

Clinical and histopathological analysis of conjunctival tumors

Osman Melih Ceylan (*), Yusuf Uysal (*), Fazıl Cüneyt Erdurman (*), Kenan Gültekin (**), Ali Hakan Durukan (*), Serkan Köksal (***), Fatih Mehmet Mutlu (*), Gökhan Özge (*)

SUMMARY

The aim of our study was to analyze the clinicopathologic features of conjunctival tumors followed at a tertiary care hospital in Turkey. One hundred and sixty four patients with surgically excised conjunctival tumors followed between March 1995 and March 2010 were retrospectively reviewed. Clinical data were collected from medical records. Age and gender of patients, and clinical and histopathologic findings of lesions were identified. Of all the patients 139 (84.75%) were male and 25 (15.24%) were female. The mean age of the patients was 26.4 years (range 4 to 65 years). Of the 164 conjunctival lesions, 115 (70.12%) were nevus, 12 (7.31%) were chronic inflammation, 9 (5.48%) were pyogenic granuloma, 6 (3.65%) were limbal dermoid, 5 (3.04%) were racial melanosis, 4 (2.43%) were benign lymphoid hyperplasia, 3 (1.82%) were hemangioma, 2 (1.21%) were primary acquired melanosis, 2 (1.21%) were inflammatory polyp, 2 (1.21%) were squamous cell carcinoma, 1 (0.6%) was malignant melanoma, 1 (0.6%) was squamous papilloma, 1 (0.6%) was keratoacanthoma and 1 (0.6%) was non-Hodgkin lymphoma. In our study, we found that the most common conjunctival benign tumor was nevus. Although squamous cell carcinoma is a rare conjunctival malignant tumor, it may be encountered in young age population.

Key words: *Conjunctiva, eye, tumor*

ÖZET

Konjonktival tümörlerin klinik ve histopatolojik analizi

Bu çalışmanın amacı Türkiye’de üçüncü basamak bir sağlık merkezinde takip edilen konjonktival tümörlerin klinik ve histopatolojik özelliklerinin değerlendirilmesiydi. Mart 1995 ile Mart 2010 arasında konjonktiva tümörü cerrahi rezeksiyonu uygulanan 164 hasta retrospektif olarak değerlendirildi. Klinik veriler hasta dosyalarından toplanarak elde edildi. Hastaların yaş ve cinsiyetleri ile lezyonun klinik ve histopatolojik özellikleri belirlendi. Çalışmadaki hastalardan 139’u (%84.75) erkek, 25’i (%15.24) kadın idi. Hastaların ortalama yaşı 26.4 (aralık, 4-65) yıl idi. Yüz altmış dört konjonktival lezyondan 115’i (%70.12) nevüs, 12’si (%7.31) kronik inflamasyon, 9’u (%5.48) piyojenik granülom, 6’sı (%3.65) limbal dermoid, 5’i (%3.04) ırksal melanozis, 4’ü (%2.43) benign lenfoid hiperplazi, 3’ü (%1.82) hemanjiyom, 2’si (%1.21) primer kazanılmış melanozis, 2’si (%1.21) inflamatuvar polip, 2’si (%1.21) skuamöz hücreli karsinom, 1’i (%0.6) malign melanom, 1’i (%0.6) hastada skuamöz papillom, 1’i (%0.6) keratoakantoma ve 1’i (%0.6) non-Hodgkin lenfoma olarak belirlendi. Çalışmamızda konjonktivanın en sık gözlenen iyi huylu tümörü nevüs olarak saptanmıştır. Yassı hücreli karsinoma nadir görülen kötü huylu konjonktiva tümörü olmakla birlikte, genç yaş grubunda da karşılaşılabılır.

Anahtar kelimeler: *Konjonktiva, göz, tümör*

* Department of Ophthalmology, Gulhane Military Medical Faculty

** General Practitioner, Private Doctor

***Elazığ Military Hospital

This study was presented as a poster presentation in the 15th Balkan Military Medicine Meeting (Athens, May 30-June 3, 2010)

Reprint request: Dr. Osman Melih Ceylan, Department of Ophthalmology, Gulhane Military Medical Faculty, Etik-06018, Ankara

E-mail: drmelihceylan@hotmail.com

Date submitted: July 02, 2010 • **Date accepted:** September 14, 2010

Introduction

The conjunctival neoplasms are clinically and histopathologically similar to the tumors which arise from other mucous membranes in the body, and these tumors may originate from both epithelial and stromal structures. The broad spectrum of conjunctival tumors ranges from non-neoplastic benign tumors to aggressive malignancies, such as melanoma or Kaposi’s sarcoma which may threat visual function and life of the patient (1-5). These tumors are mainly classified into melanocytic and non-melanocytic tumors based on clinical evidence of intrinsic pigment and histopathologic findings (3). The aim of this study was to analyze the clinicopathologic features of conjunctival tumors followed at a tertiary care hospital in Turkey.

Material and Methods

This retrospective study included 164 eyes of 164 patients with conjunctival tumors who were operated between March 1995 and March 2010. Medical records of patients including age, gender, clinical (visual acuity, slit lamp biomicroscopy, fundus evaluation, applanation tonometry) and histopathologic findings were reviewed retrospectively. Ethical guidelines of the Declaration of Helsinki were followed throughout, and the study was approved by the Ethics Committee of Gulhane Military Medicine Academy Review Board. The clinical diagnosis of conjunctival tumor was based on the patients’ history and biomicroscopic features of the lesion. The most common indication for tumor resection was suspected growth of the tumor according to the patients’ history. The therapeutic options included periodic observation with digital photographs (Nikon D-100, Japan), surgical excision and administration of antitumor agent. For the confirmation of diagnosis, sections from each biopsy specimen were stained with hematoxylin and eosin stain (1,4).

Results

Of the 164 patients who had conjunctival tumor resection, 139 (84.75%) patients were male and 25 (15.24%) patients were female. The mean age of the 164 patients was 26.4 years (range 4 to 65 years). In our series, the most common histopathologic diagnosis of 164 excised lesions was nevus in 70.12% (n=115), followed by chronic inflammation in 7.31% (n=12), pyogenic granuloma in 5.48% (n=9), limbal dermoid in 3.65% (n=6), racial melanosis in 3.04% (n=5) (Figure 1), benign lymphoid hyperplasia in 2.43% (n=4), hemangioma in 1.82% (n=3), primary acquired melanosis (PAM) in 1.21% (n=2), inflammatory polyp in 1.21% (n=2), squamous cell carcinoma (SCC) in 1.21% (n=2), malignant melanoma in 0.6% (n=1) (Figure 2), squamous papilloma in 0.6% (n=1), keratoacanthoma in 0.6% (n=1) and non-Hodgkin lymphoma (NHL) in 0.6% (n=1), respectively (Table I). The most common indication for tumor resection was suspected growth of the tumor. In all cases, the tumor was excised surgically, 2 (1.21%) SCC and 1



Figure 1. Racial melanosis



Figure 2. Malignant melanoma

Table I. Histopathological classification of conjunctival tumors

Conjunctival tumors (n=164)	n	%
Nevus	115	70.12
Chronic inflammation	12	7.31
Pyogenic granuloma	9	5.48
Limbal dermoid	6	3.65
Racial melanosis	5	3.04
Lymphoid hyperplasia	4	2.43
Hemangioma	3	1.82
Primary acquired melanosis	2	1.21
Inflammatory polyp	2	1.21
Squamous cell carcinoma	2	1.21
Malignant melanoma	1	0.6
Squamous papilloma	1	0.6
Keratoacanthoma	1	0.6
Non-Hodgkin lymphoma	1	0.6

(0.6%) malignant melanoma were treated with topical mitomycin C after tumor resection. None of the malignant lesions had systemic metastasis and local recurrence.

Discussion

Tumors of the conjunctiva have a large spectrum which range from benign lesions to aggressive life and vision threatening malignancies. Conjunctiva is a readily visible mucous membrane and it is easy to evaluate clinical features of lesions by slit lamp biomicroscopy (2). Management of conjunctival tumors depend on the size and extent of the lesion, which consist of observation, biopsy, cryotherapy, chemotherapy, radiotherapy, enucleation, orbital exenteration and author's personal experience. Chi and Baek reported that most common conjunctival tumors were melanocytic nevi in 54.2%, and 29.2% of these tumors was compound nevus (1). Amoli and Heidari reported that the most common benign primary conjunctival tumor was nevus 38.7% (mean age of the patients 22.27) and the most common malignant tumor (25.1%) was SCC (mean age of the patients 58.63) in their series (2). In the present study, the most common tumor was conjunctival nevus in 115 (70.12%) of the patients and the compound nevus was the most common type (Figure 3). Conjunctival SCC is generally seen in elderly male patients. It occurs with increased frequency in patients with long time exposure to sunlight and xeroderma pigmentosum (2). Studies of large populations in Congo, Uganda, and United States have shown that AIDS is an increased risk factor for the development of conjunctival SCC (6-8). In our study, SCCs were 1.21% (mean age of patients 21) of all conjunctival tumors, and none of



Figure 3. Conjunctival melanocytic lesion including cyst covering corneal surface. Histopathologic diagnosis was compound nevus

the patients were affected by HIV or had a history of long time sunlight exposure and xeroderma pigmentosum. Conjunctival defects more than 4 clock hours due to excision of large SCCs have been used to repair with tissue replacement techniques (9,10). The disadvantages of conjunctival tissue replacement techniques such as symblepharon, pseudopterygium, tissue foreshortening and recurrence of tumor have encouraged clinicians to investigate alternative or adjuvant treatment options such as topical mitomycin C, 5-fluorouracil and interferon alpha-2B (11-15). In our study, SCC was treated with topical mitomycin C in 2 (1.21%) cases and mean age of the patients was younger than that of the previously reported cases in the literature. It is important to recognize the precursor lesions of malignant melanoma including PAM with atypia and an enlarging or atypical nevus (16). In our study, malignant melanoma was arised in the area of PAM with atypia. Racial melanosis, which is especially bilateral in more heavily pigmented races is a benign proliferation of melanocytes, but rarely is unilateral, acquired and can be a precursor of melanoma (16,17).

Ocular adnexal lymphoid tumors may commonly be seen in the sixth to seventh decade with slightly female preponderance (18). Non-Hodgkin lymphoma may involve the eyelids, conjunctiva, orbital connective tissue or lacrimal gland (18). The present study showed 1 (0.6%) male patient presented with conjunctival metastasis of previous NHL which is a rare route of systemic spread. Conjunctival lymphomas often appear to masquerade as conjunctivitis and a number of misdiagnoses have been reported (19). Other conjunctival tumors that have malignant potential in our study group were 2 (1.21 %) PAM, 1 (0.6%) squamous cell papilloma, 1 (0.6%) keratoacanthoma. One

form of conjunctival papilloma is squamous cell papilloma which is caused by infection with HPV (type 6, 11, 16, 33), and papilloma represents 7-10% of conjunctival tumors in childhood and young ages (20,21). Squamous cell papilloma has a low risk of malignant transformation and can be treated either by surgical excision or cryotherapy, but the recurrence rate is unfortunately high (20,22). Conjunctival keratoacanthoma preferentially occurs in the limbic region and can be mistaken as SCC which has very similar clinical and histopathological findings (23). PAM presents as a unilateral patchy area of conjunctival pigmentation, mostly found in middle-aged or elderly white patients. The presence or absence of atypia is helpful in determining the potential for malignancy, because PAM without atypia is usually benign (24). In our series, 2 (1.21%) PAM, 1 (0.6%) squamous papilloma and 1 (0.6%) keratoacanthoma that have suspected to be malignant potential were surgically excised and no presence of atypia was seen except for 1 case with PAM in histopathologic evaluation.

In conclusion, the present study demonstrated that nevus was the most common benign conjunctival tumor and malignant tumors of conjunctiva may show variable features. Conjunctival SCC is a rare malignant tumor and also can be seen in young patients. Malignant lymphoid tumors of the conjunctiva should be considered in the differential diagnosis of conjunctivitis especially in elderly adults and must be kept in mind as a rare presentation of systemic metastasis of NHL. Conjunctival melanoma is a potentially lethal neoplasm, and early recognition of precursor lesions have markedly reduced the late diagnosis.

References

1. Chi MJ, Baek SH. Clinical analysis of benign eyelid and conjunctival tumors. *Ophthalmologica* 2006; 220: 43-51.
2. Amoli FA, Heidari AB. Survey of 447 patients with conjunctival neoplastic lesions in Farabi Eye Hospital, Tehran, Iran. *Ophthalmic Epidemiol* 2006; 13: 275-279.
3. Shields CL, Demirci H, Karatza E, Shields JA. Clinical survey of 1643 melanocytic and nonmelanocytic conjunctival tumors. *Ophthalmology* 2004; 111: 1747-1754.
4. Shields CL, Fasiuddin AF, Mashayekhi A, Shields JA. Conjunctival nevi: clinical features and natural course in 410 consecutive patients. *Arch Ophthalmol* 2004; 122: 167-175.
5. Shields CL, Shields JA. Tumors of the conjunctiva and cornea. *Surv Ophthalmol* 2004; 49: 3-24.
6. Ateenyi-Agaba C, Weiderpass E, Smet A, et al. Epidermodysplasia verruciformis human papillomavirus types and carcinoma of the conjunctiva: A pilot study. *Br J Cancer* 2004; 90: 1777-1779.

7. Kaimbo Wa Kaimbo D, Parys-Van Ginderdeuren R, Missotten L. Conjunctival squamous cell carcinoma and intraepithelial neoplasia in AIDS patients in Congo Kinshasa. *Bull Soc Belge Ophtalmol* 1998; 268: 135-141.
8. Yoon YD, Grossniklaus H. Tumors of the cornea and conjunctiva. *Curr Opin Ophthalmol* 1997; 8: 55-58.
9. Tseng SC, Prabhasawat P, Lee SH. Amniotic membrane transplantation for conjunctival surface reconstruction. *Am J Ophthalmol* 1997; 124: 765-774.
10. Shields CL, Shields JA, Armstrong T. Management of conjunctival and corneal melanoma with surgical excision, amniotic membrane allograft, and topical chemotherapy. *Am J Ophthalmol* 2001; 132: 576-578.
11. Shields CL, Naseripour M, Shields JA. Topical mitomycin C for extensive, recurrent conjunctival-corneal squamous cell carcinoma. *Am J Ophthalmol* 2002; 133: 601-606.
12. Zaki AA, Farid SF. Management of intraepithelial and invasive neoplasia of the cornea and conjunctiva: a long-term follow up. *Cornea* 2009; 28: 986-988.
13. Poothullil AM, Colby KA. Topical medical therapies for ocular surface tumors. *Semin Ophthalmol* 2006; 21: 161-169.
14. Herold TR, Hintschich C. Interferon alpha for the treatment of melanocytic conjunctival lesions. *Graefes Arch Clin Exp Ophthalmol* 2010; 248: 111-115.
15. Lee GA, Hirst LW. Ocular surface squamous neoplasia. *Surv Ophthalmol* 1995; 39: 429-450.
16. Brownstein S. Malignant melanoma of the conjunctiva. *Cancer Control* 2004; 11: 310-316.
17. Folberg R, Jakobiec FA, Bernardino VB, Iwamoto T. Benign conjunctival melanocytic lesions. Clinicopathologic features. *Ophthalmology* 1989; 96: 436-461.
18. Das D, Deka P, Bhattacharjee K, et al. Ocular adnexal lymphoma in the Northeast Indian population. *Indian J Ophthalmol* 2008; 56: 153-155.
19. Akpek EK, Polcharoen W, Ferry JA, Foster CS. Conjunctival lymphoma masquerading as chronic conjunctivitis. *Ophthalmology* 1999; 106: 757-760.
20. Okan G, Ayan İ, Karşlıoğlu Ş, Altıok E, Yenmiş G, Vural G. Conjunctival papilloma caused by human papillomavirus type 11 treated with systemic interferon in a five-year-old boy. *Turk J Pediatr* 2010; 52: 97-100.
21. Sjö NC, Heegaard S, Prause JU, von Buchwald C, Lindeberg H. Human papillomavirus in conjunctival papilloma. *Br J Ophthalmol* 2001; 85: 785-787.
22. de Keizer RJ, de Wolff-Rouendaal D. Topical alpha interferon in recurrent conjunctival papilloma. *Acta Ophthalmol Scand* 2003; 81: 193-196.
23. Perdigão FB, Pierre-Filho Pde T, Natalino RJ, Caldato R, Torigoe M, Cintra ML. Conjunctival keratoacanthoma. *Rev Hosp Clin Fac Med Sao Paulo* 2004; 59: 135-137.
24. Lin SM, Ferrucci S. Primary acquired melanosis of the conjunctiva. *Optometry* 2006; 77: 223-228.