Imaging of Retinoblastoma

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Summary

Even after multiple awareness programmes, retinoblastoma still presents late in developing country like India where major crowd is still uneducated. Most of the patients present at advanced stage when eye / vision preserving treatment has no role and enucleation becomes essential. In this pictorial study we have tried to show various features of retinoblastoma on imaging modalities with its complication and its differential diagnosis. We have also discussed role of imaging in post treatment patients. Imaging features of retinoblastoma may help doctors to diagnose retinoblastoma earlier thus help the patient to opt for eye/vision preservating treatment options.

Keywords: Retinoblastoma, USG, CT, MRI, Ocular, Childhood

Introduction

The most common primary ocular malignancy of childhood is retinoblastoma. It is highly malignant tumor. In 1970, Tso and colleagues established that the tumor arises from photoreceptor precursors.[1] Common incidence of retinoblastoma is 1 case per 18,000-30,000 live births. In developed countries retinoblastomas are detected early while in developing and underdeveloped countries, they are often detected after they have invaded the orbit or brain. High-resolution sonography (HRSG) is highly sensitive method for diagnosing small intra-ocular retinoblastoma. Computerized Tomography (CT) and MRI are good modalities to determine local extension of lesion, distal metastasis and to demonstrate post treatment residual /recurrent lesion or complication.

Material and Methods

We studied 100 patients of retinoblastoma over period of 3 years from year 2009-2012. Out of 100 cases, 40 were females and 60 were males. Age was between 2 months to 8 years. We have performed USG of orbit on SIEMEN G50 machine and LOGIQ P5 machine using 7.5-10 MHz linear probe. CT scan was performed on six slice Siemens Somatom machine and MRI was performed on Hitachi Aperto system. The images shown in this article are representative cases of our study.

Discussion

The most common presenting sign of retinoblastoma is leucocoria, accounting for about 56.1% of cases. Retinoblastoma can cause secondary changes in the eye, including glaucoma, strabismus, retinal detachment, and inflammation secondary to tumor necrosis. Proptosis is a more common presenting symptom in most underdeveloped countries while leucocoria is common presenting symptom in developed country.

Most retinoblastomas are quite advance at the time of diagnosis hence enucleation or external beam radiotherapy (EBRT) remains the only therapeutic option in such cases. Laser ablation, photocoagulation, and cryotherapy are newer modalities of treatment. Early diagnosis of retinoblastoma is necessary because if it is diagnosed early enough, it can be managed with new treatment modalities without enucleation or any form of irradiation. It is apparent that if all retinoblastoma could be recognized either in utero or shortly after birth, most of them could be treated promptly by the aforementioned methods, thus saving the child's life and salvaging vision.[2] Routine clinical screening of all parents and sibling of retinoblastoma patient is recommended to provide early detection of retinoblastoma and treatment at presymptomatic disease stage.[3]

HRSG is a prime imaging modality for superficial and small parts scanning. Excellent tissue details with anatomical landmarks are the hallmark of the technique. The prerequisite for HRSG is high frequency transducers ranging from 5 MHz to 15 MHz with short focus. The advantages of HRSG are that it is a noninvasive, cost effective and rapid investigation. No specific preparation or sedation is required. USG is very useful for the detection and differentiation of intraocular masses and in diagnosis of retinoblastoma.[4]

Intraocular Retinoblastoma -patterns of tumor growth

Endophytic growth

Endophytic growth occurs when the tumor breaks through the internal limiting membrane. Small Retinoblastoma is smooth, dome shaped and shows homogenous hypoechoic echopattern (Figure 1) however, large tumors are highly irregular and heterogeneous in texture. Usually it arises from retina and fills the posterior segment (Figure 2,3). But in rare case, tumor involving all the surfaces of retina can be found on HRSG known as retinoblastoma circumference. Calcification is typical feature of retinoblastoma and is accompanied with acoustic shadowing. The presence of intraocular calcium in children under three years of age is highly suggestive of retinoblastoma (Figure 4). Rarely calcification is absent (Figure 5).[5] Effected eye may show normal or

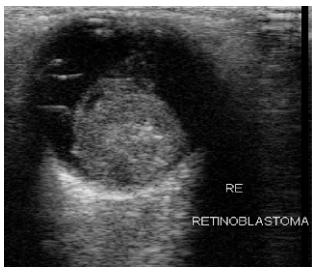

Figure 1: A 3 years old boy with endophytic retinoblastoma in right eye. USG shows well-defined hypoechoic mass in vitreous cavity forming acute angle with retina and showing few echogenic calcified spots

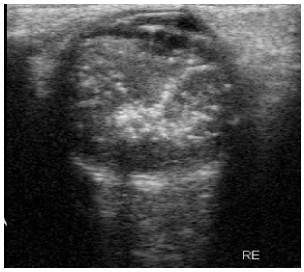

Figure 2: Huge retinoblastoma in right eye. USG showing hetero-geneous echopattern mass lesion almost completely filling vitreous cavity with internal dense calcification. Anterior chamber appears normal

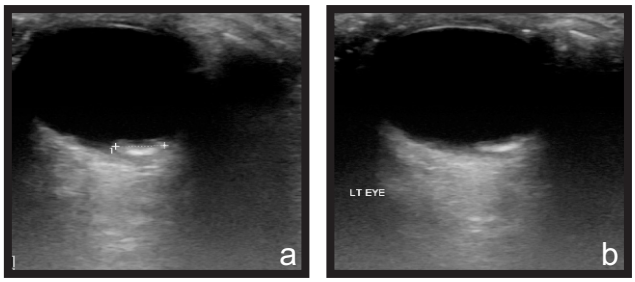

Figure 4: A 3 years old male child presented with complain of diminished vision in both eyes. USG of right eye showed presence of 6 mm sized calcification (a) and 8 mm sized calcification in left eye (b)

higher than normal axial length. Retinoblastoma in microophthalmic eye is extremely rare. HRSG can also tell about the extra-ocular extension of the tumor. The eye is usually of normal size or larger than normal.[6] Retinoblastoma may be unilateral or bilateral (Figure 6, 7), focal or multifocal (Figure 6).[7]

Endophytic tumor growth pattern can be associated with vitreous seeding. Here small fragments of tissue are separated from the main tumor. In some instances, vitreous seeding may be extensive allowing tumor cells to be visible as spheroid masses floating in the vitreous and anterior chamber. Secondary deposits or seeding of tumor cells into other areas of the retina may be confused with multicentric tumors. Differentiation between multifocal lesion and tumor seedling may be difficult.[7] Vitreous seedling produces vitreous echogenic debris on HRSG. Vitreous echogenic debris may also results from hemorrhage or increased globulin content.

Retinoblastoma can extend to involve anterior chamber. On HRSG few solid and cystic nodules can be seen. Tumor can be discovered posterior to iris, on the lens capsule and over ciliary process. Other HRSG findings include angle closure related to iris, neovascularization and uveal thickening.[8]

Retinoblastoma can locally extend and involve retro bulbar space (Figure 8) and optic nerve (Figure 9)**.** CT is better modality to see intra-lesional

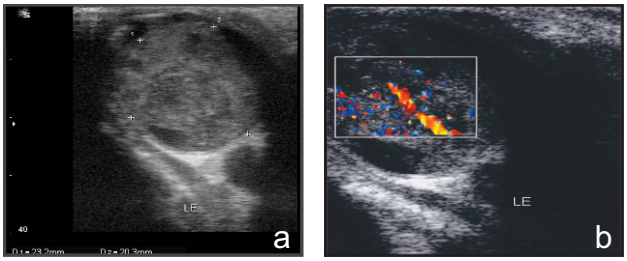

Figure 3: USG showing huge retinoblastoma in left eye with thickened optic nerve suggestive of optic nerve involvement (a), Doppler study of lesion shows high vascularity within mass suggestive of high grade malignant nature (b)

calcification (Figure 10), widening of optic canal (Figure 11) and local bony erosion (Figure 12)**.** MRI is modality of choice to detect optic nerve involvement (Figure 13)**.**

Retinoblastoma can lead to metastasis at different site. Cases have been reported with metastasis to cerebrum (Figure 14), dura matter (Figure 15), leptomeninges (Figure 16), cerebellum (Figure 17), brain stem (Figure 18), liver (Figure 19), ovary,[9] skin (Figure 20), bone (Figure 21, 22) and lung (Figure 23). MRI is modality of choice for metastasis in brain and dura matter.[10] The vascularity indicates tumor activity-hypervascular and active lesion. Vascularity regresses with treatment.[11] Echography is also useful in monitoring size of tumor and complication in post chemotherapy or radiotherapy status. In most instances, tumors that recur or continue to grow after radiotherapy tend to exhibit low to medium reflectivity and do not show calcification. Tumor tends to outgrow their blood supply resulting in areas of necrosis.[7,12]

Large size retinoblastoma and retinoblastoma located at macular region responses more to chemotherapy. While lesion less than 2 mm in size and in patient less than 2 months of age responses less to chemotherapy.[13] If the tumor extends beyond the lamina cribrosa even if the cut end of the nerve is free of tumor cells, chances of survival decrease to 60%. If the tumor cells are found at the surgical transection sight, chances of survival rates decrease to less than 20%. Intracranial extension of tumor can lead to death.[13]

Exophytic growth

Exophytic growth occurs in the subretinal space. This growth pattern often is associated with subretinal fluid accumulation and retinal detachment (Figure 24). The tumor cells may infiltrate through the bruch membrane into the choroid and then invade either blood vessels or ciliary nerves or vessels. Tumor may grow outside eyeball. Typically retinoblastoma growing outside eyeball does not show presence of calcification (Figure 25).

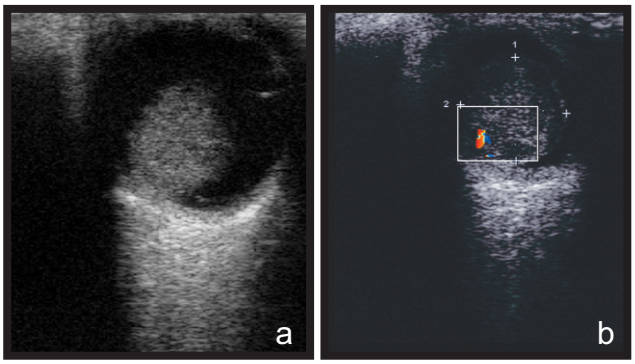

Figure 5: A 2 years old girl presented with complain of Leucocoria in right eye. USG examination revealed large well-defined homogenous hypoechoic lesion in vitreous cavity without presence of calcification which is forming acute angle with retina (a), Color doppler study of lesion showed presence of vascularity within (b)

Diffuse infiltrating growth

It is a rare subtype that comprises 1.5% of all retinoblastoma. There is relatively flat infiltration of the retina by tumor cells and without a discrete tumor mass. It exhibits slow growth pattern. It typically lacks calcification, seen in older patient and readily stimulate inflammatory or hemorrhagic process.[8,12]

Reese and Ellsworth have developed a generally adopted classification system for intraocular retinoblastoma that has been shown to have prognostic significance.

Group I: very favorable for maintenance of sight

1. Solitary tumor, smaller than 4 disc diameters, at or behind the equator
2. Multiple tumors, none larger than 4 disc diameters all at or behind the equator

Group II: favorable for maintenance of sight

1. Solitary tumor, 4-10 disc diameters at or behind the equator
2. Multiple tumors, 4-10 disc diameters behind the equator

Group III: possible for maintenance of sight

1. Any lesion anterior to the equator
2. Solitary tumor, larger than 10 disc diameters behind the equator

Group IV: unfavorable for maintenance of sight

1. Multiple tumors, some larger than 10 disc diameters
2. Any lesion extending anteriorly to the ora serrata

Group V: very unfavorable for maintenance of sight

1. Massive tumors involving more than one half the retina
2. Vitreous seeding

Retinocytomas are rare tumors that are composed entirely of benign-appearing cells. Genetic implications of retinocytoma are the same as that of retinoblastoma. Family members of patients with retinoblastoma should be closely examined for retinocytoma and if positive, they are followed for rest of their lives.[14]

Trilateral retinoblastomas are cases of bilateral retinoblastoma associated with an ectopic intracranial retinoblastoma usually involving the pineal gland or the parasellar region. Trilateral retinoblastomas contribute significantly to the overall mortality in patients with hereditary retinoblastoma in the first decade of life accounting for approximately 50% of deaths. To reduce the mortality of trilateral retinoblastoma, screening efforts should be made in patients who have bilateral or multifocal disease and those with a positive family history. Patients and their siblings should be assessed periodically for any signs of developing retinoblastoma.

Standard therapy comprises enucleation for unilateral disease and radiation therapy with or without enucleation for bilateral disease. However, contemporary treatment for retinoblastoma is transitioning to front-line chemotherapy to improve disease control while preserving vision and minimizing adverse sequel of enucleation and

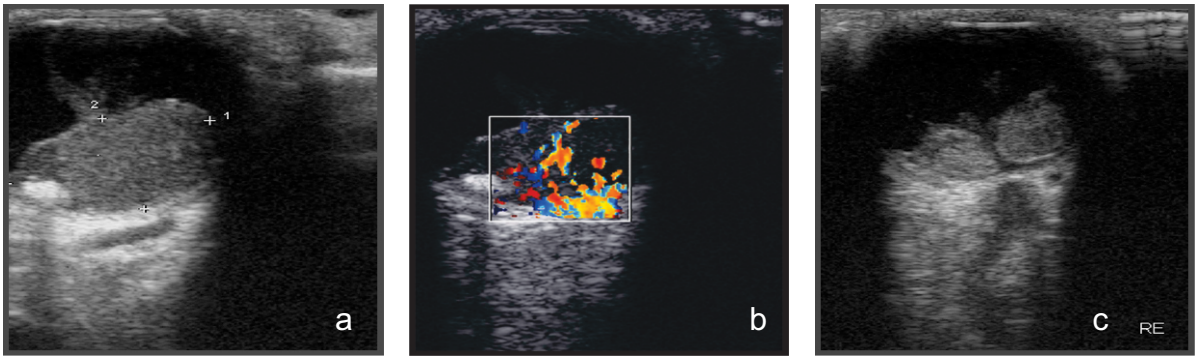

Figure 6: A 5 years old male patient presented with complain of bilateral loss of vision for 3 months. USG of left eye showed presence of large well-defined homogenous hypoechoic mass with presence of dense calcified area (a), Color Doppler study of lesion showed presence of high vascularity within, suggestive of high grade malignancy (b), USG of right eye also shows presence of large retinoblastoma with thickening of optic nerve (c)

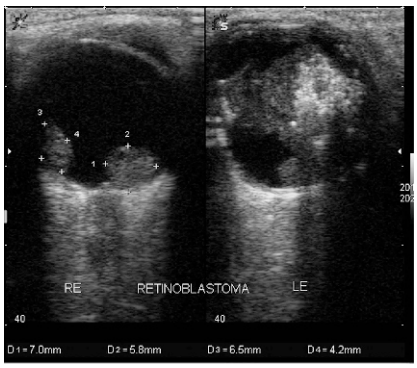

Figure 7: USG of both eyes in 4 years old boy shows presence of large calcified mass lesion in left eye with two small hypoechoic noncalcified mass lesions in right eye suggestive of bilateral multiple retinoblastomas

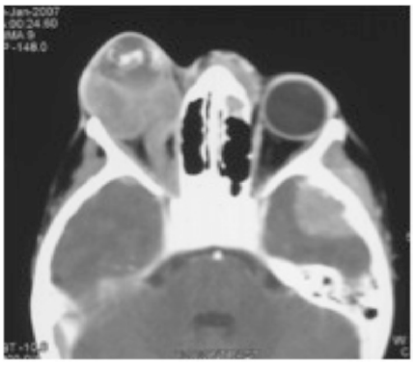

Figure 8: Axial CT scan at level of orbit shows mass in right orbit with extension into retrobulbar space

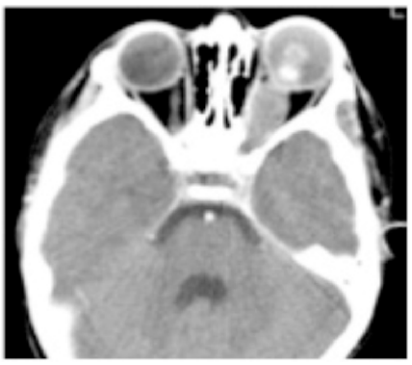

Figure 9: Axial CT scan at level of orbit shows mass in left eye-ball with thickened left optic nerve

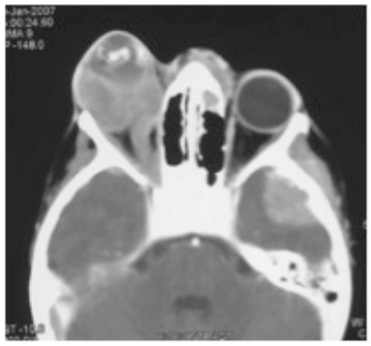

Figure 10: Axial CT scan at level of orbit shows mass in right eye-ball extending into right retrobulbar space with thickened right optic nerve. Intra-ocular component shows calcification spot within

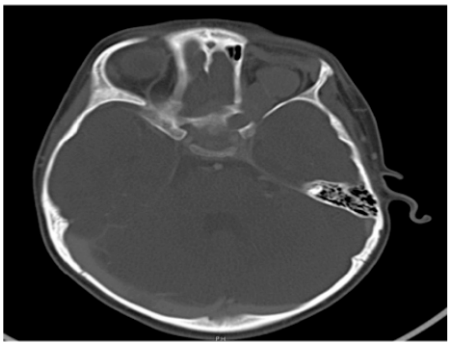

Figure 11: Patient with left eye retinoblastoma, bone window image of CT scan shows widening of left optic canal

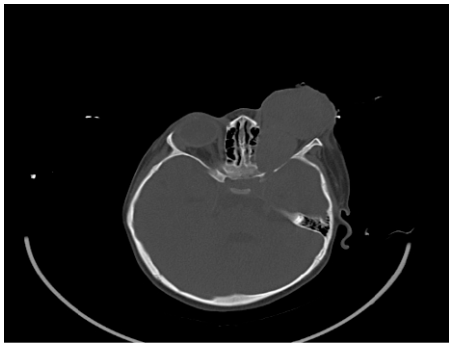

Figure 12: Patient with left eye retinoblastoma, bone window image of CT scan shows thinning of greater wing of sphenoid

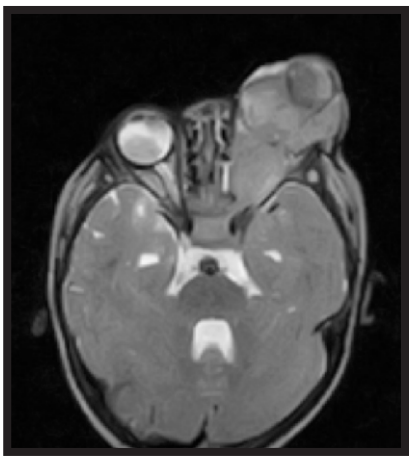

Figure 13: Patient with bilateral retinoblastoma, MR T2w image shows thickened liftt optic nerve. Left optic nerve appears hyperintense, suggestive of retroocular extension of lesion

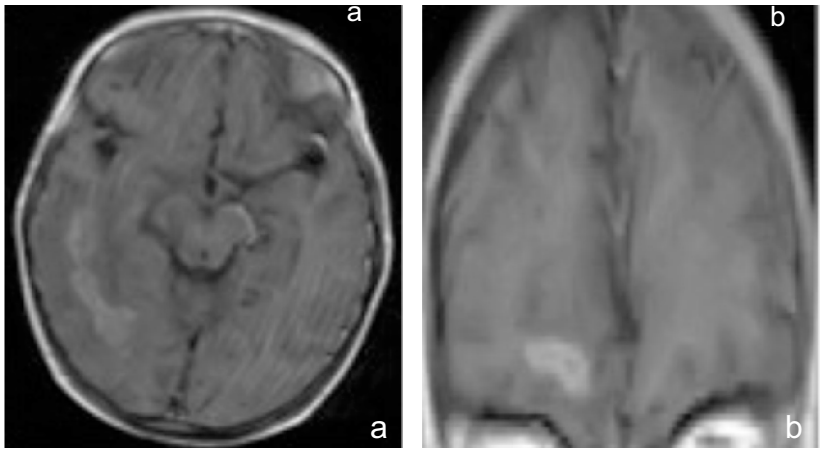

Figure 14: A 6 year old male child with retinoblastoma of right eye. MRI brain T1w post contrast axial image shows few well-defined nodular enhancing lesions in right parietal lobe (a), Coronal section of MRI brain shows similar metastasis in right temporal lobe

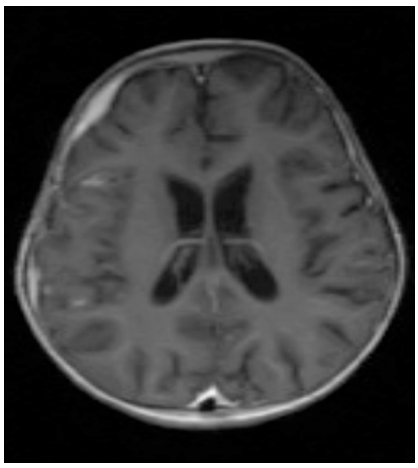

Figure 15: A 9 year old male child with retinoblastoma of right eye. T1w post contrast image of MRI brain shows dural based enhancing lesions along right frontal lobe and parietal lobe

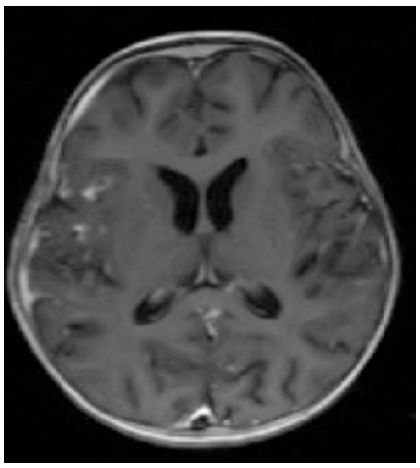

Figure 16: A 9 year old male child with retinoblastoma of right eye, T1w post contrast image of MRI brain shows focal leptomeningeal enhancement along right parietal lobe

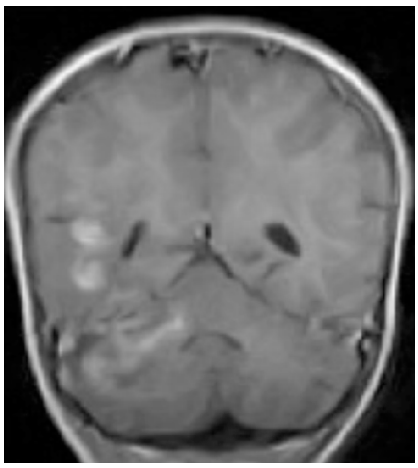

Figure 17: A 6 year old male child with retinoblastoma of right eye. T1w post contrast axial image of MRI brain shows few well-defined nodular enhancing lesions-metastasis in right cerebellar hemisphere

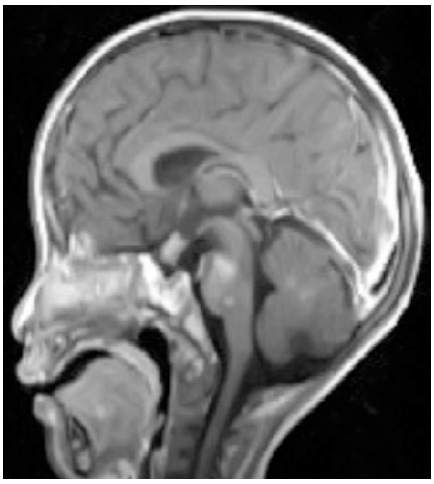

Figure 18: A 6 year old male child with retinoblastoma of right eye. T1w post contrast axial image of MRI brain shows few well-defined nodular enhancing lesions-metastasis in brain stem

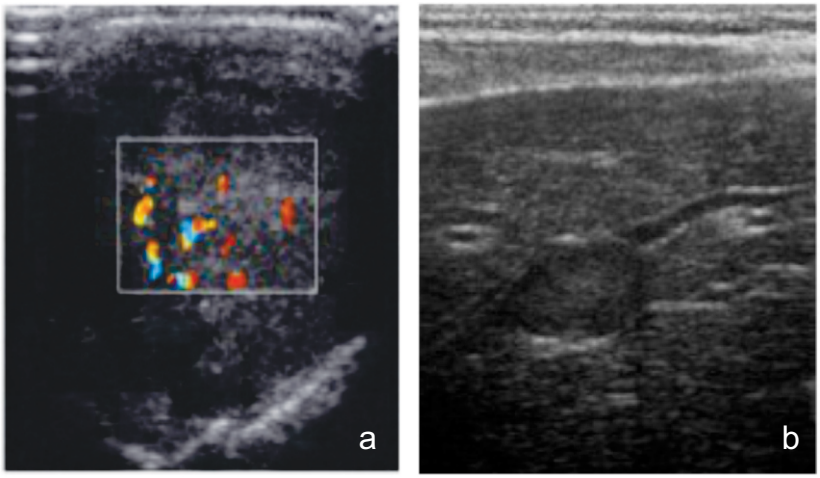

Figure 19: A 3 years old boy presented with leucocoria in left eye. USG revealed exophytic retinoblastoma in left eye with internal vascularity (a), USG of liver shows presence of hypoechoic liver metastasis (b)

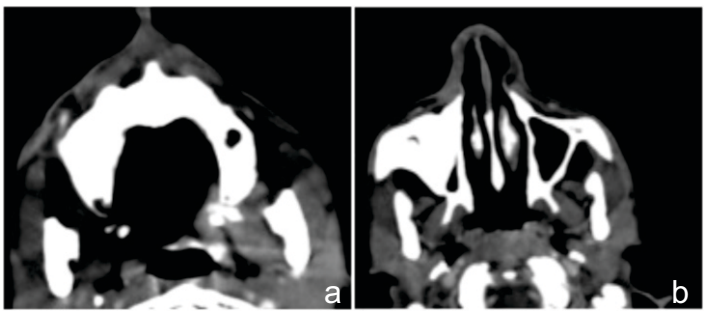

Figure 20: A 12 years old boy had right eye retinoblastoma. Enucleation surgery was performed. After 2 years he presented with swelling over nose (a, b). Biopsy confirmed metastasis

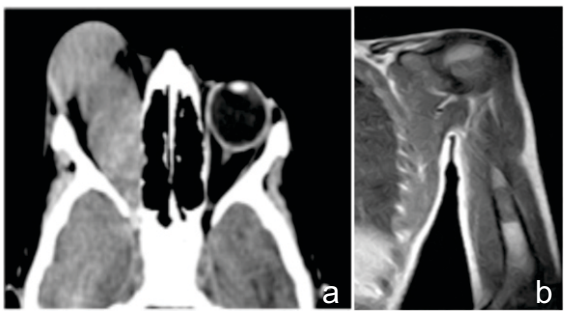

Figure 21: A 5 years old girl with right eye retinoblastoma, MRI shows retrobulbar extension of lesion with involvement of right optic nerve (a) and metastasis in left humerus (b)

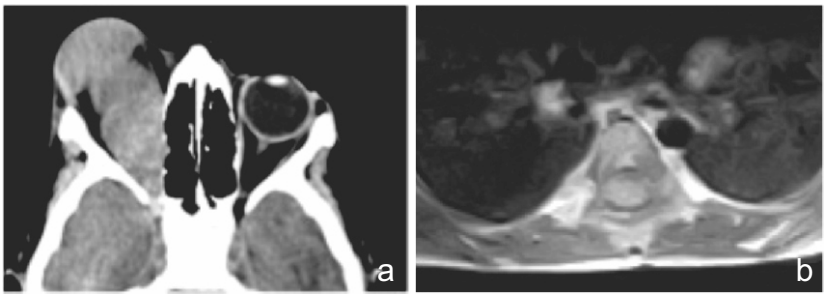

Figure 22: MRI images of 10 years old boy presented right eye retinoblastoma (a) and vertebral body metastasis (b)

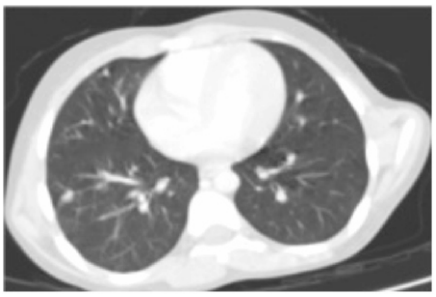

Figure 23: CT scan of 7 years old male child with retinoblastoma, lung window images show few well-defined metastatic lung nodules

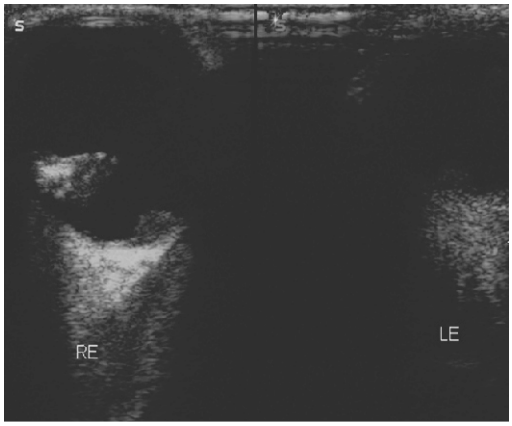

Figure 24: USG of both eyes shows presence of two small hypoechoic mass lesions in right eye with presence of dense calcification in one of the lesion. Single small hypoechoic lesion is also noted in left eye, suggestive of bilateral multiple retino-blastoma

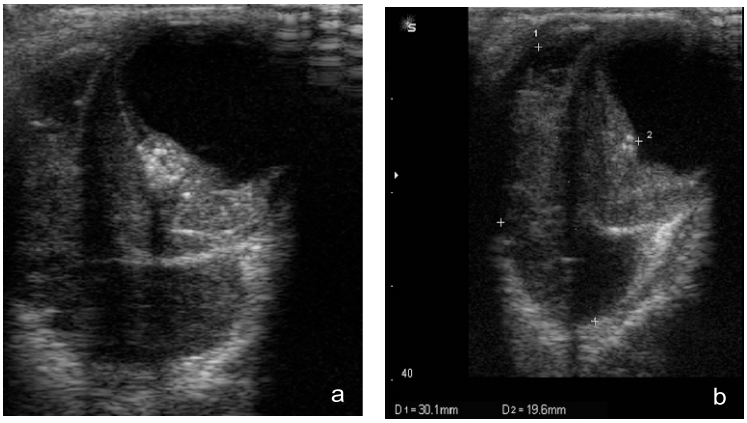

Figure 25: A 3 years old boy presented with complains of exophthalmous in right eye. USG revealed exophytic calcified retinoblastoma in right eye with large extra-bulbar component. The extrabulbar component typically doesn't show presence of calcification (a), measuring 30X19 mm (b)

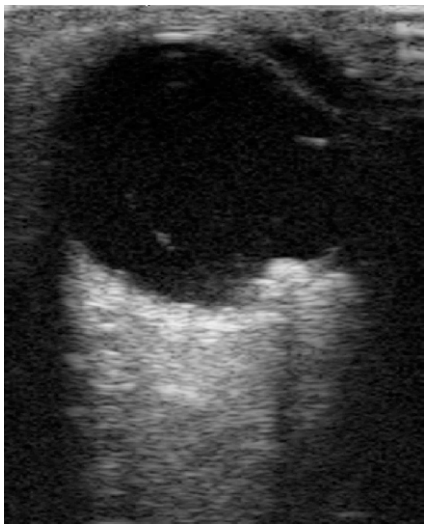

Figure 26: Known case of bilateral retinoblastoma with enucleation of right eye. Patient was also given concurrent radiotherapy. After completion of radiotherapy, USG of left eye was performed. It showed calcified residue of retinoblastoma

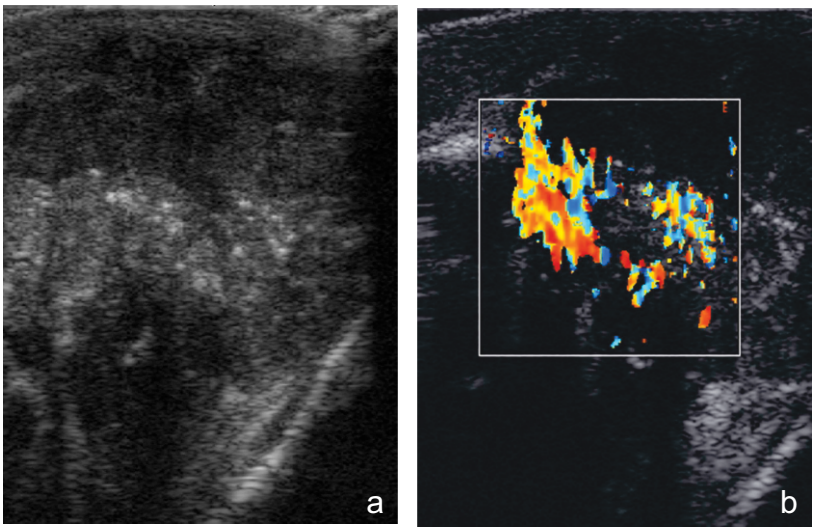

Figure 27: Known case of right eye retinoblastoma - post enucleation status. Patient presented with swelling in right orbit. USG showed presence of large hypoechoic lesion in orbital cavity with internal calcification (a), Color doppler study showed high vascularity of lesion (b). All findings suggestive of recurrent retinoblastoma in same side

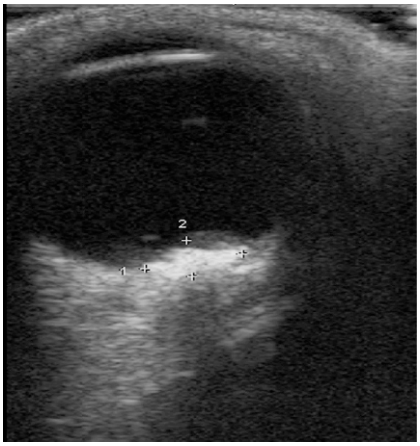

Figure 28: Old case of retinoblastoma of left eye - post enucleation status. Follow up USG showed presence of small calcified lesion in right eye, suggestive of development of retinoblastoma in opposite eye

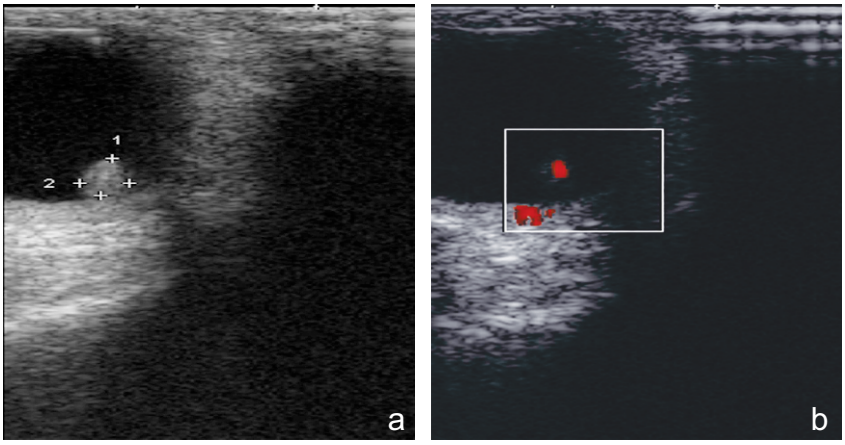

Figure 29: Treated case of right eye retinoblastoma. Follow up USG revealed small hypodense lesion in left eye without calcification (a), Color doppler study showed vascularity within the lesion (b). Findings are suggestive of retinoblastoma in opposite eye

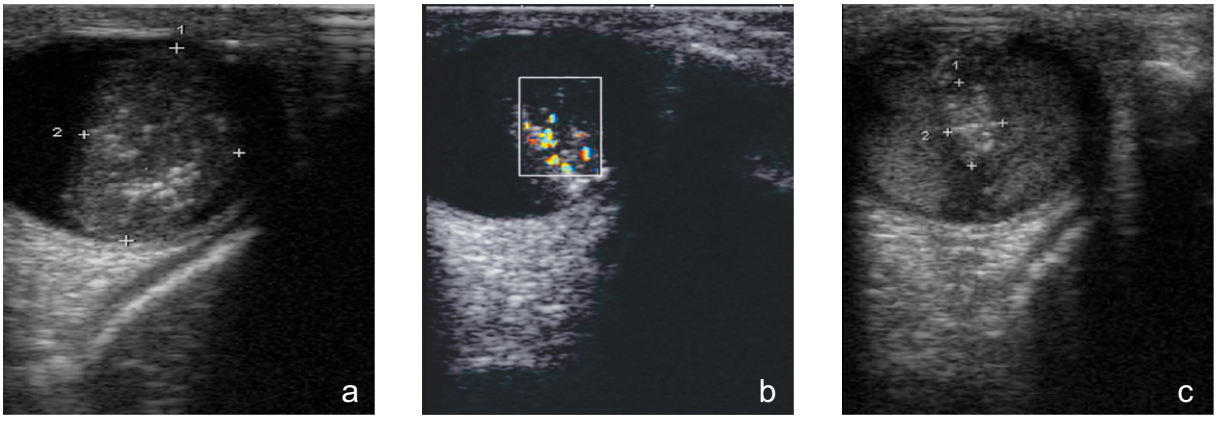

Figure 30: A 4 years old girl presented with complain of leucocoria in left eye. USG of left eye shows presence of large heterogeneous echopattern mass lesion with internal calcification, suggestive of retinoblastoma (a), Color Doppler study revealed presence of vascularity within the lesion (b). Patient was given two doses of chemotherapy. Post chemotherapy USG orbit showed complete retinal detachment with subretinal echoes. Residual mass is seen as small heterogeneous echopattern lesion with calcification. Size of mass is reduced as compared to previous USG (c)

radiation therapy. Retinoblastoma contracts, calcifies, and becomes hypovascular in response to therapy.[15] Long term follow up is essential for managing retinoblastoma after eye preserving conservative therapy.[15]

Imaging of retinoblastoma after treatment is major concern. Post conservative treatment, the size of tumor decreases, with ultimately calcified spot, fibrosis remains as residue of previous treatment (Figure 26). In post enucleation status, USG is very sensitive modality to detect residual/recurrent mass on the same side (Figure 27) or development of tumor in opposite eye (Figure 28, 29, 30).

EBRT can lead to various complications. Radiation can lead to cataract formation in 18 months to 3+ years. Hypoplasia of bone and soft tissue structures after treatment with radiation doses exceeding 3500 cGy may occur. The maxillary molar tooth buds located high in the maxilla just inferior to the posterior apex of the orbit may become irradiated with treatment. Numerous reports of failure of tooth eruption have been noted in patients with retinoblastoma treated with irradiation.

Secondary monocular tumors can develop in survivors of retinoblastoma, in order of decreasing frequency: osteosarcoma[16,17](Figure 31), various soft tissue sarcomas, malignant melanoma, various carcinomas, leukemia and lymphoma, and various brain tumors.[17] Patients treated with EBRT appear to be at a much greater risk of developing second tumors. Dunkel et al demonstrated that by age 40 years 6% of those patients who did not receive EBRT had developed second primary malignant neoplasms as compared to 35% for those who did receive EBRT.

Differential diagnosis of retinoblastoma includes PHPV, retinopathy of prematurity, coat's

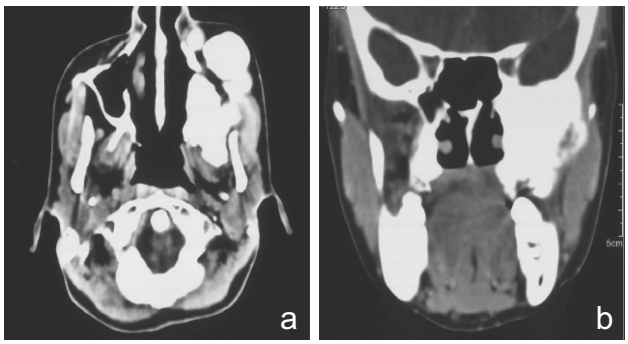

Figure 31: Known case of retinoblastoma post radiotherapy status. Axial CT (a) and coronal CT (b) scan shows sclerotic lesion involving maxilla suggestive of sclerotic variety of osteosarcoma

disease, retinal astrocytoma, toxocariasis and optic nerve head drusen.

Conclusion:

Retinoblastoma is curable intra-ocular childhood malignancy if it is diagnosed at an early stage. Various radiological modalities help in early diagnosis and staging of disease. In follow up cases during post treatment period, imaging modality help to rule out any residual or recurrent lesion.

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