Indian Journal of Pathology and Oncology 2023;10(1):64–68

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Indian Journal of Pathology and Oncology

Journal homepage: www.ijpo.co.in

Case Series

Histopathological findings of enucleated specimen of eye in children - A case series of 4 cases

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ARTICLE INFO

Article history:
Received 13-06-2022
Accepted 16-02-2023
Available online 16-03-2023

Keywords:
Retinoblastoma
Retinal dysplasia
Phthysis bulbi

ABSTRACT

Retinoblastoma is one of the common intraocular malignancy in childhood. It's incidence varies between 1 in 3300 to1 in 20,000 live birth. Retinal dysplasia is a rare disorder which can mimic retinoblastoma. Retinal dysplasia is a rare cause of childhood leucocoria, which can cause considerable diagnostic difficulty in the differentiation of benign and malignant intraocular pathologies Enucleation is often required for both these conditions. In this series we are discussing 4 cases of enucleated eyeball. Out of these 4 cases three cases were of retinoblastoma.4^{th} case was done for post traumatic phthysis bulbi. In this case series we are discussing diagnostic and prognostic indicators of Retinoblastoma as well as retinal dysplasia.

1. Introduction

Enucleation is the removal of the entire globe and a section of the optic nerve. It is sometimes an unavoidable end-stage solution for several ophthalmic diseases. This procedure may be required after severe ocular trauma, tumours, infections, or painful blind eye.[1] Indications for enucleation—since the first description of the surgery in 1583 by Bartisch—may differ over time, with changing incidences of different ophthalmic conditions (e.g., diabetes mellitus, secondary glaucoma, and tumours) and therapeutic regimens (e.g., panretinal photocoagulation, intravitreal injections, and chemotherapies).[2]

Retinoblastoma is the commonest intraocular malignancy of childhood[3] and needs enucleation. It's incidence varies between 1 in 3300 to1 in 20,000 live birth.[4,5] Average age at diagnosis is 12 months for unilateral cases and 24 months for bilateral cases. However, it has been reported in older children up to the age of 16years.[6,7] Cases of retinoblastoma have also been reported in adults up to the age of 37 years.[8,9] The tumour have been found to be due to a mutation in the retinoblastoma gene (RB1), located in the 14 band of chromosome 13.[10,11] Being a tumour suppressor gene, it's loss is said to lead to tumour formation. Clinically, the tumour commonly presents as leucocoria (60%) and strabismus(20%) and rarely as secondary glaucoma, pseudouveitis, orbital inflammation, proptosis, metastatic features and raised intracranial pressure in trilateral cases among others (20%).[12,13]

Retinal dysplasia is a rare cause of childhood leucocoria, which can cause considerable diagnostic difficulty in the differentiation of benign and malignant intraocular pathologies. When they are present as the component of a group of congenital disorders, the ocular findings are mostly bilateral. Clinically, retinal dysplasia may present itself in a wide range of severity. Leucocoria and retinal detachment in children require prompt further investigation because retinoblastoma should be included in the differential diagnosis.

In this case series we are discussing 4 cases of enucleation cases 3 of which are for retinoblastoma and 1

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https://doi.org/10.18231/j.ijpo.2023.012

for phthysis bulbi.

2. Case Reports

2.1. Case 1

4 year male presented with leucocoria in the ophthalmology department Gauhati Medical College. On ocular examination, visual acuity in the right eye was no perception of light. There was mild lid retraction, moderate temporal sclera injection and clear cornea in same eye. Pupils were fixed and dilated and there was a white pupillary reflex. Fundal view was not possible. The left eye was normal. The anterior chamber was normal. CEMRI brain and Orbit: Heterogenously enhancing intraconal soft tissue lesion (measuring 1.5X1.2X1.7 in cross-sectional and craniocaudal dimensions) with resultant retinal detachment and haemorrhage, showing significant diffusion retraction with possible optic nerve infiltration, suggestive of neoplastic etiology (possibly retinoblastoma). Enucleation of eyeball was done and specimen was sent to histopathology.

Specimen was 2.6 cm in anteroposterior diameter, 2.5 cm in horizontal diameter and 2 cm in vertical diameter. Externally leucocoria was noted. Optic nerve stump was 1.1 cm in length. On cut section a tumour mass noted measuring 2X1.5X1.1 cm involving the inferotemporal and inferonasal quadrant. Cut section of the tumour is solid, greyish white with few areas of calcification (Figure 1). The tumour is confined to the posterior compartment. Grossly, optic nerve, choroid, sclera appear uninvolved. Optic nerve cut margin is 1.2 cm away from tumour.

On microscopy, Tumour cell show features of Poorly differentiated Retinoblastoma. Tumour cells are arranged in sheets, round to oval in shape, high neucleocytoplasmic ratio, moderate to severe nuclear pleomorphism, irregular nuclear membrane and scant amount of cytoplasm (Figure 2). Few Flexner Winterstainer and Homer Wright rosettes seen (<1/3 of tumour population). Tumour additionally shows areas of calcification, necrosis and ossification at places. Tumour was confined to posterior segment. Choroid was involved by the tumour and the invasion is massive. Vitreous seeding noted. Optic nerve is involved by the tumour and the involvement is at the level of the lamina cribrosa upto post lamina cribrosa and upto a maximum length of 1 cm. Optic nerve cut margin is also involved by tumour(Figure 3). Cornea, sclera and iris are not involved.

2.2. Case 2

5 year old male presented to the ophthalmology department Gauhati Medical College for diminish of vision and phthysis bulbi. Patient has a past history corneal injury for which coreal repair was done under general anaesthesia 5 months back. No radiological investigation was done. Enucleation

Fig. 1:

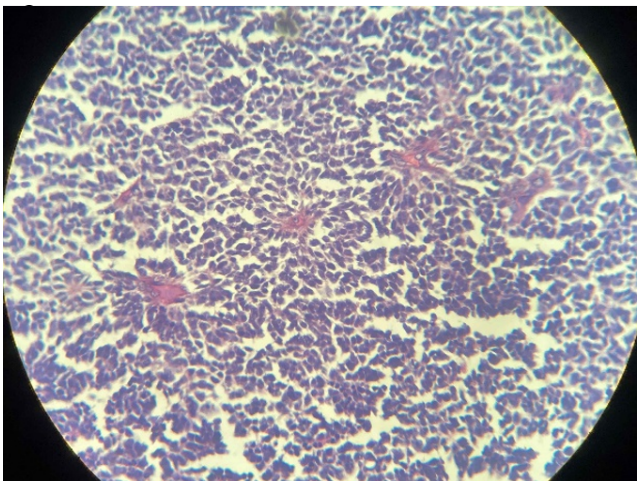

Fig. 2:

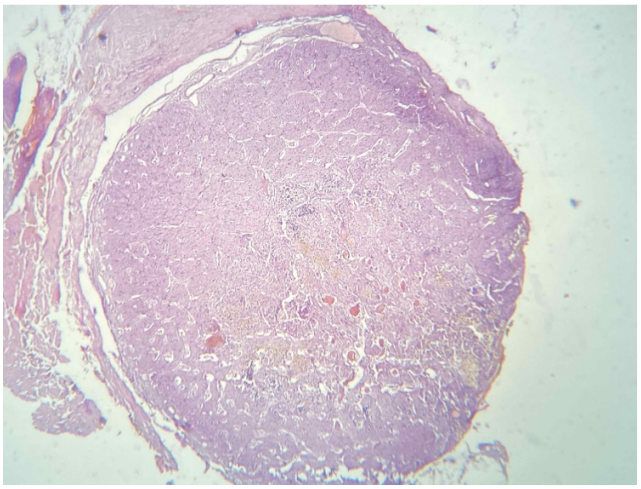

Fig. 3:

was done under general anaesthesia for phthysis bulbi.

Enucleated eyeball was 1.7 cm in anteroposterior diameter and 1.5 cm in vertical diameter. Externally the eyeball appears normal. On cut open an ill defined endophytic solid mass noted in the vitreous chamber just behind the lens measuring 1.5X1X0.8 cm. Mass is confined to the posterior chamber grossly (Figure 4). Grossly optic nerve was not involved. Optic nerve cut margin was 0.4 cm away from the mass. Soft tissue cut margins were uninvolved grossly and 0.9cm away from mass.

On microscopy, disorganised mass of well differentiated retinal tissue seen of which nuclear layer of retina infolds/thrown into folds forming large sized rosettes and some tubular structures the rosettes showed well delineated limiting membrane towards the luminal side and surrounded by rows of uniform rounded nuclei (Figure 5). There was no atypia or mitotic activity retinal detachment was seen with exudates filling in subretinal space. Areas of exudates, mixed inflammatory cells, cholesterol clefts, histiocytic giant cells and metastatic ossification also seen. Final diagnosis of retinal dysplasia associated with phthysis bulbi was made.

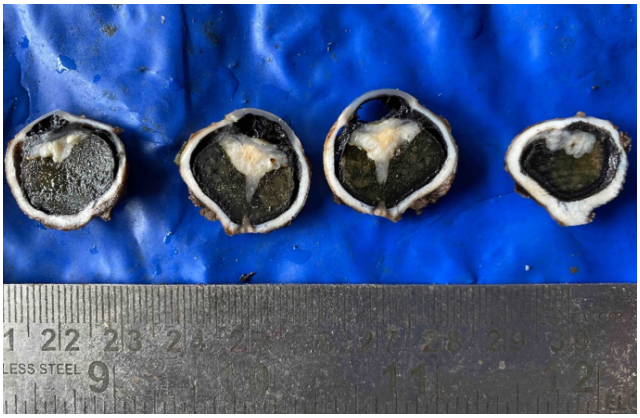

Fig. 4:

2.3. Case 3

2 year 6 months male was presented to the ophthalmology department Gauhati Medical College for decreased vision and ocular pain in the right side. Leucocoria was not there.CEMRI of brain and orbit showed a heterogeneously enhancing soft tissue lesion (1.8X1.5X1.5 cm) arising from the right globe showing significant diffusion restriction causing mild proptosis, suggestive of malignant neoplastic etiology (possibly retinoblastoma). Histopathological examination was advised. Patient undergone enucleation of right eye ball under GA and tissue was sent for HPE.

Specimen was 2.2 cm in anteroposterior diameter, 2.0 cm in horizontal diameter and 2 cm in vertical diameter. Externally no leucocoria was noted. Optic nerve stump was

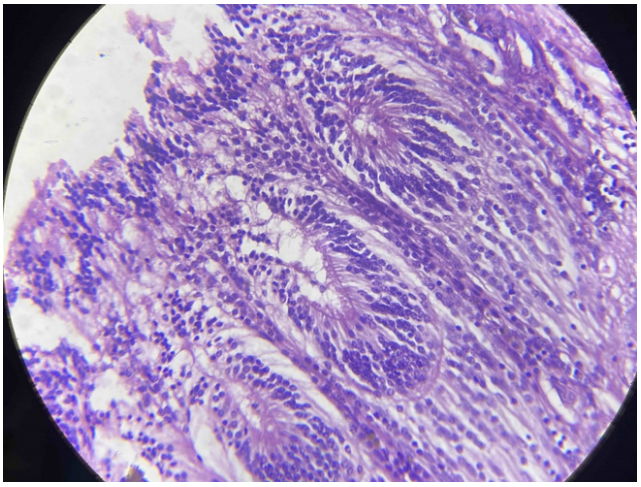

Fig. 5:

0.2 cm in length. On cut section an endophytic tumour mass noted measuring 1.5X1.5X1.5 cm is seen in the posterior compartment of the eyeball arising from posterosuperior wall. Cut section of tumour is solid and greyish grossly optic nerve, choroid, sclera, iris and cornea are uninvolved by the tumour. Optic nerve cut margin is 0.6 cm away from tumour.

Microscopically tumour shows features of Poorly differentiated Retinoblastoma with extensive areas of necrosis (Figure 6). Tumour is confined to posterior chamber. Choroid is involved by the tumour and invasion was found to be massive. Vitreous seeding seen. Cornea, sclera, optic nerve and iris are uninvolved by the tumour(Figure 7). Optic nerve cut margin was free. Areas of fibrosis seen.

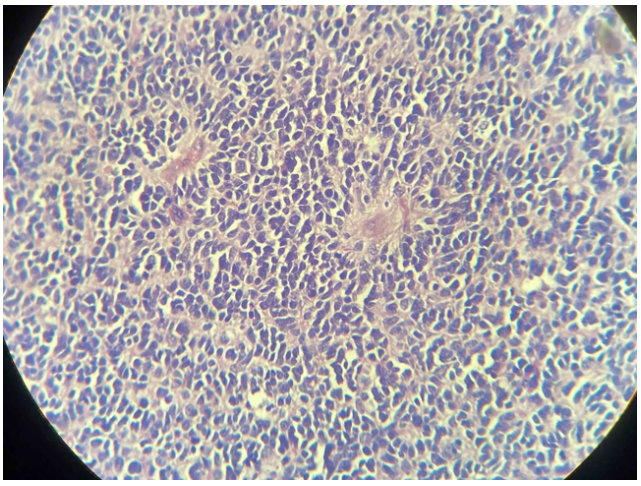

Fig. 6:

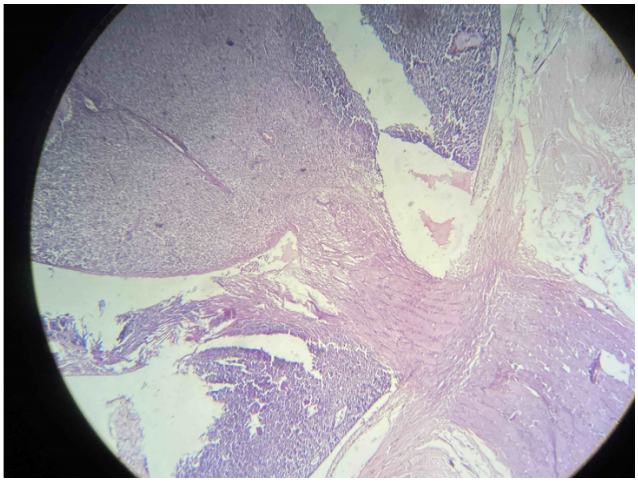

Fig. 7:

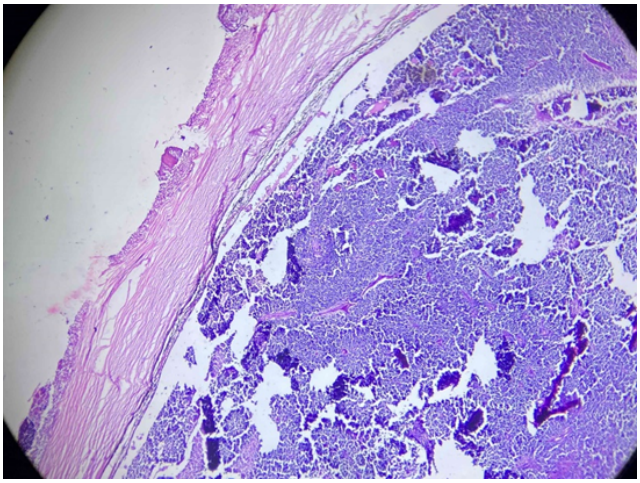

Fig. 8:

2.4. Case 4

1 year 10 months old female child presented with ocular pain. Ocular examination and CEMRI suggest it be a intraocular tumour, likely to be Retinoblastoma. Enucleation was done.

Grossly enucleated eyeball with optic nerve stump measures 3.3 cm anteroposteriorly, 2.7cm horizontally and 1.2 cm vertically. Optic nerve stump was 0.5 cm. Tumour is seen superotemporaly and superonasally measuring 2X1.6X1.5 cm which was endophytic in nature and grossly confined to the posterior chamber. Grossly choroid and sclera were univovled by the tumour.

Microscopically tumour shows features of Poorly differentiated Retinoblastoma with presence of occasional rosettes(Figure 8). Anterior chamber, iris and sclera is found to be involved by the tumour. Choroid is massively involved by the tumour. Vitreous seeding seen. Optic nerve was also involved and it was prelamina cribrosa type as well as at the lavel of the lamina cribrosa. Optic nerve cut margin is free. Cornea is not involved.

3. Discussion

The survival and management of high risk retinoblastoma has improved by identification of high-risk factors and appropriate adjuvant therapy. Histopathological high risk factors (HRFs) are evaluated and identified after enucleation for predicting metastasis. Prognostic factors like massive choroidal invasion, retrolaminar invasion and involvement of resected end of optic nerve, iris and ciliary body involvement, anterior chamber involvement, scleral and extrascleral involvement by tumour cells are associated with a greater risk of orbital recurrence and predictive of metastasis. There is a still debate regarding anterior chamber as a high-risk factor for retinoblastoma. Recently, Sreelakshmi et al[14] concluded in their study that anterior chamber seeds do not, by themselves, constitute an independent risk factor for metastasis in retinoblastoma. Kashyap et al[15] described various clinical features like older age at presentation, longer lag period, presence of hyphema, pseudohypopyon, staphyloma, and orbital cellulitis. These factors were associated with occurrence of HRFs and may be a useful indicator for considering adjuvant chemotherapy especially in developing countries. Also, poorly differentiated retinoblastomas present at a later age and are associated with presence of multiple HRFs and necrosis. Cases with presence of HRFs need systemic adjuvant chemotherapy which improves the survival of children at risk for metastatic disease.[16] Therefore, histopathologic HRFs can provide important basis for clinicians to determine treatment plan.

The normal histology of the retina is characterized by the ordered orientation of cells forming a multilayered tissue. When this orderly arrangement of the retinal layers is disrupted, retinal dysplasia results. The term “retinal dysplasia” was first described by Reese and Blodi in 1950.[17] Retinal dysplasia may be unilateral or bilateral; the latter is often associated with congenital conditions like Trisomy 13, Norrie’s syndrome and Warburg syndrome.[18–20] An X-linked dominant inheritance has been described.[18] Retinal dysplasia is an extremely rare condition; the exact incidence cannot be ascertained as the term “retinal dysplasia” has been used in various contexts to indicate any congenital anomaly of the retina. The major histopathologic differential diagnosis to be considered while making a diagnosis of retinal dysplasia is retinoblastoma, both having in common the presence of rosettes. The rosettes of retinoblastoma are composed of anaplastic cells with poor differentiation while cells of rosettes in retinal dysplasia are more uniform and bland. Moreover, the rosettes in retinal dysplasia show a fundamental alteration in arrangement as observed on immunohistochemical study – the outer

nuclear layer is present centrally and the lumen is lined by outer limiting membrane, while the inner nuclear layer is present more peripherally.[18] In addition, the cells lining the rosettes in retinal dysplasia have been shown by immunohistochemistry to be populated by a more diverse population than the rosettes in retinoblastoma. The cells in retinoblastoma are positive for cone opsin while those of retinal dysplasia stain for rod opsin and focally for Muller cells.[18,21]

4. Conclusion

Pathological analysis of enucleated eye does provide absolute confirmation of the pathological processes inside the eye removed. It also allows for pathologists to maintain ocular diagnostic skills. In eyes with unexpected or unexplained findings on clinical examination and where examination may not be complete (opaque ocular media), the information from a pathological report may be extremely valuable. When the history, examination, or surgical findings are unclear or unaccounted for, we suggest a histological

5. Examination

We would advise efficient use of resources, considering clinical history and examination findings, when sending a specimen for histopathological examination.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Soares IP, França VP. Evisceration and enucleation. *Semin Ophthalmol*. 2010;25(3):94–7.
2. Stiebel H, Sela M, Peer J. Changing indications for enucleations in Hadassah University Hospital, 1960-1989. *Ophthalmic Epidemiol*. 1995;2(3):123–7.
3. Abdul-Salam AA, Adenipekun AA, Akinlade BJ, Elumelu TN. Pattern of Paediatric malignancies seen at the Radiotherapy department of University College Hospital. *Nig Q J Hosp Med*. 2007;17(4):152–4.
4. Freedman J, Goldberg L. Incidence of retinoblastoma in the Bantu of South Africa. *Br J Ophthalmol*. 1976;60(9):655–6.
5. Suckling RD, Fitzgerald PH, Stewart J, Wells E. The incidence and epidemiology of retinoblastoma in New Zealand: A 30-year survey. *Br J Cancer*. 1982;46(5):729–36.
6. Karcioglu ZA, Abboud EB, Al-Mesfer SA, Al-Rashed W, Pilapil DH. Retinoblastoma in older children. *J AAPOS*. 2002;6(1):26–32.
7. Park JJ, Gole GA, Finnigan S, Vandeleur K. Late presentation of unilateral sporadic retinoblastoma in a 16 year old girl. *Aust N Z J Ophthalmol*. 1999;27(5):365–8.
8. Shrestha A, Adhikari RC, Saiju R. Retinoblastoma in a 37 years old man in Nepal: a case report. *Kathmandu Univ Med J (KUMJ)*. 2010;8(30):247–50.
9. Biwas J, Mani B, Shanmugam MP, Patwardhan D, Kumar KS, Badrinath SS. Report of three cases and review of the literature. *Surv Ophthalmol*. 2000;44:409–14.
10. Dryja TP, Rapaport JM, Joyce JM, Peterson RA. Molecular detection of deletions involving band q14 of chromosome 13 in retinoblastomas. *Proc Natl Acad Sci U S A*. 1986;83(19):7391–4.
11. Cavenee WK, Dryja TP, Phillips RA. Expression of recessive allele by chromosomal mechanism in retinoblastoma. *Nature*. 1983;305(5937):779–84.
12. Abrahamson DH, Frank CM, Susman M. Presenting signs of retinoblastoma. *J Paediatr*. 1998;132:505–8.
13. Kanski JJ. Clinical Ophthalmology: a systematic approach. Butterworth Heinemann: Butterworth Heinemann, Elsevier; 2007. p. 545–8.
14. Sreelakshmi KV, Chandra A, Krishnakumar S, Natarajan V, Khetan V. Anterior Chamber Invasion in Retinoblastoma: Not an Indication for Adjuvant Chemotherapy. *Invest Ophthalmol Vis Sci*. 2017;58(11):4654–61.
15. Kashyap S, Meel R, Pushker N, Sen S, Bakhshi S, Sreenivas V, et al. Clinical predictors of high risk histopathology in retinoblastoma. *Pediatr Blood Cancer*. 2012;58(3):356–61.
16. Eagle RC. High-risk features and tumor differentiation in retinoblastoma: a retrospective histopathologic study. *Arch Pathol Lab Med*. 2009;133(8):1203–9.
17. Reese AB, Blodi FC. Retinal dysplasia. *Am J Ophthalmol*. 1950;33(1):23–32.
18. Chan A, Lakshminrusimha S, Heffner R, Gonzalez-Fernandez F. Histogenesis of retinal dysplasia in trisomy 13. *Diagn Pathol*. 2007;2:48.
19. DeGraaf P, Valk PVD, Moll AC, Imhof SM, Schouten-Van Meeteren A, Castelijns JA. Retinal dysplasia mimicking intraocular tumor: MR imaging findings with histopathologic correlation. *AJNR Am J Neuroradiol*. 2007;28(9):1731–3.
20. Lloyd IC, Colley A, Tullo AB, Bonshek R. Dominantly inherited unilateral retinal dysplasia. *Br J Ophthalmol*. 1993;77(6):378–80.
21. Gonzalez-Fernandez F, Lopes MB, Garcia-Fernandez JM, Foster RG, DeGrip WJ, Rosemberg S, et al. Expression of developmentally defined retinal phenotypes in the histogenesis of retinoblastoma. *Am J Pathol*. 1992;141(2):363–75.

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Cite this article: Barman M, Aziz N, Devi J. Histopathological findings of enucleated specimen of eye in children - A case series of 4 cases. *Indian J Pathol Oncol* 2023;10(1):64-68.