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PATTERN OF OPHTHALMIC LESIONS AT TWO HISTOPATHOLOGY CENTRES IN ETHIOPIA
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# PATTERN OF OPHTHALMIC LESIONS AT TWO HISTOPATHOLOGY CENTRES IN ETHIOPIA

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## ABSTRACT

***Objective:*** **To describe the distribution of ocular, orbital and eyelid lesions that required histopathologic analysis in Ethiopian children and adults.**
***Design:*** **A retrospective study.**
***Setting:*** **Tikur Anbessa and Menelik II Teaching hospitals, Addis Ababa, Ethiopia, during 1995 and 1999 period.**
***Results:*** **Two hundred and ninety ophthalmic specimens were examined, 20% of which came from children. Half of the lesions had epithelial origin, about 30% were malignant, 22.6% were benign and 16.4% were potentially malignant. Squamous cell carcinoma was the leading conjunctival (26%), eyelid (33%), orbital (33%) and ocular (20%) lesion among adults and elderly people whereas only 6% of eyelid lesion were basal cell carcinomas. In children the most frequent intra-ocular as well as orbital tumour was retinoblastoma, 39%, followed by miscellaneous benign lesions (24%). More than half of the request forms were incomplete.**
***Conclusions:*** **In Addis Ababa, squamous cell carcinoma and retinoblastoma should be considered when evaluating ophthalmic lesions in adults and children, respectively. Clinicians and pathologists should improve their communication by filling in request forms, providing clear reports and making dialogue.**

## INTRODUCTION

Ocular, orbital and eyelid tumours are frequently encountered in ophthalmic practice. These are usually benign or locally invasive, but some tumours may pose a threat to the patient's life in addition to causing severe visual impairment. Ocular or orbital metastases can be the initial manifestations of malignancies elsewhere in the body(1). Although history and physical findings provide much of the information for diagnosis, histopathological confirmation is usually required to direct a particular therapy according to the nature of the lesion. In addition to this epidemiological data on the pattern and incidence of different lesions would be very helpful.

Tumours that originate from the eye and its adnexae contribute a small share of the overall incidence of malignancies in Ethiopia where lymphoreticular, skin, hepatic, cervical, breast and ovarian cancers dominate the scene(2-6). Ophthalmic lesions accounted for 4.0% and 2.8% malignant tumours observed during a ten-year period in southern Ethiopia among males and females, respectively(2). The distribution of ocular, orbital and eyelid tumours remains unknown in Ethiopia. Only few isolated cases have been reported on different ophthalmic tumours in the past(1,7,8).

Communication between the pathologist and the ophthalmic surgeon should always be complete. This is usually made through request and report forms, although a verbal contact may be necessary in many cases. Nonetheless, the pathologist usually complains of incomplete request forms while clinicians may receive reports with vague descriptions.

The objective of this analysis was to describe the histopathologic distribution of ophthalmic lesions from Ethiopian patients; and to evaluate the degree of communication through ophthalmic biopsy request and report forms used by these centres.

## MATERIALS AND METHODS

The department of ophthalmology, in Addis Ababa University, submits most of the ophthalmic biopsy material to the main histopathology centre in the teaching department of pathology at Tikur Anbessa hospital. Since 1998, the second centre based at the Menilik II hospital, where the teaching department of ophthalmology is affiliated, also started to undertake histopathological analysis. The two centres also accept formalin-fixed biopsy materials from all over the country. Each specimen was examined for gross appearance, sliced, embedded in paraffin and stained for microscopic analysis. Haematoxylin-Eosin is the routine stain although PAS, Alican Blue and others were used when indicated. Immunohistochemical stains and electron microscopy were not available. However, suspicious slides were sent to a collaborative centre in Switzerland for immunohistochemical studies and other special stains.

A retrospective review of all biopsy request forms and pathology reports for ophthalmic specimens submitted and analysed in the two centres during a five-year period (1995-1999) was made. Those missing, confused or inconclusive and inadequate specimens were also included and so reported to indicate the efficiency of the centres. Age, sex, submitting hospital, anatomical origin, histological diagnosis and nature of the lesion were recorded in a structured format. Further analysis

was made to determine predominant eyelid lesions by anatomic origin and in different age groups. Classifications commonly used by ocular and general pathology textbooks were adopted to group lesions and to report specific diagnosis(9-12). Dysplasia of any degree, carcinoma in-situ and known pre-malignant lesions were categorised as potentially-malignant lesions(10). Orbital lesions were classified as primary or secondary, and benign or malignant(11). The percentage of tumour type was calculated from the total number of biopsy reports for the age group and from the number of specimens from the particular anatomical origin.

The pathology request forms were analysed to determine if they were complete. A total of 13 parameters were specified in request form. These included name, age, sex, hospital number, submitting hospital, duration of lesion, size, clinical appearance and consistency, local invasion, clinical impression, relevant laboratory data and the name of the doctor who sent the specimen. The form was labelled incomplete if any single variable was missing or not legible. The agreement between clinical and pathologic diagnosis was assessed. Data were processed using EPI-Info version-6 statistical software. Finally the information was presented for discussion in a clinico-pathological conference.

## RESULTS

A total of 290 ophthalmic biopsy specimens were examined at the two pathology centres. Ophthalmic specimens accounted only for 1.4 % of 21,415 biopsy materials submitted to the two centres during a five-year period. A bigger proportion of the specimens was sent from the university department of ophthalmology based at Menelik II hospital. The mean age was 31.6 years. General information including socio-demographic data are presented in Table 1.

**Table 1**

*General description of ophthalmic specimens submitted for analysis at the two pathology centers*

| Description | No. (290) | % |
|---|---|---|
| *Pathology centre* | | |
| Tikur Anbessa Hospital | 244 | 84.1 |
| Menilik II Hospital | 46 | 15.9 |
| *Submitting hospital/source* | | |
| Menilik II Hospital | 261 | 90.0 |
| Others and regional hospitals | 26 | 10.0 |
| Not specified | 3 | 1.0 |
| *Age of patients* | | |
| 0-14 [paediatric] | 59 | 20.3 |
| 15-59 [adults] | 209 | 72.1 |
| 60+ [elderly] | 20 | 6.9 |
| Unclassified | 2 | 0.7 |
| *Gender* | | |
| Male | 190 | 65.5 |
| Female | 100 | 34.5 |

**Table 2**

*Clinical and histopathological characteristics of ophthalmic lesions analysed at the two pathology centres*

| Characteristic | No. (290) | % |
|---|---|---|
| *Anatomical origin* | | |
| Conjunctiva | 176 | 60.7 |
| Eye ball/ intra-ocular | 53 | 18.3 |
| Eyelid | 35 | 12.1 |
| Orbit | 26 | 9.0 |
| *Cyto-histological origin* | | |
| Epithelial non- pigmented | 128 | 44.1 |
| Pigmented epithelial | 20 | 6.9 |
| Neuroblastic | 21 | 7.2 |
| Mesenchymal | 15 | 5.2 |
| Lymphoid | 4 | 1.4 |
| Others/normal/ inconclusive | 102 | 35.2 |
| *Nature / behaviour* | | |
| Malignant | 87 | 30.0 |
| Benign | 65 | 22.4 |
| Potentially malignant | 47 | 16.2 |
| Inflammations, infections | 38 | 13.1 |
| Degenerations | 25 | 8.6 |
| Others/ normal/ inconclusive | 28 | 9.7 |

Almost all neoplasms were primarily ophthalmic tumours. The anatomical origin, histological pattern and nature of the lesions is summarised in Table 2. Fifty four different types of pathologies were reported excluding normal biopsies and inadequate or lost specimens. The most frequent diagnosis among patients of all age were squamous cell carcinoma, 66; chronic inflammations, 25; dysplasia, 25; retinoblastoma, 21; pterygium, 19; carcinoma *in situ*, 19; and naevus, 16. There was no significant difference in the relative incidence of these lesions between the two sexes. The distribution of ocular, orbital and eyelid lesions in children and adults is presented in Tables 3 and 4.

**Table 3**

*Distribution of ophthalmic lesions from children by anatomical origin, at the two pathology centres*

| Anatomic origin | Lesion | No. (59) | % |
|---|---|---|---|
| Conjunctiva (19) | Naevus | 7 | 11.8 |
| | Miscellaneous benign lesions | 6 | 10.1 |
| | Chronic inflammations | 3 | 5.0 |
| | Others | 3 | 5.0 |
| Intra-ocular (27) | Retinoblastoma | 18 | 30.5 |
| | Other benign lesions | 3 | 5.0 |
| | Chronic inflammation | 2 | 3.4 |
| | Squamous cell carcinoma | 1 | 1.7 |
| | Others | 3 | 5.0 |
| Orbit (12) | Retinoblastoma | 5 | 8.5 |
| | Miscel. benign lesions | 3 | 5.0 |
| | Glioma | 2 | 3.4 |
| | Others | 2 | 3.4 |
| Eyelids (2) | Cyst, chronic inflammation | 2 | 3.4 |

**Table 4**

*Distribution of ophthalmic lesion in adults by anatomical origin, at the two pathology centres*

| Anatomic origin | Lesion | No. (231) | % |
|---|---|---|---|
| Conjunctiva (156) | Squamous cell carcinoma | 41 | 17.7 |
| | Carcinoma in-situ | 18 | 7.8 |
| | Dysplasia | 22 | 9.5 |
| | Pterygium pingueculae | 24 | 10.4 |
| | Naevus and melanosis | 11 | 4.7 |
| | Other benign lesions | 18 | 7.8 |
| | Chronic inflammations | 9 | 3.9 |
| | Kaposi's sarcoma | 1 | 0.4 |
| | Inconclusive or normal | 12 | 5.1 |
| Eyelids (32) | Squamous cell carcinoma | 11 | 4.7 |
| | Chronic inflammations | 5 | 2.1 |
| | Chalazion, naevi, benign lesions | 11 | 4.7 |
| | Basal cell carcinoma | 2 | 0.8 |
| | Normal | 3 | 1.3 |
| Intra-ocular (25) | Squamous cell carcinoma | 8 | 3.5 |
| | Chronic inflammation and, endophthalmitis | 7 | 3.0 |
| | Choroidal melanoma | 2 | 0.8 |
| | Other malignant lesions | 2 | 0.8 |
| | Others, missing or normal | 6 | 2.6 |
| Orbit (16) | Squamous cell carcinoma | 5 | 2.1 |
| | Benign lesions | 5 | 2.6 |
| | Sarcomas | 3 | 1.3 |
| | Non-Hodgkins lymphoma | 2 | 0.8 |
| | Inconclusive | 1 | 0.4 |

**Table 5**

*Efficiency of the centres and communication between the clinician and the pathologist in relation to ophthalmic biopsy specimens analysed at the two pathology centres*

| Description | No (290) | % |
|---|---|---|
| Request forms | | |
| Incomplete | 154 | 53.1 |
| Complete | 135 | 46.6 |
| Missing | 1 | 0.3 |
| Pathology reports | | |
| Complete and clear | 274 | 94.5 |
| Inadequate specimens | 6 | 2.1 |
| Vague, confused, record lost | 3 | 1.0 |
| Specimen lost or inconclusive | 4 | 1.4 |
| Clinical versus pathologic diagnosis | | |
| Same | 69 | 23.8 |
| Different | 78 | 26.9 |
| Not written (clinical) | 143 | 49.3 |

One or more important variables were missing, in more than half of the request forms. The most frequently forgotten variable was clinical impression (50%). The quality of request forms, the fate of the specimens and agreement between the presumed clinical impression and histological diagnosis are described in Table 5. Histological analysis was essential to rule out or change the clinical impression in many cases. The degree of agreement between pathologic and clinical diagnosis was highest for retinoblastoma (98%) making it clinically the most easily diagnosed ophthalmic tumour. One specimen from left lower lid was confusedly reported as carcinoma of the left lower leg. This happened because of inappropriate abbreviation used by the clinician on the request form to denote left lower lid with "LLL", which could also mean left lower leg.

## DISCUSSION

Most reviews about ophthalmic tumours originate from referral pathology centres or major hospitals. Such reports are therefore unavoidably biased. There is no cancer registry in Ethiopia and most of the lesions remain under-diagnosed and under-reported. This review is certainly biased concerning age, sex, geographical distribution, access to health care, nature of the clinical and histopathology evaluation facility and others, to reflect the national situation in Ethiopia. However, considering this inherent factor, one can make certain useful observations from this clinical-based review.

Childhood ophthalmological lesions and most ocular tumours in paediatric age group are benign. Not infrequently, however, certain malignant neoplasms can threaten the child's life as well as the child's sight(21). Long period of analyses showed that benign and cystic lesions are more common than malignancies and the trend of reduction in frequency of secondary and metastatic orbital tumours were perhaps due to improved care(13). The two aggressive and potentially fatal tumours in childhood, rhabdomyosarcoma and retinoblastoma, are extensively reviewed elsewhere(14). Retinoblastoma comprises 3% of all malignant tumours, with an incidence of 1 in 23,000 births in Britain(1). In this review, this fatal tumour was the leading indication for ophthalmic pathology analysis in children. Its clinical diagnosis usually matched the histological report making it the most easily diagnosed tumour perhaps due to very late presentation of cases.

In adults, squamous cell carcinoma (SCC) was found to be the most frequent conjunctival lesion. This is similar to the review of conjunctival lesions from 2,455 adults over a 61-year period(16). They reported that the most common benign lesions in decreasing order were pterygium, naevus, dysplasia, non-specific non-granulomatous inflammation and epithelial inclusion cyst. SCC was the leading malignancy followed by melanoma and sebaceous gland carcinoma. Secondary squamous cell carcinomas of the orbit almost always originate from the conjunctiva. Aggressiveness of this tumour depends on geographic location, genetic factors, immunology status, chronic irritation among other factors(17). Rarely, intra-ocular invasion may be the initial presentation(18).

This review re-confirmed that SCC of both the conjunctiva and the eyelid is more common than basal cell carcinoma in heavily pigmented individuals like Ethiopians. This is contrary to many reports from western geographic locations where SCC is 40 times less common than basal cell carcinoma (BCC)(19,20). Mamalis *et al* (21), reported that basal cell carcinoma as the most common

cancer of the eyelid and ocular adnexae followed by squamous cell carcinoma whereas malignant melanomas and sebaceous cell carcinoma were rare. SCC is reportedly the commonest skin cancer in Tanzania where, the head and neck area is the most affected next to the lower-limb(22). Many skin lesions such as senile keratosis, follicular keratosis, Bowen's disease, basal cell carcinoma adeno-acanthoma and kerato-acanthoma can be erroneously diagnosed as SCC(19). Human immuno-deficiency virus (HIV) infection is positively associated with the incidence of aggressive SCC(23). However, trend analysis of the incidence of SCC through the five years revealed no association with the HIV epidemic in the country.

The triggering factor for SCC is not clearly known. Polymerase chain reaction studies suggested that papilloma virus as the cause of SCC in HIV patients(24). SCC arises from progressive stages of mild, moderate and severe dysplasia but these lesions have a low malignant potential. A large number of potentially malignant lesions were also diagnosed. The histological hallmark of carcinoma-in-situ or conjunctival intraepithelial-neoplasia (CIN) is the presence of intact basement membrane not penetrated by cancerous cells. The term Bowen' s disease was sometimes used to report CIN of the conjunctiva in the two centres. Some authorities, however, strictly reserve the term for lesions of the skin and the eyelid and not that of mucus membranes(11,19). Although further confirmatory data are needed, CIN was recently considered as a possible marker for human immunodeficiency virus infection(24). Surgical excision with wide margins is the preferred method of treatment for squamous cell carcinoma due to the lethal nature of the tumour. Advanced cases may require exenteration(25).

Degenerations such as pterygium and pinguccullae were frequently observed which are expected in a tropical country. Pigmented lesions, particularly naevi, were common. Conjunctival pigmented lesions exhibit a wide range of malignant potential, but those with no junctional activity rarely, if ever, become malignant(11). Conjunctival deposition was rare. Despite the general fact that secondary tumours are more common than primary malignancies, no metastatic carcinoma was diagnosed in our series.

Conjunctiva and eyelid tumours may mimic benign conditions. Early diagnosis needs high index of suspicion and biopsy of the lesion is often necessary to confirm or rule out certain malignancies. Histological analysis made in the two centers was useful to rule out or change the clinical impression in more than half of the cases. On the other hand, the use of conjunctival biopsy and exfoliative cytology as a diagnostic procedure is low in these centres. The conjunctiva provides a relatively accessible site for diagnostic biopsy for systemic conditions like sarcoidosis(11). Impression cell cytology can be used for the diagnoses of vitamin A deficiency and viral conjunctivitis(25,26). Other diseases of ophthalmic importance which may require temporal artery biopsy is giant cell arteritis, a single case was reported from these centres(27).

The impact of the degree of communication between the ophthalmologist and the pathologist on patient care cannot be directly assessed from request and report forms. The patients' clinical outcome was not followed for each case. However, the review has shown that there are some drawbacks, which can indirectly hamper the quality of patient care. It is quite worrisome to learn that most of the request forms were incompletely filled. Ophthalmic surgeons seemed reluctant in making the pathologist know their clinical impression, which was a very important guide to rule out or reach a specific pathological diagnosis. The use of abbreviations and words, not known by both parties, resulted in confusion and misinterpretaion. The surgeon, who usually looks for the final diagnosis, might not understand pathology report terms such as "consistent", "suggestive of" among others.

In conclusion, malignant and potentially malignant neoplasms of epithelial origin, from the conjunctiva, were the major indications for ophthalmic biopsy analysis among adults at the two centers. SCC of the conjunctiva, eyelid and the orbit, is by far the leading ophthalmic cancer among Ethiopian adults whereas retinoblastoma and benign lesions of the conjunctiva predominate in children. These two fatal malignant neoplasms should be considered when evaluating lesions of the conjunctiva, eyelid or advanced intraocular and orbital tumours. As facilities are limited at the centres, socio-demographic and clinical data on the request forms are very important for making correct histological diagnosis. Clinicians and pathologists should improve their communication by making complete request forms and clear reports. A verbal communication between the two parties would clear ambiguities and maintain efficient diagnostic service and quality patient care.

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