoblastoma. Males were more susceptible 32(83%) as compared to females 7(17%).

Unilateral to bilateral ratio was 25:14. CT scan allows more accurate and rapid detection of tumor size and location with detailed visualization of retro-orbital or intracranial extension. These finding are essential in planning treatment and determining the prognosis. As the tumor is extended outside the confines of the globe, the prognosis becomes poor. In this study tumor was confined to the globe only, which could be favorable prognostic sign. Contrast enhancement was not commonly associated with tumor extending beyond the globe. The three tumor grades are: grade I tumor confined to the globe; grade II, tumor extending retro-orbitally into the soft tissues or involving the optic nerve; and grade III, tumor extending beyond the confines of the orbit or intracranially[13-16]. In children, the risk of retinoblastoma should always be suspected in the presence of leukocoria, strabismus or any other unexplained sign[17]. Leukocoria is the early of retinoblastoma and initially apparent when the tumor is still contained within the eye. The life-threatening white tumor reflects light and blocks view of the red retina. Retinoblastoma which remained intraocular is curable within 3–6 months. In the study, of newly diagnosed cases of retinoblastoma[17,18], only 6% are familial and 94% are sporadic[19,20]. Programs or campaigns on retinoblastoma should be focused on early diagnosis for better prognosis[21,22].

Recent studies show that retinoblastoma tumors may differ in the mutagenic pathway as some of retinoblastoma tumors are caused by RB1 mutation others also caused by amplification of MYCN

proto-oncogene. Singh et al.[23] demonstrated prognostic significance of CDC25 phosphatases and polo-like kinases in retinoblastoma. Thus CDC25B might be used as a prognostic marker in the pathogenesis of retinoblastoma and contribute to the development of the disease by causing genomic instability through deregulation of cell division. In their study, PLK1 was more frequently expressed and deregulated in poorly differentiated retinoblastoma tissue as compared to PLK3 protein that might serve as a poor prognostic marker in retinoblastoma[24].

For diagnosis, ultrasonography can be attempted primarily to detect a retinal mass with calcification and neuroimaging (MRI of the brain and orbit with and without contrast) is performed to assess the orbital segment of the optic nerve and to detect pinealoblastoma (trilateral retinoblastoma)[23]. CT scanning has shown high sensitivity and specificity in the detection of intraocular tumors[25].

CONCLUSION

This study shows that CT scan, is more accurate for the assessment of tumor size, localization, retro-orbital and intracranial extension of the retinoblastoma rather than other modalities. Thus CT scan, found to be affective in diagnosis, planning treatment and determining the prognosis of this disease.

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