Ocular Pathology
Free Papers
AIOC in Mobile App

‘AIOS Edu’ app on your mobile from play store or visit www.aiosedu.org
OCULAR PATHOLOGY

The Correlation of International Classification of Retinoblastoma and High-Risk Retinoblastoma ------------------------------------------ 985
Dr. Swathi Kaliki, Dr. Visweswaran S, Dr. Mohd Javed Ali, Dr. Milind Naik

Retinoblastoma in Adults: A Study of 6 Cases -------------------------- 988
Dr. Adit Gupta, Dr. Swathi Kaliki, Dr. Milind Naik

Orbital Cellulitis, An Indicator of High Mortality in Retinoblastoma? - 991
Dr. Rajesh Ramanjulu, Dr. Mahesh Shanmugam P

Intravitreal Topotecan Injection in the Management of Refractory Vitreous Seeds in Retinoblastoma ----------------------------- 992
Dr. Vishalsharma, Dr. Santosh G Honavar, Dr. Fairooz PM, Dr. Vijay Anand P Reddy

Comparison of Clinical Classification Systems of RB with Histopathology of Primarily Enucleated Eyes----------------------------- 996
Dr. Ashwin Mallipatna, Dr. Payal Shah, Dr. Kushal Kacha, Dr. Sanket Bhatnagar, Dr. Ashwin Mallipatna

Clinical Profile of Eccentric Proptosis in Southern Odisha ---------- 1003
Pranati Sahu, Dr. Subudhi B N R

15-Year Prospective Outcome of Medical Management of Recurrent Ocular Surface Squamous Neoplasia----------------------------- 1005
Prof. Anita Panda. Dr. Jatinder Bali, Dr. Jatinder Bali, Dr. Seema Kashyap, Dr. Sasikala Nindra Krishna

Clinicopathologic Features and outcome of Ocular Medulloepithelioma----------------------------------------------- 1011
Dr. Bhavna Chawla, Dr. Ashutosh Kumar Singh, Dr. Seema Sen, Prof. Mandeep Singh Bajaj, Dr. Pradeep Venkatesh
The Correlation of International Classification of Retinoblastoma and High-Risk Retinoblastoma

Dr. Swathi Kaliki, Dr. Visweswaran S, Dr. Mohd Javed Ali, Dr. Milind Naik

International Classification of Retinoblastoma (ICRB) is an indispensable tool in predicting the success following chemoreduction. Shields and associates analyzed 249 eyes of retinoblastoma treated with systemic intravenous chemotherapy and concluded that treatment success was achieved in 100% group A, 93% group B, 90% group C, and 47% group D eyes. Treatment with intra-arterial chemotherapy achieves 100% globe salvage in group C and D eyes, and 33% in group E eyes.

Enucleation is the treatment of choice in advanced retinoblastoma or if there is a concern for invasion of the tumor into the optic nerve, choroid or orbit. The histopathologic diagnosis of high-risk retinoblastoma is an indication of adjuvant systemic chemotherapy to prevent the risk of metastatic disease. The assessment of prognosis and prediction of high-risk retinoblastoma before enucleation creates an environment of successful communication with the parents of a child diagnosed with retinoblastoma. In this study, we explored the reliability of ICRB and RE classification for the prediction of high-risk retinoblastoma.

MATERIALS AND METHODS

This study was a retrospective, non-randomized, non-comparative, interventional case series. Institutional review board approval was obtained. The medical records of all patients with retinoblastoma (RB) managed with enucleation at the Ocular Oncology Service at L V Prasad Eye Institute, Hyderabad, India in Philadelphia from June 1, 1999 through May 31st, 2014 were reviewed. Patients who underwent primary enucleation as treatment of retinoblastoma were included, and those who underwent secondary enucleation following failure of other treatment modalities were excluded from this study. The histopathologic features of the enucleated specimen were reviewed. High-risk histopathologic features were defined as the presence of one or more of the following features: tumor invasion into the anterior chamber, iris invasion, ciliary body invasion, massive choroid invasion >3 mm, post-laminar optic nerve involvement, or any choroidal invasion with any optic nerve involvement, scleral invasion, extrascleral extension.
The charts were reviewed for clinical and histopathologic findings. International Classification of Retinoblastoma (ICRB) was recorded in all enucleated eyes. In eyes with high-risk retinoblastoma, the detailed clinical data was recorded. The histopathologic data was recorded.

**RESULTS**

There were 403 eyes that underwent primary enucleation for retinoblastoma during the study period. Of 403 primarily enucleated eyes, 49 (12%) were classified as group D and 354 (88%) as group E based on the International Classification of Retinoblastoma. High-risk retinoblastoma was identified in 36% (145/403) of enucleated eyes including 14% (7/49) group D and 39% (138/354) group E eyes.

High-risk histopathologic features of retinoblastoma included anterior chamber involvement [0/7 (0%) group D eyes, 25/138 (18%) group E eyes], iris infiltration [0/7 (0%) group D eyes, 12/138 (9%) group E eyes], ciliary body infiltration [0/8 (0%) group D eyes, 19/138 (14%) group E eyes], isolated massive posterior uveal invasion >3mm [7/7 (100%) group D eyes, 64/138 (46%) group E eyes], isolated post-laminar optic nerve invasion [1/7 (25%) group D eyes, 73/138 (53%) group E eyes], any combination of minor posterior uveal invasion and prelaminar/laminar optic nerve involvement [0/7 (0%) group D eyes, 16/138 (12%) group E eyes], scleral invasion [0/7 (0%) group D eyes, 20/138 (14%) group E eyes], and extrascleral extension [0/7 (0%) group D eyes, 8/138 (6%) group E eyes] respectively. Of 145 patients with high-risk retinoblastoma, systemic adjuvant chemotherapy was administered in 139 (96%) patients. Systemic metastasis and death occurred in 0% (0/7) of those with high-risk group D and 4% (5/138) of those with high-risk group E retinoblastoma over mean follow-up period of 32 months (median, 36; range 1 to 67 months). There was no metastasis in any patient (n=258) classified as non-high-risk retinoblastoma.

**DISCUSSION**

Clinical features at presentation have been reported to predict high-risk retinoblastoma. In a retrospective analysis of 164 retinoblastoma patients by Chantada et al., patients presenting with glaucoma (p=0.025, specificity=97.2%, sensitivity=21%) and buphthalmos (p=0.00017, specificity=74.3%, sensitivity=58.9%) had a higher risk of high-risk retinoblastoma. In contrast, Wilson et al. found no significant association between clinical features of glaucoma and buphthalmos and high-risk retinoblastoma. The other clinical features predictive of high-risk retinoblastoma include older age at presentation (>2 years), longer lag period (>3 months), hyphema, pseudohypopyon, staphyloma and orbital...
A significant association has been found between choroidal invasion and iris neovascularization, glaucoma and optic nerve invasion, and shallow anterior chamber and iris invasion.

In a clinicopathological correlation of 67 primarily enucleated eyes by Wilson et al., high-risk retinoblastoma was present in 15% (7/47) group D and 50% (10/20) group E eyes based on ICRB. In a study of 519 primarily enucleated eyes by Kaliki et al., histopathologic evidence of high-risk retinoblastoma was evident in 17% (15/87) group D eyes and 24% (102/432) of group E eyes based on ICRB. In our study of 403 primarily enucleated eyes in Asian-Indian patients, high-risk retinoblastoma was noted in 14% (7/49) group D and 39% (138/354) group E eyes.

The prediction and diagnosis of high-risk retinoblastoma is crucial since untreated high-risk retinoblastoma carries at least a 24% risk for metastatic disease, and adjuvant systemic chemotherapy reduces the risk to 0-4%. ICRB can predict high-risk retinoblastoma. In this study, histopathologic evidence of high-risk retinoblastoma was noted in 14% group D eyes and 39% group E eyes in Asian-Indian population. This finding is useful in selection of cases for enucleation and counseling parents of retinoblastoma children regarding the probable need of adjuvant chemotherapy following enucleation.

REFERENCES


---

**Retinoblastoma in Adults: A Study of 6 Cases**

**Dr. Adit Gupta, Dr. Swathi Kaliki, Dr. Milind Naik**

Retinoblastoma is an intraocular malignancy with postulated primitive neuroendocrine origin, which usually affects children. Retinoblastoma represents about 6.1% of all the cancers in children less than 5 years of age. More than 90% of the children present within this age group. Epidemiological studies estimate the incidence of this disease to be varying from 3.4 to 42.6 cases per million live births.\(^1\)\(^2\) It may be hereditary or non-hereditary. Most of the unilateral cases are non-hereditary and sporadic. It affects males and females equally and 60% of the cases are unilateral at presentation while the remaining 40% are bilateral.\(^3\) Patients with a positive family history are diagnosed early in their life.

Sometimes this tumor may even present in adults as evident by 27 such cases, which have been reported in literature dating as early as back to 1919.\(^4\) Although, there have been many case reports published, there is no clarity as to how this tumor arises in adults. Is it the reactivation of a regressed retinoblastoma? Is it a retinocytoma undergoing malignant transformation? Or is it just de-novo appearance of the malignancy due to mutations already present in such patients? We present the single largest case series of retinoblastoma presenting in adults from a single ophthalmic tertiary care institute and their presentation characteristics.

**MATERIALS AND METHODS**

This is a retrospective case series study in which the patients with retinoblastoma presenting after age of 20 between the years 2000-2013 were included. This study was conducted at the ocular oncology clinic of a tertiary eye care institute in South India dealing with a high volume of
retinoblastoma patients. The clinical and histopathology records of all these patients were reviewed.

After recording a detailed clinical history and a proper ophthalmological examination, a detailed fundus evaluation was done with the indirect ophthalmoscope including peripheral scleral depression. All the findings were recorded with the help of standardized fundus diagrams. Ultrasonography B-scan was done in every patient to look for any evidence of calcification and possible scleral extension. CT scan was also done in all the patients to look for any extraocular extension. In patients with high-risk features or extraocular disease, a cerebrospinal fluid analysis and bone marrow biopsy was done to exclude any metastatic disease.

RESULTS

There were 6 patients with adult retinoblastoma of which 3 were males and 3 females. The mean age of the group was 26.5 years ± 5.43 (22-37). The presentation characteristics of these patients are depicted in table 1. There was no significant family history in any of the 6 patients. Two patients had extraocular disease at presentation of which one was enucleated elsewhere and was referred to us due to the recurrence of the disease after enucleation. One patient with extraocular disease underwent exenteration after chemoreduction and succumbed after one year of treatment due to meningitis.

DISCUSSION

Retinoblastoma is the commonest intraocular malignancy in children. Retinoblastoma is a neoplasm arising from the photoreceptor precursor cells. Even though it is commonly found in children cases in adults have been reported. What causes this late presentation of retinoblastoma in adults is not yet clearly known. Retinomas, retinocytomas or spontaneously regressed retinoblastomas are considered to be similar entities today. Retinocytoma is considered to be the benign counterpart of a retinoblastoma usually found in adults on routine examination. It usually remains quiescent but there is a possibility of oncogenic mutations and malignant transformations of the retinocytoma. In a study by Singh et al., the risk of malignant transformation of a retinocytoma was 4%. There are no studies to prove whether retinoblastoma in an adult arises de novo or from a retinocytoma. Another hypothesis is reactivation of previously undiagnosed spontaneously regressed tumors.

In children, retinoblastoma presents with the classical clinical features of leucocoria and strabismus in majority of patients. However, in adults the patients present with atypical manifestations such as diminution of vision,
floaters and pain. These symptoms along with the age pose a challenge in diagnosing this tumor when presenting late.

Adult onset retinoblastoma is very rare which is evident by the fact that only few case reports have been published in literature. A maximum of 3 patients has been reported from a single group till now.\(^6\) It poses a diagnostic dilemma, as the usual differentials of an amelanotic mass lesion in adults would first include an amelanotic melanoma, metastasis, leukemia and other inflammatory disorders with retinoblastoma coming way down in the list. Large lesions with vitreous seeds can be easily diagnosed but it is the smaller lesions, which pose a diagnostic challenge. Many techniques like ultrasonography, fine needle aspiration cytology aid in diagnosis but histopathological examination is usually needed to clinch the diagnosis. All the reported cases of adult-onset retinoblastoma in literature are sporadic and unilateral. Also calcification is not an important feature in an adult onset retinoblastoma except in a case report by Singh et. al.\(^7\) Most of the reported cases in literature have been managed by enucleation as the treatment modality.

In our series, out of the 6 patients, 2 presented with proptosis and extraocular disease. Both of them received primary high dose chemotherapy followed by exenteration later on. One patient died after 12 months of follow up due to meningitis. There was no evidence of any systemic metastasis at the time of his death. The other patient has completed 12 cycles of high dose chemotherapy along with external beam radiotherapy to the exenterated socket and is alive and doing well at 3 year from the time of diagnosis.

REFERENCES

Orbital Cellulitis, An Indicator of High Mortality in Retinoblastoma?

Dr. Rajesh Ramanjulu, Dr. Mahesh Shanmugam P

Retinoblastoma is the most common eye tumour in the paediatric age group with a reported incidence ranging from 1 in 15,000 to 1 in 18,000 live births. Children presenting with Group A to C do have a good prognosis as far as salvaging the eye and vision is concerned. Children with Group D have eye salvage can be achieved in as much as 70%, while in group E most of them undergo enucleation. Incidence of Mortality differs from centre to centre and is more in children with extraocular retinoblastoma for obvious reasons. As we know Rb can present with various complaints, among which leucocoria is the commonest followed strabismus. Orbital cellulitis as a initial presentation is quite rare. There is lacunae in knowledge regarding the correlation of the initial presentation and the mortality in children with retinoblastoma.

Purpose
To report the incidence of mortality in children suffering from retinoblastoma with initial presentation of orbital cellulitis.

MATERIALS AND METHODS
Retrospective analysis of 167 children (85 with unilateral tumor, 80 with bilateral and 2 with trilateral) from July 2009 to Sep. 2013 suffering from retinoblastoma was done. Grouping according to the IRC included Group A-21 eyes, Group B-26 eyes, Group C-19 eyes and Group D-76 eyes. The largest in our series was with Group E of 107 eyes. Lecocoria was the most common followed by strabismus. Initial presentation of Pseudo-orbital cellulitis was very less and found in 9 children only, the second least common presentation only after buphthalmos.

All the children were confirmed of the diagnosis after a thorough evaluation which included detailed clinical evaluation under anaesthesia and with imaging modalities (CT or MRI scans of the head and the orbit). Once the diagnosis was confirmed, the staging was done as per the IRC and the new TNM staging of Retinoblastoma. The treatment options as per the guidelines were discussed with the parents. Children with Group A and B underwent direct focal treatment. Neo-adjuvant chemotherapy was the primary treatment in Group C and D. In these children, after the initial 2 cycles the child was re-evaluated to see for the response. In cases with favourable outcome the chemotherapy was continued for 6 cycles with intermittent focal therapy at 6 weekly intervals.
Children with Group E unilateral retinoblastoma, were subjected to primary enucleation. The enucleated eye were subjected to careful histological dissection to mark out for high risk indicators for external spread as per the CAP (College of American Pathologists). If these factors were present then an additional adjuvant chemotherapy of 6 cycles was provided. If histologically residual tumor persisted then External beam radiotherapy was also given in addition to the systemic chemotherapy.

The children were longitudinally followed up. In this presentation we looked closely on the children who attained mortality. Its correlation with initial presentation and the clinical and histological classification were retrospectively analysed. 7 of the total children with initial pseudo-orbital cellulitis expired within 18 months of initial diagnosis as opposed to a total of 17 deaths in the entire series. The detailed charting showed that most of these children had a Clinical staging of cT2a to c3b and a histological staging of pT3a to cT4, both suggestive of massive choroidal involvement and optic nerve involvement without the cut section involved. These children had received additional adjuvant chemotherapy and EBRT on case to case basis.

**RESULTS**
High mortality rate in children suffering from retinoblastoma with initial presentation of orbital cellulitis.

**CONCLUSION**
Cumulative Data of multiple centres will be essential to consolidate the above evidence. Proven, children with pseudo-orbital cellulitis may require more aggressive adjuvant chemotherapy irrespective of the histological outcome.

---

**Intravitreal Topotecan Injection in the Management of Refractory Vitreous Seeds in Retinoblastoma**

**Dr. Vishalsharma, Dr. Santosh G Honavar, Dr. Fairooz PM, Dr. Vijay Anand P Reddy**

Vitreous seeding, a condition characterized by tumor cells floating within the vitreous cavity, is one of the key limiting factors in salvaging eye with retinoblastoma. Systemic combination chemotherapy has been the standard of care for patients with advanced retinoblastoma;
however, success rates in cases with vitreous seeds have been low, despite the concurrent use of radiation therapy. Other potential treatment options include brachytherapy and local chemotherapeutic delivery methods, including subtenon injection and the recently described technique of ophthalmic artery catheterisation with chemotherapy infusion. Injecting chemotherapy directly into the eye is another potential method for focal antineoplastic agent delivery however has not yet gained wide acceptance because of the apprehension of possible extraocular dissemination and pending standardization of dose and frequency of administration.

The risk of extraocular dissemination may be further reduced by the use of safety-enhancing injection techniques. In our study we have evaluated the safety and efficacy of intravitreal Topotecan injection in management of retinoblastoma with refractory vitreous seeds.

**MATERIALS AND METHODS**

Prospective non-comparative case series included 15 consecutive patients that received safety-enhanced injections of transconjunctival pars-plana intravitreal topotecan (20-30 μg in 0.1-0.15 ml) with injection site triple freeze-thaw cryotherapy. We planned 3-weekly injections until regression + an additional injection for consolidation. The ocular status was objectively monitored under anaesthesia with fundus photography.

**RESULTS**

15 eyes of 15 consecutive patients with refractory vitreous seeds received intravitreal topotecan injections. Complete vitreous seeds regression was achieved in 14 of 15 patients (93%). 5 eyes belonged to International Classification of Retinoblastoma (ICRB) group C and 10 eyes belonged to group D. Male : Female ratio observed was 2:1. Age ranged from 14 to 54 months (mean, 36). All patients had primarily received prior cycles of VCE (vincristine+etoposide+carboplatin) intravenous chemotherapy that ranged from 6 to 18 (mean, 10). The total number of intravitreal topotecan injections ranged from 2-6 (mean, 3) (Table 1). Patients who required 3 or more injections had residual retinal tumor and were treated with concurrent Trans-pupillary Thermo Therapy (TTT). 13 patients had received prior periocular carboplatin chemotherapy along with concurrent systemic combination chemotherapy while 3 patients had received intravitreal melphalan earlier in the course of management.

There was no local recurrence at 6 months and 3 months following the last injection in 8 eyes and 6 eyes respectively. One eye (7%) with a recurrent retinal tumor needed enucleation, which further on histopathological examination, was free of tumor dissemination at injection port site. In rest
of the 14 patients, no ocular or systemic complication was observed, and the
visual acuity remained stable.

**Case 1**
A 18-month-old male child with bilateral retinoblastoma, status post 6 cycles of high-dose chemotherapy; RE enucleated and LE treated for residual tumor by TTT and refractory vitreous seeds by intravitreal injections of topotecan x 6 (left) shows complete regression at 6 months following the last injection (right).

**Case 2**
A 38-month-old child with bilateral retinoblastoma, status post 12 cycles of high-dose systemic chemotherapy; RE enuclated and LE treated for residual tumor by TTT and refractory vitreous seeds by intravitreal injection topotecan X 3 (left) shows complete regression 3 months following the last injection (right).

**Case 3**
A 22-month-old male child with bilateral retinoblastoma, status-post 12 cycles of standard-dose chemotherapy; LE enucleated and RE treated with periocular carboplatin x 1. Refractory vitreous seeds were than treated with intravitreal injections of topotecan x 3 (left) shows complete regression at 6 months following the last injection (right).

**DISCUSSION**
Ericson and Rosengren\textsuperscript{14} were the first to use intravitreal injections of thiotepa as heroic treatment in six only eyes with recurrent vitreous disease
in 1960s. Seregard et al. treated three eyes using the same approach. More recently, Kivela et al. reported the use of intravitreal methotrexate in five eyes from four patients with relapse following chemoreduction, only one of the four patients having vitreous seeding. Each eye received 20–27 injections of methothrexate over a period ranging between 10 and 12 months. Francis L Munier et al. required 2–8 injections of melphalan within a 2–12 week period in their study. In our study number of injections needed was between 2-6 (mean, 3).

**CONCLUSION**

Intravitreal topotecan injection appears safe and potent and provides impressive control of refractory vitreous seeds in a carefully selected subset of patients with retinoblastoma

**REFERENCES**


Comparison of Clinical Classification Systems of RB with Histopathology of Primarily Enucleated Eyes

Dr. Ashwin Mallipatna, Dr. Payal Shah, Dr. Kushal Kacha, Dr. Sanket Bhatnagar, Dr. Ashwin Mallipatna

Retinoblastoma is the most common primary intraocular malignancy in childhood.\textsuperscript{1} Estimated incidence of retinoblastoma in India is about 2000 cases per year.\textsuperscript{2} Various systems of classification of retinoblastoma (RB) exist in literature, with little evidence of how they correlate with pathological severity of the enucleated eye.
The Reese-Ellsworth Classification scheme (Table 1), developed by Algernon Reese, MD and Robert Ellsworth, MD at Columbia Presbyterian Medical Center in the 1960s, has been for many years the most commonly used classification system for describing intraocular tumors. It was originally developed to predict prognosis in eyes that were treated with lateral photons via external beam irradiation and other vision preserving techniques. In recent years, however, its usefulness has been questioned by many ophthalmic oncologists who feel it is no longer appropriate, given the current trend away from the use of external beam radiation.3

IIRC system of classification developed by Linn Murphree et. al. predicts the outcome when treated with combination chemotherapy and laser/cryotherapy. Grouped A to E (Table 2), this system was validated through the World Retinoblastoma Survey involving 25 retinoblastoma treatment centres on six continents.4 Diagnostic features/classification and treatment outcome data was submitted to a secure online database for 1,527 children (1,919 eyes) diagnosed from 1997-2002. This survey found the IIRC to be an effective tool in predicting potential for eye salvage children with retinoblastoma.

The International Classification Of Retinoblastoma (ICRB) was later developed by Shields et. al. (Table 3), to predict the outcome of success with chemoreduction.5

The TNM system of classification was introduced by the American Joint Commission on Cancer and the Union for International Cancer Control (AJCC/UICC).6 This classification includes both clinical and pathological staging represented as cTNM and pTNM.

The standard treatment of retinoblastoma even today remains enucleation although various newer modalities like chemotherapy and focal laser therapy have evolved in recent years. Based on the histopathological findings after enucleation, pTNM classification grades the stage of the tumor.

In 2001, the pediatric cooperative group effort was strengthened by the merger of four previously separate groups, including the Childrens Cancer Group (CCG) and Pediatric Oncology Group (POG), into a single Children’s Oncology Group (COG). The COG is currently developing four different retinoblastoma protocols for treatment based on high and low risk pathology.

**MATERIALS AND METHODS**

This was a retrospective, nonrandomized, interventional case series. Approval from the review board of the institution was obtained. We studied 60 eyes of 56 patients with retinoblastoma who underwent enucleation or
had orbital metastases. These patients were examined and followed up in Narayana Nethralaya, Bangalore from 2009 to 2013 by a single experienced doctor who heads the Retinoblastoma clinic in our centre. Out of the 60 eyes, we excluded 19 eyes as they received pre-enucleation chemotherapy. This was done in order to eliminate the bias due to alteration in histopathology that might be due to receiving pre-enucleation chemotherapy. Two eyes were eliminated as they had orbital metastases at presentation, because they cannot be included in intraocular classifications. Out of the 39 eyes that underwent primary enucleation classification at presentation was determined using the IIRC system (A-E), the Shield’s classification (A-E) and TNM classification.

Post-enucleation histopathology was according to risk using the COG criteria for high-risk pathology. High-risk histopathologic features were defined as the presence of 1 or more of the following features: tumor invasion into the anterior chamber, an area of massive posterior uveal invasion ≥3 mm in diameter, post-laminar optic nerve invasion, or a combination of any non-massive posterior uveal invasion (<3 mm in diameter) with any degree of non-retrolaminar optic nerve invasion. The histopathological findings recorded included growth pattern, tumor differentiation, involvement of anterior chamber, iris, ciliary body, choroid (focal or massive), sclera and extrascleral structures. Optic nerve invasion was classified as pre-laminar, laminar, post-laminar, or to the site of transection. In the eyes with high-risk histopathological features, the number of high risk features was recorded.

Basic demographic data like age at presentation, sex, medical record number, duration of follow up, laterality and extra ocular manifestations if any were noted.

RESULTS

Analysis of data collected from patient medical records and histopathology samples was done using Microsoft Excel. Descriptive data was obtained from this.

Of the 39 eyes included in the study, according to IIRC system, 7 eyes fall into Group D while 32 eyes fall into Group E category. According to Shield’s ICRB classification, 3 eyes belong to Group D and 36 eyes belong to Group E category. cTNM classification showed 3 eyes with T2b, 4 eyes with T3a, 30 eyes with T3b and 2 eyes with T4a.

On histopathological examination using pTNM classification showed 11 eyes with pT1, 7 eyes with pT2a, 3 eyes with pT2b, 9 eyes with pT3a, 6 eyes with pT3b, 3 eyes with pT4a. 18 eyes had high risk features while 21 eyes had low risk according to COG criteria.
Table 1: Reese-Ellsworth Classification for Intraocular Retinoblastoma

<table>
<thead>
<tr>
<th>Group I</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Solitary tumor, less than 4 disc diameters in size, at or behind the equator</td>
<td></td>
</tr>
<tr>
<td>b. Multiple tumors, none over 4 disc diameters in size, all at or behind the equator</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group II</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Solitary tumor, 4 to 10 disc diameters in size, at or behind the equator</td>
<td></td>
</tr>
<tr>
<td>b. Multiple tumors, 4 to 10 disc diameters in size, behind the equator</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group III</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Any lesion anterior to the equator</td>
<td></td>
</tr>
<tr>
<td>b. Solitary tumors larger than 10 disc diameters behind the equator</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group IV</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Multiple tumors, some larger than 10 disc diameters</td>
<td></td>
</tr>
<tr>
<td>b. Any lesion extending anteriorly to the ora seratta</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group V</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Massive tumors involving over half the retina</td>
<td></td>
</tr>
<tr>
<td>b. Vitreous seeding</td>
<td></td>
</tr>
</tbody>
</table>

Prelaminar optic nerve involvement was seen in 26 eyes, 14 eyes were found with optic nerve involvement, 10 eyes with retrolaminar involvement and 3 eyes with cut end of optic nerve involved. 7 eyes showed focal choroidal involvement while 16 eyes showed massive choroidal involvement. 12 eyes showed vitreous seeds; 34 eyes showed necrosis and 23 eyes showed haemorrhage.

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>IIRC Group D</th>
<th>IIRC Group E</th>
<th>ICRB Group D</th>
<th>ICRB Group E</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>1</td>
<td>17</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>Low risk</td>
<td>6</td>
<td>15</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>32</td>
<td>3</td>
<td>36</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>cT1</th>
<th>No data</th>
<th>No data</th>
</tr>
</thead>
<tbody>
<tr>
<td>cT2a</td>
<td>No data</td>
<td>No data</td>
</tr>
<tr>
<td>cT2b</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>cT3a</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>cT3b</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>cT4a</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>cT4b</td>
<td>No data</td>
<td>No data</td>
</tr>
</tbody>
</table>
Table 2: International Intraocular Retinoblastoma Classification

<table>
<thead>
<tr>
<th>Group</th>
<th>Risk</th>
<th>Defining features</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Very low risk</td>
<td>Eyes with small discrete tumors away from critical structures. All tumors 3 mm or smaller, confined to the retina, and located at least 3 mm from the fovea and 1.5 mm from the optic nerve. No vitreous or subretinal seeding is allowed.</td>
</tr>
<tr>
<td>B</td>
<td>Low risk</td>
<td>Eyes with no vitreous or subretinal seeding and discrete retinal tumor of any size or location. Retinal tumors may be of any size or location not in Group A. No vitreous or subretinal seeding allowed. A small cuff of subretinal fluid extending no more than 5 mm from the base of the tumor is allowed.</td>
</tr>
<tr>
<td>C</td>
<td>Moderate risk</td>
<td>Eyes with only focal vitreous or subretinal seeding and discrete retinal tumors of any size and location. Any seeding must be local, fine, and limited so as to be theoretically treatable with a radioactive plaque. Retinal tumors are discrete and of any size and location. Up to one quadrant of subretinal fluid may be present.</td>
</tr>
<tr>
<td>D</td>
<td>High risk</td>
<td>Eyes with diffuse vitreous or subretinal seeding and/or massive, nondiscrete endophytic or exophytic disease. Eyes with more extensive seeding than Group C. Massive and/or diffuse intraocular disseminated disease may consist of fine or &quot;greasy&quot; vitreous seeding or avascular masses. Subretinal seeding may be plaque-like. Includes exophytic disease and more than one quadrant of retinal detachment.</td>
</tr>
<tr>
<td>E</td>
<td>Very high risk</td>
<td>Eyes that have been destroyed anatomically or functionally by the tumor with one of the following: irreversible neovascular glaucoma, massive intraocular hemorrhage, aseptic orbital cellulitis, tumor anterior to anterior vitreous face, tumor touching the lens, diffuse infiltrating retinoblastoma, phthisis or pre-phthisis.</td>
</tr>
</tbody>
</table>

**DISCUSSION**

In our study, we found that high risk histopathological features were present in 18 cases, i.e. 14% of Group D and 53% of Group E according to IIRC showed high risk features while none of the Group D and 50% of Group E according to ICRB classification showed high risk features.

Earlier studies by Kalki *et. al.* and Wilson *et. al.* compared ICRB with RE classification. Wilson and associates found high-risk histopathologic features in 15% (7/47) of group D and 50% (10/20) of group E eyes according to ICRB9. Kalki and associates found high-risk features were evident in 17%
**Table 3: International Classification of retinoblastoma (ICRB)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Quick reference</th>
<th>Specific Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Small tumor</td>
<td>Retinoblastoma ≤3 mm</td>
</tr>
<tr>
<td>B</td>
<td>Larger tumor</td>
<td>Retinoblastoma &gt;3 mm or macular retinoblastoma location (≤3 mm to foveola) juxtapapillary retinoblastoma location (≤1.5 mm to disc) additional subretinal fluid (≤3 mm from margin)</td>
</tr>
<tr>
<td></td>
<td>Macula Juxtapapillary Subretinal fluid</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Focal seeds</td>
<td>Retinoblastoma with subretinal seeds ≤3 mm from retinoblastoma vitreous seeds ≤3 mm from retinoblastoma both subretinal and vitreous seeds ≤3 mm from retinoblastoma</td>
</tr>
<tr>
<td>D</td>
<td>Diffuse seeds</td>
<td>Retinoblastoma with subretinal seeds &gt;3 mm from retinoblastoma vitreous seeds &gt;3 mm from retinoblastoma both subretinal and vitreous seeds 3 mm from retinoblastoma</td>
</tr>
<tr>
<td>E</td>
<td>Extensive retinoblastoma</td>
<td>Extensive retinoblastoma occupying &gt;50% globe or neovascular glaucoma opaque media from hemorrhage in anterior chamber, vitreous or subretinal space invasion of postlaminar optic nerve, choroid (&gt;2 mm), sclera, orbit, anterior chamber</td>
</tr>
</tbody>
</table>

(15/87) of group D eyes and 24% (102/432) of group E eyes on the basis of the ICRB.\(^{10}\)

We also compared these results with pTNM classification which revealed ¼ (25%) eyes of T3a, 15/30 (50%) eyes with T3b and 2/2 (100%) eyes with T4a showed high risk pathological features in our study.

Studies by Kalki and associates showed 17 (15%) eyes with T1, 9(8%) eyes with T2a, 20 (17%) eyes with T2b, 52 (44%) with T3a, 12 (10%) eyes with T3b, 4 (3%) eyes with T4a and 3 (3%) eyes with T4b showed high risk features.

Our study showed that various clinical systems of classification differed in their ability to predict the high risk pathological features. This results in a confusion to decide which system of classification should be followed to get the highest predictive outcome of high risk histopathological features. There is no single clinical system which can be considered as the best to correlate with the high risk pathological features.

**Limitations of our study**

- It was not a prospective study.
• The sample size was smaller in our study because of which we could not get compare enough Group D eyes with its high risk histopathology.
• We could not derive a significant difference in correlation between IIRC and ICRB with COG criteria for high risk features due to smaller sample size.
• We did not have sufficient data on pT1, pT2 and pT3a eyes to predict the high risk features in these groups and compare them with other systems of classification.
• Enucleation was done mainly on Group E eyes which might have led to selection bias in the study.

Our observations revealed that, we need a larger sample size to decide which system of classification has the best ability to predict high risk histopathological features. Further studies are required to compare high risk features in Group C and Group D eyes of both IIRC and ICRB systems. Studies with higher sample size to compare IIRC with COG criteria can reveal greater correlation with high risk histopathology than ICRB system.

CONCLUSION

From our study, we can see that high-risk pathology segregates well across the TNM classification system. Group E eyes according to the Shield’s classification had 50% with high-risk pathology, and according to the IIRC system 53% had high-risk pathology. This study shows that using different systems of classifications of RB can predict different proportions of high-risk pathology.

REFERENCES


Clinical Profile of Eccentric Proptosis in Southern Odisha

Pranati Sahu, Dr. Subudhi B N R

The fact that orbit is in close proximity with the cranial cavity, the nose and the paranasal sinuses around it making it vulnerable to many disorders that might involve the orbit by contiguity or through venous drainage.

Aim of the study to eccentric proptosis being a multidisciplinary problem the solution has become more complex. In view of the wide spectrum of the extension, the progress is not satisfactory as it should be. In most of the patients and most of the ophthalmologists it still stands as a strong obstacle. Even if a correct diagnosis is made it is not the solution. Management is not satisfactory in view of the extensive etiological background.

In view of the problem this work is aimed to study the clinical profile of eccentric proptosis in this part of the state with available scope with expectation that it will help to eradicate some of the problem.

**Type of study:** Prospective

**Period of study:** January 2013 to March 2014.

**MATERIALS AND METHODS**

All the patients presenting with eccentric proptosis were evaluated after excluding axial proptosis.

A detailed history (systemic & ocular) was taken. Detailed ocular examination was done to note the direction of proptosis (to localize the site of pathology), horizontal and vertical displacement of eye ball.

Routine blood investigations, X-Ray orbit P-A and Lateral view, USG orbit, CT, MRI (Few cases), FNAC, Excisional biopsy were done. ENT and Neurosurgical opinion taken wherever necessary.
**RESULTS**

1. Age and Sex distribution-Out of 52 cases 28 were males (53.84%) and 24 were females (46.16%). 30 cases were within 30-60 years age group (57.69%).

2. Amount of Proptosis-Out of 52 cases 37 cases show proptosis more than 6 mm (71.15%). Among these 37 neoplastic origin seen in 14 cases.

3. Visual loss-27 cases show visual acuity <6/12 at presentation (51.92%). Rest 25 cases have vision >6/12 (48.07%).


5. Etiological Distribution-14 cases (26.92%) show neoplastic origin, 10 cases (19.23%) show infectitious etiology.

6. Duration of Presentation-38 cases have (73.07%) chronic onset.

7. Clinical Presentation- All 52 cases have chief complain of proptosis. 47(90.38%) cases have proptosis with reduced vision. But 16 cases (30.76%) have diplopia.

8. Direction of Proptosis-34 cases show down and out, 15 cases show down and in, 3 cases up and out direction.

9. Management option-Medical management given to 42 cases, surgical treatment to 10 cases. 20 cases referred.

**CONCLUSION**

Majority of cases are in middle age group with out any sex prevalence. More than half of the cases have chronic onset. Neoplasms were the most common cause in adults where as trauma and infections in paediatric age group

**DISCUSSION**

In the present study peak incidence noted in 30-60 years. Rootman and Dallow reported the same. Masud et al. reported proptosis as c/c followed by defective vision in 80% cases in their study. Seregard and Sahalin reported 30% cases of neoplastic origin in their study. Bhatacherjee et al. reported 36% cases of infectitious etiology, Rootman 7%, but it is 20% in present study.

Early diagnosis with appropriate management and timely referral can result in reduction of proptosis and visual improvement.
15-Year Prospective Outcome of Medical Management of Recurrent Ocular Surface Squamous Neoplasia

Prof. Anita Panda, Dr. Jatinder Bali, Dr. Jatinder Bali, Dr. Seema Kashyap, Dr. Sasikala Nindra Krishna

The incidence of OSSN of conjunctiva and cornea has been estimated to range from 0.13/100,000 (Uganda, Templeton, 1967) to 2.2 per 100,000 persons (Tanzania, Furahini and Lewallen, 2010) in developed world the incidence of 1.9/100,000 population in the Brisbane metropolitan area, Australia (Lee and Hirst, 1992) and 0.3 million per year in United States (Sun et. al., 1997) has been reported.

Highest risk of OSSN was associated with male sex, Caucasian race and tropical stay (latitudes closer than 30° latitude to the equator). It is speculated that dysfunctional limbal stem cells altered by various mutagenic agents give rise to OSSN. The factors implicated for development of ocular surface squamous neoplasia include but are not limited to the following: exposure to ultraviolet B radiation, human papilloma virus infection, exposure to petroleum products, smoking, chemicals such as trifluridine, arsenicals, beryllium, recurrent ocular surface injury, vitamin A deficiency, defective DNA repair, HIV infection, Xeroderma Pigmentosum, family origin in the British Isles, Austria, or Switzerland and other immunocompromised states.

Objective: To report the effect of topical MMC in recurrent OSSN.

MATERIALS AND METHODS

62 recurrent OSSN eyes were prospectively evaluated with slit lamp biomicroscopy, Ultrasound Biomicroscopy (UBM), Impression cytology (IC), central corneal thickness (CCT) and Specular microscopy. Complete pictorial documentation of the lesion on the ocular surface was made. Then with Whatman’s filter paper No. 16 the excised lesion, mucosal surface facing up, was placed on the filter paper and allowed to dry adequately (approx. 2–3 min) on the filter paper to aid adhesion of the tissue on the filter paper. It was transported in 10% buffered formal saline to histopathology laboratory. Margins when not sent separately were submitted for grossing as superior/inferior/medial and/or lateral in separate filter papers submitted in separate cassettes.

Grades of dysplasia were classified according to the level and thickness of epithelial involvement: in mild dysplasia lower one third of the epithelium
showed abnormal transformation while in moderate dysplasia lower two thirds of the epithelium shows abnormal transformation. In severe dysplasia the abnormal transformation involved more than 2/3rds of the epithelial thickness with surface maturity being preserved. carcinoma in situ referred to the involvement of full thickness of epithelium with integrity of epithelial basement membrane not being disturbed.

Topical MMC 0.04-0.02% QID was employed cyclically till complete resolution. The drug was instilled four times a day for 1 week followed by one week off. The schedule was repeated up to 1 week after complete remission.

Post resolution CCT and Specular were performed at 1,3,6 and IC at 6 months. Thereafter annual clinical photography and IC were performed to look for recurrence.

**RESULTS**

62 eyes presenting with recurrent OSSN were prospectively evaluated in a tertiary care hospital in Delhi. The eyes had previously undergone single or multiple surgical excisions for different indications. The findings are enumerated in table 1 and Figure 1.

The number of clock hours involved varied from 2 to complete limbus. A tabular and pictorial representation is given in table 2 and Figure 2.

The biopsy was required in only one case for confirmation while impression cytology was positive in all cases. UBM was offered to all patients when it became available in the institute. Only 12 underwent the modality. Among these no evidence of intraocular involvement was detected in any of the patients. Intraocular pressure was not elevated in any of the patients. All these patients had been worked up for surgical intervention earlier and a rigorous ascertainment of lack of intraocular involvement was therefore already built into the evaluation.

Irritation was reported in 6 eyes (9.68%) and frank dry eye was reported from 1 eye (1.61%). One complained Flu like symptom after one week of medication which resolved gradually. Post resolution CCT and Specular were performed at 1,3,6 and IC at 6 months. The endothelium showed a normal mosaic and there was no difference in pre and post treatment endothelial cell counts or pre and post treatment central corneal thickness. Topical MMC 0.04-0.02% QID was employed cyclically till complete resolution. Thereafter annual clinical photography and IC were performed to look for recurrence. The mean duration of instilllation was 24.36 (SD=4.82) days. The total follow up ranged from 10-121 months with a mean of 72.46 (SD=2.43) months. All lesions resolved.
OSSN is uncommon and can present in many forms ranging from a sessile, fleshy, elevated lesion adjacent to limbus in interpalpebral region to diffuse, flat and poorly-demarcated lesions. Sometimes tumours infiltrating the deeper corneal stroma and covering entire ocular surface and infiltrative OSSN mimicking necrotizing scleritis can be seen. Dilated conjunctival blood vessels feeding and draining the lesion should be seen with suspicion. Rarely pigmented variants of OSSN are seen which are difficult to differentiate from conjunctival melanoma. Aggressive variants of OSSN are less common. Examples include mucoepidermoid carcinoma with a propensity for intraocular and orbital invasion and spindle cell carcinoma. It is usually non-progressive and has an interpalpebral area involvement. Intraocular invasion is rare and has devastating consequences.

The gold standard for diagnosis of OSSN is sample material after incisional or excisional biopsy examined by histopathologically. Diagnosis is based on the presence of the universal cytological criteria which include nuclear
enlargement, hyperchromasia, irregular nuclear outline, coarse nuclear chromatin, and prominent nucleoli. Impression cytology on cellulose acetate paper has a reasonably high reported predictability rate of 77% (55/71) in diagnosing moderate dysplasia to microinvasive carcinoma. Nolan et. al. reported that severe OSSN was associated with presence of keratin, inflammatory cells and fewer diagnostic cells on impression cytology. Bio pore membrane used for impression cytology correlated with histological diagnosis in 80% (20/25) [Tole et. al.]. It is easy and fast for use in routine clinical practice as compared to longer preparation and transport time in impression cytology with cellulose acetate paper. The cells differentiate less as the spectrum moves from mild to severe dysplasia. Eventually the full thickness of epithelium is made of undifferentiated/immature atypical cells. There is increase in the size of nuclei, irregularity
of nuclear membrane, hyperchromasia and shift from fine to coarse chromatin in the dysplastic cells

Management modalities in OSSN range from complete excision for well delineated tumours to chemotherapy for diffuse poorly delineated and unresectable lesions. Exenteration is reserved for cases with anterior chamber involvement or in cases with documented intraocular involvement (IOI) on UBM/CT. Complete excision with adequate margins is advocated for well delineated localized lesions. Alcohol assisted keratoepitheliectomy and lamellar sclerokeratoconjunctivectomy are used for cornea and infiltration. double-freeze cryotherapy to the resected margins and base of the lesion is management of choice. Complete resection can be confirmed by histopathological examination of conjunctival margins. Impression cytology is of importance and fornical extension must be ruled out. Negative infiltration of the resected surgical margin is the most important predictor for tumour recurrence which ranges from 5% to 33% after negative margins and upto 56% for margins with positive infiltration. The residual defect after excision is covered by different methods like amniotic membrane transplant or buccal mucous membrane graft. The extent of corneoscleral invasion in OSSN can be evaluated by UHR, OCT and ultrasound biomicroscopy. Resection of fibrous coat of eyeball or modified enucleation to resect the tumour may be required for suspected intraocular invasion by OSSN. Special attention needs to be paid to cases of uveitis associated with raised intraocular pressure. OSSN with orbital invasion can be treated with local resection and/or irradiation to eyelid sparing orbital exenteration with or without chemotherapy.

Medical management includes topical applications 5 Fluorouracil (5FU) and mitomycin C (MMC). Topical MMC 0.04% was found to be safe and effective as the first line of therapy for proved OSSN without intra ocular involvement in recurrent cases in the present study. For localised OSSN and recurrent lesions both MMC and 5FU have been used as primary and adjuvant therapy. Extensive OSSN with a mean diameter of 40 mm have shown 57% reduction in tumour base after chemoreduction with MMC. All recurrent lesions except one were associated with favorable outcomes (n=61, 98.38%) in the present study. The lone case was managed with interferon IFNa2b. Hence MMC 0.04% should be the first line of therapy for proved OSSN without intra ocular involvement. This is the largest prospective clinical study on recurrent OSSN in world literature and it highlights efficacy of MMC in recurrent and extensive lesions with satisfactory anatomic and visual restoration. However, close follow up is necessary in all cases where this modality is offered.

Modern treatment strategies have made the prognosis reasonably good
with local recurrence rates of 5% and regional lymph node metastasis below 2% in most series. However, prognosis is poorer in immunocompromised patients and aggressive variants of OSSN like spindle cell and mucoepidermoid carcinoma.  

**CONCLUSION**

This is the largest prospective clinical study on recurrent OSSN in world literature and it highlights efficacy of MMC in recurrent and extensive lesions with satisfactory anatomic and visual restoration. However, close follow up is necessary in all cases where this modality is offered.

**REFERENCES**

1011

Clinicopathologic Features and outcome of Ocular Medulloepithelioma

Dr. Bhavna Chawla, Dr. Ashutosh Kumar Singh, Dr. Seema Sen, Prof. Mandeep Singh Bajaj, Dr. Pradeep Venkatesh

Medulloepithelioma is a rare neoplasm of the brain and the eye. Ocular medulloepithelioma is a congenital tumor of the nonpigmented ciliary epithelium, usually diagnosed in the first decade of life. It is an extremely rare tumor, with an average incidence of 1 case per 4,50,000 – 10,00,000 population. Medulloepithelioma can be classified as teratoid or non-teratoid medulloepithelioma. The teratoid variant arises due to the pluripotential nature of the medullary epithelium and shows areas of hyaline cartilage, rhabdomyoblast, undifferentiated mesenchymal tissue or neuroglial tissue. The objective of this study is to describe the clinical presentation, management, histopathologic features and outcome of ocular medulloepithelioma.

MATERIALS AND METHODS

This retrospective case series included four patients of histopathologically proven ocular medulloepithelioma who were diagnosed and treated at our centre between 2010-14. Data noted included age at presentation, gender, clinical features, imaging findings, histopathological and immunohistochemical features, and the final outcome.

RESULTS

The mean age at presentation was 9.6 years (Range, 4.2-15.4 years). There were 3 males and one female. At presentation, two out of 4 cases (50%) had extraocular spread. The follow-up period ranged from 6 months to 3.5 years. At last follow-up, all cases were doing well, with no local recurrence. A detailed description of the cases is as follows:

Case 1

A 4 year old male child presented with a history of loss of vision in the left...
eye, associated with pain and redness since two months. The visual acuity in the right eye was 6/6 and in the left eye, there was no light perception. On examination of left eye, a retro-lental white fluffy mass was visible. On USG, a mass with calcification was seen in the ciliary body region of the left eye, with intra-lesional calcification. Contrast enhanced MRI of the brain and orbits showed an enhancing mass arising from the ciliary body region, without any evidence of extra-ocular spread. Ultrasound biomicroscopy (UBM) revealed a heterogenous mass with multiple cystic cavities arising from the ciliary body. FNAC was performed from the mass through a clear corneal incision. On cytopathology, a round cell tumor with multiple rosettes was identified. Enucleation surgery was done. Histopathological examination showed numerous undifferentiated neuroepithelial cells with rosettes and foci of calcification, cartilage formation and glial differentiation. IHC staining showed variable positivity for cytokeratin (CK), glial fibrillary acidic protein (GFAP), S-100, neuron-specific enolase (NSE) and synaptophysin. The diagnosis was consistent with teratoid medulloepithelioma.

Case 2
A 7 year old boy presented with a history of pain and leucocoria in the right eye since one month. Visual acuity was no perception of light in the right eye and 6/6 in the left eye. On examination of the right eye, a whitish retro-lental mass was visible through the dilated pupil. USG and CT-scan showed a mass with calcification in the ciliary body region of the right eye. MRI showed an enhancing mass arising from the ciliary body, but no extraocular spread. Cytological examination of the aspirate from the mass showed a round cell tumor with multiple rosettes. On enucleation of the right eye, histopathology showed medullary cords of undifferentiated neuroepithelial cells and rosette formation, consistent with medulloepithelioma.

Case 3
A 15 year-old boy presented with a fungating mass of the right orbit since 3 years. Five years ago, he had been diagnosed as glaucoma elsewhere and had undergone glaucoma filtering surgery. The visual acuity was absence of light perception in the right eye and 6/6 in the left eye. On examination, a fungating mass was noted protruding through the palpbbral aperture. Contrast enhanced MRI of the brain and the orbits showed an enhancing intraocular mass with extraocular spread. Incisional biopsy showed features consistent with ocular medulloepithelioma. The patient underwent exenteration of the right orbit. Histopathology and immunohistochemical studies were consistent with medulloepithelioma.

Case 4
A 12 year-old girl presented with painful proptosis of the right eye since 2 years. The visual acuity was absence of light perception in her right eye and
6/6 in the left eye. On examination, a pink fleshy mass was noted protruding through the inferior fornix in the right eye, extending into the orbit. Dilated vessels were visible on the surface of the mass. MRI showed an enhancing intraocular mass with extraocular spread. An incisional biopsy showed features suggestive of medulloepithelioma. Exenteration of the right orbit was performed. Histopathology and IHC studies were consistent with medulloepithelioma.

**DISCUSSION**

Medulloepithelioma is a rare embryonal neoplasm seen in the first decade of life. To the best of our knowledge, 11 cases have been reported in patients older than 20 years. It has no gender or racial predilection. No known risk factors have been identified for this tumor. Surgical management by enucleation is the mainstay of treatment. Eye-sparing surgery e.g., iridocyclectomy has also been described in the literature, with varying degrees of success. Our series consisted of 4 cases of this rare tumor that were managed at a tertiary referral centre in North India. The median age at diagnosis was higher (9.6 years) in our series as compared to that reported by Broughton and Zimmerman (3.8 years), Kaliki et. al. (5 years) and Shields et. al. (5 years). Interestingly, the incidence of orbital spread (50%) and teratoid features (75%) were also higher in our series as compared to published literature. The incidence of orbital spread was reported as 12% by Broughton and Zimmerman, 10% by Kaliki et. al. and in none of the cases by Shields et. al. The incidence of teratoid features was noted in 37% of cases by Broughton and Zimmerman and Kaliki et. al., and in 50% of cases by Shields et. al.

In conclusion, the management of ocular medulloepithelioma can be challenging. The clinical presentation can simulate other intraocular conditions, and a high degree of clinical suspicion is required. Imaging and cytological investigations are useful tools for accurate diagnosis. Management is by surgery and close follow up is required.

**REFERENCES**