INVENTORY ARTICLE

A 10-year review of histopathological findings of enucleated eyes from a tertiary-care center, Pakistan

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Abstract

Objective: To determine the histopathology of enucleated eye specimens.

Methods: The 10-year inventory was conducted at Aga Khan University Hospital, Karachi, and comprised all histopathology reports of enucleated eye specimens received from January 2007 to December 2016 by the Section of Histopathology, Department of Pathology. SPSS 19 was used for data analysis.

Results: A total of 232 ocular tissue specimens from 231 patients were evaluated. Ocular tumours were the most common histopathological diagnosis 186(80%). Among tumours, retinoblastoma was the most common 137(59%) followed by malignant melanoma 31(13%) and squamous cell carcinoma 15(6.5%). Overall, 16(6.9%) specimens had degenerative changes secondary to different ocular disorders. Staphyloma and Coat's disease was diagnosed in 3(1.3%) cases each. In 4(1.7%) cases, there was no formal diagnosis.

Conclusions: Early identification of tumours may allow for conservative management and limit the need for enucleations.

Keywords: Enucleations, Histopathology, Ocular tumours. (JPMA 70: 289; 2020)
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Introduction

Enucleation is a last-resort therapeutic procedure typically performed for end-stage ophthalmic conditions causing significant patient discomfort and/or in cases non-responsive to standard medical management.[1] Although the frequency with which enucleation is performed has reduced over time, it is still occasionally necessary in this day and age for the management of certain conditions such as intraocular tumours or to alleviate patient's symptoms from a painful, blind eye.[2]

The histopathological diagnosis of enucleated eyes has been studied in different settings, albeit most of it in developed countries.[3-6] There is currently insufficient data from Pakistan[7] on the histopathology of enucleated eyes and, therefore, such an analysis would help address this gap in knowledge and help provide scope for its comparison between different geographic locations. The current study was planned to review the histopathological diagnosis from a tertiary healthcare centre in Pakistan over 10 years.

Material and Methods

The 10-year inventory was conducted at Aga Khan University Hospital, Karachi, and comprised all histopathology reports of enucleated eye specimens received from January 2007 to December 2016 by the Section of Histopathology, Department of Pathology. After approval from the institutional ethics review committee, data was collected using a structured proforma which included information on patient demographics, diagnosis and immuno-profile. Diagnosis was broadly categorised as tumours, inflammatory pathology, infections and degenerative/traumatic conditions. SPSS 19 was used for data analysis. Means with standard deviation (SD) and median with interquartile range (IQR)were computed to express continuous data, while frequencies and percentages were calculated to express categorical data.

Results

A total of 232 ocular tissue specimens from 231 patients were evaluated. The specimens had been received from across Pakistan. Overall, 190(82%) specimens were from outside the AKUH. Ocular tumours were the most common histopathological diagnosis 186(80%) (Table). Among the tumours, retinoblastoma was the most common 137(59%) followed by malignant melanoma 31(13%) and squamous cell carcinoma (SCC) 15(6.5%). The mean age of children with retinoblastoma was 3.47±3.66 years. Of the 136(58.8%) retinoblastoma patients, 69(50.7%) were boys and 67(49.3%) were girls. Tumour was located in the right eye in 56(41.2%) cases and in the left eye in 58(42.6%). It was bilateral in 1(0.7%) case.

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Table: Histopathology reports of enucleated eye specimens of 231 patients.

Histopathological findings	Frequency (N)	Percent (%)
Retinoblastoma	137	59.1
Melanoma	31	13.4
Degenerative changes	16	6.9
Squamous cell carcinoma	15	6.5
Fungus	6	2.6
Phthisis bulbi	5	2.2
Choroidal haemangioma	3	1.3
Staphyloma	3	1.3
Coat's disease	3	1.3
Retrolental fibroplasia	2	0.9
Pilocytic astrocytoma	2	0.9
Melanocytic lesion - could not be further characterized	2	0.9
Medulloepithelioma	1	0.4
Embryonal rhabdomyosarcoma	1	0.4
Ependymoma	1	0.4
Unremarkable	4	1.7
Total	232	100

Laterality was not known in 21(15.4%) cases. Optic nerve was involved in 39(28.7%) cases and free-from-tumour invasion in 76(55.9%). Optic nerve status was unknown in 21(15.4%) specimens. Immunohistochemical (IHC) stain synaptophysin was positive in all the 59(43.3%) cases in which it was performed. Both synaptophysin and CD56 marker were positive in 21(15.4%) cases. Desmin, leukocyte common antigen (LCA) and CD99 were negative in all 25(18.4%), 27(19.8%) and 25(18.4%) cases, respectively.

The mean age of patients with malignant melanoma was 49.61±13.38 years. Of them, 17(54.8%) were males and 14(45.2%) were females. Tumour involved right eye in 10(32.2%) cases, and left eye in 16(51.6%). Laterality was not known in 5(16.1%) cases. Optic nerve invasion was found in 5(16.1%) melanomas. IHC stains S100, Melan A and HMB45 were positive in all 16(100%) cases, 14(87.5%) of 16 cases and 19(90.4%) of 21 cases in which they were used respectively. There were 2(0.86%) melanocytic lesions that could not be characterised further.

The mean age of SCC cases was 49.47±17.93years, and 12(80%) of them were males. Among SCC cases, 4(26.6%) were well-differentiated, 6(40%) were moderately differentiated, and 5(33.3%) were poorly differentiated. A5-year old-male patient with history of xeroderma pigmentosa also had SCC.

Overall, 3(1.3%) cases were diagnosed on pathology as choroidal haemangioma; 2(66.6%)of them were females. Individual ages of those with choroidal haemangioma were 35, 49 and 58 years. All 3(100%) had been clinically suspected of being melanomas. The haemangiomas were of cavernous subtype with no evidence of cellular proliferation.

Of the total 231 subjects, glial tumours were identified in 4(1.7%). Of them, 2(50%) had pilocytic astrocytomas; 1(50%) 41-year-old female and 1(50%) male aged 50 years. Of the remaining 2(50%), 1(50%) 3-year-old girl had medulloepithelioma, and 1(50%) 45-year-old male had ependymoma. Embryonal rhabdomyosarcoma was diagnosed in 1(0.43%) 12-year-old boy.

Also, 6(2.6%) cases had fungal infection; 4(66.6%) of them were males. Mucor and aspergillus accounted for 4(1.7%) and 2(0.86%) cases. Phthisis bulbi was the histological diagnosis in 5(2.2%) cases. Further, 16(6.9%) specimens were diagnosed to have degenerative changes secondary to different ocular disorders (trauma/ glaucoma/ perforation/ haemorrhage/ inflammation). Staphyloma and Coat's disease was the diagnosis in 3(1.3%) cases each. In 4(1.7%) cases, there was no formal diagnosis.

Discussion

To date, to the best of our knowledge, the current study presents the largest review of histopathology of enucleated eyes in Pakistan. Intraocular tumours, in particular retinoblastoma, constituted an overwhelming majority (80%) of the final histopathological diagnosis.

The relative frequency of tumour at the study site was relatively higher than previous reports citing 51-74.8%.[6,8,9] A possible explanation for the predomination of tumours over other causes might be the high percentage of referred patients with malignant ocular tumours.[9]

In continuing advancements in medical management, a preference for globe-preserving surgical techniques have combined to reduce the frequency with which enucleation is now performed.[6] Furthermore, there has also been a change in trend for indications over the past several decades. A study in 2009 analysed pathology reports of 3264 globes over six decades. It found glaucoma, which was the most commonly reported diagnosis in the 1950s and 1960s accounting for 23% and 31% cases, respectively, accounted for just 8% cases in the 2000s. Ocular malignancy on the other hand, increased from 14% in the 1950s to 51% by 2000s. A similar changing trend in enucleations due to intractable glaucoma and ocular neoplasms was also reported.[10] Although the purpose of our study was not

to analyse how clinicopathology may have changed, our findings are consistent with increased frequency of ocular neoplasms post-2000s. Significant improvements in the treatment of different ophthalmic conditions e.g., glaucoma, retinal detachment and inflammatory/infectious disorders, combined with an increasing awareness among ophthalmologists regarding ocular malignancies, may explain this changing trend.

Retinoblastoma was the most common tumour isolated in our study, followed by malignant melanoma. The proportion of enucleations secondary to retinoblastoma is increasing[6,10] but a geographical factor also seems to be at play. The ratio of retinoblastoma to malignant melanoma was 6:1 in our study. Earlier studies[11,12] reported respective ratios of 1.43: 1 in China and 9:1 in India. In comparison, France and Poland had ratios of 1:2 and 1:13, respectively.[13,14] The geographical differences in the ratio may reflect a low incidence of malignant melanoma and a relatively high incidence of retinoblastoma in population groups originating closer to the equator.[11] Additionally, in developing countries, where the majority of retinoblastoma cases are concentrated, the infant mortality rates are declining and birth rates are comparatively higher which may also explain this difference in distribution.

The high rate of enucleation for retinoblastoma and ocular tumours in general, raises the need to create awareness at the level of primary healthcare providers and the general population for early identification of the disease. Intervention at an early stage may help manage it better with conservative measures and may not necessitate globe removal. More studies would be helpful to assess knowledge of both medical practitioners and the general public regarding ocular tumours and, to address any identified gaps.

A male predominance was noted for SCC in our sample. This observation is consistent with literature. Furthermore, SCC is more frequently observed in adults, but xeroderma pigmentosa and immunodeficiency are known risk factors for an early age of onset.[15] One such case was observed in our cohort.

For cases where a clinical history was provided, correlation of clinical diagnosis to histopathology in our sample for retinoblastoma was 98% which was in line with literature.[12] For uveal melanomas, 3 cases had been misdiagnosed, resulting in a relatively lower clinicopathological correlation rate of 91%. On histopathology, these cases were identified to be choroidal haemangiomas. Choroidal haemangiomas are well-known to masquerade choroidal melanomas, often resulting in unnecessary enucleations.[16.17] However, rate of misdiagnosis for choroidal melanoma in our sample was higher compared to literature.[11,17,18]

Staphyloma has been identified as an important cause of enucleation from developing countries[12] as was the case in our study. In a retrospective analysis of 151 enucleated specimens, anterior staphyloma accounted for 25% cases.[12] However in our study staphyloma was the histological diagnosis in only 1.3% cases.

The results of the current study are consistent with declining trends of enucleation for trauma, infectious diseases and progressive, untreated ocular conditions e.g., glaucoma.[6] Significantly improved management of traumatic and inflammatory/infectious conditions through conservative and surgical means is a plausible explanation.

Conclusion

The high rate of ocular tumours on histopathological diagnosis highlights the need to raise awareness among both medical practitioners and the general public. Early identification of tumours may allow for conservative management and may limit the need for enucleation.

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Conflict of Interest: None.

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