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آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Histopathology of Ocular Tumor Specimens in Benin City, Nigeria

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Purpose: To determine the histopathological diagnosis of ocular tumor specimens and to assess their correlation with preoperative clinical diagnosis.

Methods: Surgical records of all patients who had undergone ocular surgery yielding a tissue specimen at the ophthalmology department of the University of Benin Teaching Hospital, Benin City, Nigeria, from March 1999 to February 2007 were extracted. Parameters included age, sex, preoperative clinical diagnosis, type of surgery, and histopathological diagnosis.

Results: Overall, 148 patients including 88 male (59.5%) and 60 female (40.5%) subjects were operated during the study period. The most prevalent histopathological diagnoses included squamous cell carcinoma (SCC) of the conjunctiva and eyelids (16.9%), pterygium (12.2%) and retinoblastoma (10.8%). Excisional conjunctival biopsies were performed in 30 cases to rule out SCC which was confirmed in 16 cases (53.3%). Enucleation was performed in 19 children with suspicion of intraocular malignancy of whom 16 had retinoblastoma and one had teratoid medulloblastoma; yielding a correct clinical diagnosis in 89.5% of cases. Of 24 cases of enucleation in adults, the preoperative diagnosis was confirmed by histology in 21 cases (87.5%). The preoperative diagnosis was confirmed histologically in 8 cases (53.3%) of 15 orbital specimens and 11 cases (50%) of 22 eyelid samples.

Conclusion: The most common ophthalmic malignancies were SCC of the conjunctiva and eyelids, and retinoblastoma. Clinicopathological correlation was lowest in eyelid lesions and highest in enucleation specimens.

Key words: Orbito-ocular Tumors; Squamous Cell Carcinoma; Retinoblastoma

INTRODUCTION

Histopathology remains the mainstay of diagnosis in tumoral growths. In addition to determining the malignant potential of the lesion, histology reveals its exact nature and structure. Recent studies of orbito-ocular lesions in Nigeria suggest that retinoblastoma remains the most common ocular malignancy.1-3 Squamous cell carcinoma (SCC) was the most common malignant lesion in the conjunctiva1-3 and the most common ocular malignancy in adulthood.3 In contrast, malignant melanoma which is the most prevalent intraocular tumor in many parts of the world, was reported to be rare.4,5

Previous studies from various parts of Africa have also shown that retinoblastoma is highly prevalent in African countries whereas uveal melanoma is extremely rare.4,5 Among
tumors of the eyelids and conjunctiva, SCC occurs more frequently in Africans than in Caucasians.\(^4\) Orbital infiltration by retinoblastoma, followed by Burkitt's lymphoma, is the most common orbital tumor.\(^4,6\) Inflammatory lesions, particularly pseudotumors, endophthalmitis and panophthalmitis are however common histological findings in enucleation and excisional biopsy specimens.\(^1,3\) Benign and degenerative lesions are also fairly common.\(^3\)

Indications for enucleation and evisceration have decreased during the last decade, most probably because of improved treatment modalities.\(^7\) However, the initial clinical diagnosis does not always correlate with the histological diagnosis. This study was performed to determine the histological diagnosis of ocular tissue specimens over an 8 year period in Benin City, Southern Nigeria, to compare findings with an earlier study in the same location, and to determine whether correlation exists between histopathological and clinical diagnoses.

**METHODS**

The study was conducted at the Eye Complex of the University of Benin Teaching Hospital, Benin City, Nigeria. Surgical records of all patients who had undergone any form of surgery at the Eye Department between March 1999 and February 2007 were evaluated and cases in which tissue specimens had been obtained, mostly to rule out malignancies, were included for the purpose of the study. Relevant information including age, sex, preoperative diagnosis, type of surgery and histological diagnosis were extracted. Histopathological diagnosis was based on light microscopic examination of formalin fixed, paraffin embedded sections of orbito-ocular specimens.

Data were analysed by computer using the Instat GraphPad™ version 2.05a software. An initial frequency count of all variables was performed followed by determination of mean, median, standard deviation of mean, 95% confidence intervals (CI) and standard error of the mean (SEM). The study was approved by the ethical committee of the University of Benin Teaching Hospital.

**RESULTS**

Overall, 148 patients including 88 (59.5%) male and 60 (40.5%) female subjects were enrolled. Mean age was 31.3±21.8 years (range, 2 months to 84 years) with SEM of 1.80, median age was 30 years (95% CI, 27.8-34.8). Age and sex distribution is shown in Table 1. Tissue specimens included excisional biopsies from the conjunctiva in 67 (45.3%), enucleation specimens in 44 (29.7%), orbital samples in 15 (10.1%) and eyelid specimens in 22 (14.9%) patients.

Examination of conjunctival excisional biopsies showed the most common histological finding to be pterygia (Table 2). These specimens had been obtained to rule out SCC in 30 cases; the preoperative diagnosis was confirmed in 16 cases (53.3%) including 12 cases of invasive SCC and 4 cases of conjunctival intraepithelial neoplasia. Of 16 cases with SCC, 12 patients (75%) were HIV positive. Missed diagnosis included squamous cell papilloma, chronic non-specific inflammatory lesions, conjunctival polyp and lymphoma. The preoperative diagnosis was pterygia in 18 cases and all cases were confirmed by histology. Two cases of conjunctival biopsies were performed to rule out malignant melanoma which was confirmed by histology in one case while the other was a junctional nevus.

| Table 1 Age and sex distribution of the patients |
|-----------------------------------------------|
| **Age (yr)** | **Male (%)** | **Female (%)** | **Total (%)** |
| 0-9          | 19 (12.8)    | 13 (8.9)       | 32 (21.6)   |
| 10-19        | 8 (5.4)      | 5 (3.4)        | 13 (8.8)    |
| 20-29        | 18 (12.2)    | 9 (6.1)        | 27 (18.2)   |
| 30-39        | 11 (7.4)     | 16 (10.8)      | 27 (18.2)   |
| 40-49        | 15 (10.1)    | 5 (3.4)        | 20 (13.5)   |
| 50-59        | 8 (5.4)      | 3 (2.0)        | 11 (7.4)    |
| 60-69        | 5 (3.4)      | 4 (2.7)        | 9 (6.1)     |
| ≥70          | 4 (2.7)      | 5 (3.4)        | 9 (6.1)     |
| **Total**    | 88 (59.5)    | 60 (40.5)      | 148 (100)   |

Of 44 enucleation specimens, 20 belonged to children and 24 to adults. Retinoblastoma was the most common histological diagnosis in this category. Enucleation was performed in 19 children suspected of intraocular malignancy, specifically retinoblastoma. Histological diagnoses included retinoblastoma in 16 cases; and
teratoid medulloblastoma, chorioretinitis (an 8 month old female) and chronic endophthalmitis, each in one case (Table 3). Therefore, a correct preoperative diagnosis was made in 17 of 19 cases (89.5%). In the other case of pediatric enucleation, the eye was removed due to globe rupture from severe trauma with late presentation and the histological finding was intraocular hemorrhage. Of 24 cases of enucleation in adults, the preoperative diagnosis was confirmed by histology in 21 subjects (87.5%). Malignancy was confirmed histologically in all 10 suspicious cases including 6 cases of presumed SCC and 4 cases of malignant melanoma (9.1%). In 8 cases with ruptured globes due to trauma, a diagnosis of intraocular hemorrhage was made. Other confirmed preoperative diagnoses included endophthalmitis in 2 cases and staphyloma in one case. Missed diagnoses included 2 cases of chronic non-specific inflammation and one case of traumatic neuroma.

Table 2 Histological diagnosis in conjunctival biopsies

| Histological Diagnosis          | No. (%) |
|--------------------------------|---------|
| Pterygium                      | 18 (26.9) |
| Squamous cell carcinoma        | 12 (17.9) |
| Squamous cell papilloma        | 7 (10.5)  |
| Pyogenic granuloma             | 6 (8.9)   |
| Chronic non-specific inflammation | 5 (7.5)  |
| Conjunctival intraepithelial neoplasia | 4 (6.0)  |
| Dermoid                        | 4 (6.0)   |
| Sudoriferous cyst              | 2 (3.0)   |
| Lipoma                         | 2 (3.0)   |
| Choristoma                     | 1 (1.5)   |
| Malignant melanoma             | 1 (1.5)   |
| Junctional nevus               | 1 (1.5)   |
| Lymphoma                       | 1 (1.5)   |
| Polyp                           | 1 (1.5)   |
| Conjunctival abscess           | 1 (1.5)   |
| Capillary hemangioma           | 1 (1.5)   |
| **Total**                      | **67 (100)** |

Table 3 Histological findings in enucleation specimens

| Histological Diagnosis          | No. (%) |
|--------------------------------|---------|
| Retinoblastoma                 | 16 (36.4) |
| Intraocular hemorrhage         | 9 (20.5)  |
| Squamous cell carcinoma        | 6 (13.6)  |
| Malignant melanoma             | 4 (9.1)   |
| Endophthalmitis                | 3 (6.8)   |
| Chronic nonspecific inflammation | 2 (4.5)  |
| Teratoid medulloblastoma       | 1 (2.3)   |
| Staphyloma                     | 1 (2.3)   |
| Chorioretinitis                | 1 (2.3)   |
| Traumatic neuroma              | 1 (2.3)   |
| **Total**                      | **44 (100%)** |

Table 4 Histological findings in orbital and eyelid biopsies

| Histological Diagnosis          | No. (%) |
|--------------------------------|---------|
| Chalazion                      | 4 (10.8)  |
| Squamous cell carcinoma        | 3 (8.1)   |
| Chronic granulomatous lesion   | 3 (8.1)   |
| Lipoma                         | 3 (8.1)   |
| Lymphoma                       | 3 (8.1)   |
| Epidermal inclusion cyst       | 3 (8.1)   |
| Squamous cell papilloma        | 2 (5.4)   |
| Cyst of Moll                   | 2 (5.4)   |
| Orbital pseudotumor            | 2 (5.4)   |
| Rhabdomyosarcoma               | 2 (5.4)   |
| Choristoma                     | 1 (2.7)   |
| Fibroma                        | 1 (2.7)   |
| Optic nerve meningioma         | 1 (2.7)   |
| Pigmented nevus                | 1 (2.7)   |
| Optic nerve glioma             | 1 (2.7)   |
| Meibomian gland carcinoma      | 1 (2.7)   |
| Pseudocyst                     | 1 (2.7)   |
| Fibroepithelial polyp          | 1 (2.7)   |
| Telangiectatic hemangioma      | 1 (2.7)   |
| Malignant melanoma             | 1 (2.7)   |
| **Total**                      | **37 (100)** |

Table 4 shows the histological diagnoses of tissue samples from the orbit and eyelids. Of 15 orbital specimens, the most common orbital tumor was non-Hodgkin lymphoma including Burkitt’s lymphoma. The preoperative diagnosis was confirmed histologically in 8 cases (53.3%) including lymphoma, rhabdomyosarcoma and lipoma, each in 2 cases and optic nerve glioma and optic nerve sheath meningioma, each in one. Missed diagnoses included 3 cases of chronic granulomatous inflammatory lesions, 2 cases of pseudotumor, one case of non-Hodgkin lymphoma and one case of choristoma. Of 22 eyelid specimens, the most common mass lesions were chalazia while the most common malignancy was SCC. The preoperative diagnosis was confirmed by histology in 11 cases (50%) which included SCC, malignant melanoma, meibomian gland carcinoma, telangiectatic hemangioma, epidermal inclusion cyst and cyst of Moll. Clinical suspicion of meibomian gland carcinoma in recurrent cases of chalazia was correct in only one of 5 cases.
Cumulating all conjunctival, globe, orbit and eyelid specimens, the most common histological diagnoses were SCC in 25 (16.9%), pterygia in 18 (12.2%), retinoblastoma in 16 (10.8%), intraocular hemorrhage and conjunctival papilloma, each in 9 (6.1%), chronic non-specific inflammation in 7 (4.7%), pyogenic granuloma and malignant melanoma, each in 6 (4.1%), lipoma and dermoid cyst, each in 5 (3.4%), and orbital lymphoma, chalazia, and cyst of Moll, each in 4 (2.7%) patients. Less common histological findings included endophthalmitis, epidermal inclusion cysts and chronic granulomatous lesions, each in 3 patients (2.0%); choristoma, rhabdomyosarcoma, hemangioma, polyp, pigmented nevus and orbital pseudotumor, each in 2 patients (1.4%); staphyloma, optic nerve glioma, fibroma, chorioretinitis, meningioma, meibomian gland carcinoma, medulloblastoma, conjunctival abscess, and traumatic neurora, each in one patient (0.7%). In patients under 18 years of age (Table 5), the most common histological diagnosis was retinoblastoma (39.0%) followed by dermoid cyst (12.2%), pyogenic granuloma (9.8%), cyst of Moll (7.3%), lymphoma (7.3%) and rhabdomyosarcoma (4.9%). Some histological specimens are shown in figures 1-3.
DISCUSSION

Ophthalmic neoplasms are an important cause of morbidity and mortality. In this era of HIV pandemic, an increase in the frequency of AIDS-related ophthalmic neoplasms has been reported.\(^8\)\(^-\)\(^10\) Several studies have documented that 50-75% of adult patients with AIDS will experience ocular complications.\(^8\) It is thus possible that the pattern of ocular disorders may have undergone major changes in recent years.

In this report, males outnumbered female subjects which is similar to findings in most studies carried on the pattern of ocular tumors in Nigeria showing male predominance.\(^1\)\(^,\)\(^2\)\(^,\)\(^3\)\(^,\)\(^10\) This predominance may be due to higher attendance of male patients at hospitals in Nigeria. Male children are usually considered more important than female children, therefore both parents and the community tend to care more for male children. Male subjects are also better off financially than females and therefore more likely to afford hospital services.

The most common malignancy seen in ophthalmic specimens was SCC followed by retinoblastoma. This finding is in contrast to several other studies from Nigeria where retinoblastoma was reported as the most common ophthalmic malignancy.\(^1\)\(^,\)\(^2\)\(^,\)\(^3\)\(^,\)\(^10\) All reports from Nigeria are in agreement that retinoblastoma is the most common malignant tumor in children, while SCC is the most common malignancy in adults.\(^1\)\(^,\)\(^3\)\(^,\)\(^5\)\(^,\)\(^6\)\(^,\)\(^10\)\(^,\)\(^11\) Retinoblastoma is also reported in high numbers in other African countries whereas uveal melanoma is extremely rare.\(^4\) In Northern Nigeria, retinoblastoma and Burkitt’s lymphoma account for the majority of tumors; in Southern Nigeria however, Burkitt’s lymphoma occurs more frequently whereas the incidence of retinoblastoma is almost the same.\(^6\) This may reflect a change in the pattern of ophthalmic neoplasms due to an increased incidence of HIV/AIDS. It may also be due to differences in the frequency of specimens sent for histology. In this report, conjunctival biopsies were most common whereas in other studies, enucleation specimens were far more common.\(^1\)\(^,\)\(^3\) However even in these studies, SCC was usually the second most common tumor following retinoblastoma. In another study conducted a decade earlier at our center, conjunctival biopsies were also the most common histological specimens.\(^2\) The high incidence of pterygia in this study was due to the hospital policy over a one year period that all excised tissue must be sent for histology. There was also a high index of suspicion for SCC in any conjunctival lesion which appeared atypical or suspicious, especially in patients with HIV/AIDS. These cases also accounted for the high incidence of conjunctival biopsies.

Following retinoblastoma infiltrating the orbit, Burkitt’s lymphoma was the most common orbital tumor.\(^4\) Apart from retinoblastoma, lymphoma and rhabdomyosarcoma were the only other common malignant tumors in children in this study. Optic nerve glioma and leukemia were uncommon. These findings are in agreement with previous studies in Nigeria\(^1\)\(^,\)\(^4\)\(^,\)\(^6\) however in contrast with a comparative study on the frequencies of tumors in black Americans and Nigerian children.\(^12\) Black American children living in Washington D.C. and Caucasian children living in Manchester had similar high frequencies for leukemia and glioma, whereas the incidence of lymphoma and retinoblastoma was low. African children living in Nigeria or Uganda had the opposite frequency patterns. These differences in frequencies of tumors between two ethnically related populations suggests the influence of environmental factors in the etiology of these tumors, even when exposure is of short duration.

Lymphomas, including Burkitt’s lymphoma, were common in this report and were the most common primary orbital tumor. This is similar to what has been reported from the eastern part of Nigeria\(^10\) and another study from Ibadan, in Western Nigeria;\(^11\) but in contrast to the finding in a recent report from Lagos, Western Nigeria\(^1\) reporting rhabdomyosarcoma as the most common primary orbital malignancy. These differences may be due to regional differences, proportion of adults and children in each study, or study design.

This study also confirms findings by previous studies that uveal malignant melanoma which is the most common primary intraocular malignancy in Caucasians is rare in Africans.\(^3\)\(^,\)\(^11\)
No case of Kaposi’s sarcoma was seen which is similar to findings in previous reports from Nigeria.1,2,3

None of the previous studies from Nigeria have attempted to determine a clinicopathological correlation. In this report, the correlation between clinical diagnoses and histopathological findings has shown that we are still far from 100%. For enucleation in children, clinicopathological correlation was 89.5%; in adults, it was 87.5%. This is less than the 100% correlation for cases with a clinical diagnosis of retinoblastoma and melanoma reported from India.13 Improvement in clinicopathological correlation is particularly important in enucleation, since it is disastrous to remove the eye in benign conditions which could have been managed conservatively. Indications for enucleation have decreased over the last decade, most probably due to improved treatment options. These less aggressive therapeutic modalities are not currently in common practice in Nigeria, partly because of late presentation of patients with ocular tumors.

Orbital lesions are not easily accessible and a firm clinical diagnosis requires a detailed history, meticulous clinical examination and ancillary investigations. The high expense and lack of adequate facilities for imaging techniques such as high definition ultrasonography, computerized tomography and magnetic resonance imaging may be responsible for the low clinicopathological correlation observed in orbital lesions. The clinicopathological correlation of lid tumors was only 50% which may be due to the wide variety of lid lesions and suspicion of sebaceous gland carcinoma in recurrent chalazia which was confirmed in only 20% of cases in this study.

In conclusion, the most common opthalmic malignancies in Benin City, Nigeria, are SCC and retinoblastoma. Conjunctival excisional biopsies most commonly revealed pterygia and SCC. Enucleation was most commonly due to retinoblastoma in children but due to trauma, SCC and less commonly malignant melanoma in adults. The most common lid mass was chalazion while the most common lid malignancy was SCC. Clinicopathological correlation was poorest in lid lesions and highest for enucleation specimens.

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