Sebaceous carcinoma - An overlooked tumour in Black Africans

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Abstract

Background*: Sebaceous carcinoma is an uncommon malignant adnexal tumour with female preponderance and peak age presentation in the seventh decade of life. It is overlooked in the plethora of cutaneous tumours in general because of its rarity and diagnosis is often missed or delayed, thus increasing disease morbidity.*

Materials and Method*: Formalin fixed, paraffin processed tissue biopsies stained with haematoxylin & eosin, oil red O and immunohistochemical antibodies for EMA, S100, CD15 and Ki67 were studied over a 14year period in a Pathology laboratory.*

Results*: Six males and one female were diagnosed during the period. They had mean age of 44.7years and a range of 25years to 65years. Patients' symptoms included orbital mass and ulceration, conjunctiva mass, visual loss, ulcerated axillary mass and contact bleeding. Two patients gave history of recurrent conjunctiva growths. Clinical diagnoses included melanoma, lymphoma, basal and squamous cell carcinomas. Histology sections from all seven patients showed varying sized irregular lobular formations of undifferentiated and distinct sebaceous cells exhibiting considerable nuclear and nucleolar pleomorphism with pagetoid spread of malignant cells in the eyelid and conjunctiva epithelium. Immunoreactivity for Epithelial membrane antigen (EMA) was demonstrated in all the cases.*

Conclusion*: Middle aged males were predominantly affected. The extraocular type involved the axilla mainly as fungating masses and over seventy percent of the cases were ocular with associated extensive destruction of ocular structures and visual loss. None of the clinical diagnosis considered sebaceous carcinoma.*

Keywords: Sebaceous carcinoma, Middle aged male, Extra-ocular, Axilla, Site

Introduction

Sebaceous carcinoma is an uncommon aggressive malignant adnexal tumour. It has two subtypes of ocular and extraocular based on the anatomical site of tumour involvement and there is no morphological difference between both types. [1-5] The ocular arises from meibomian glands and glands of Zeiss, while the extraocular often involve the head and neck, genitals and the lower extremity.[3,4,6-12] It is twice common in females compared with males and it is also a disease of the elderly with a mean age of 62years at presentation.[7,13-18]

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Malignant adnexal tumours in general are rare accounting for 0.1% to 0.9% of cutaneous neoplasms and ocular sebaceous carcinoma in particular accounts for 0.5-5.5% of all eyelid malignant tumours.[8,14, 19-22] Ocular sebaceous carcinoma is rare in Caucasians with an incidence of approximately 0.5 per million people while it is common in Asians and rates as high as 28% have been recorded in this group.[8, 20, 23-25] The incidence rate for the extraocular subtype is not known due to its sporadic occurrence in different geographic settings, though its aggressiveness is comparable to its ocular counterpart.[3] There is also no literature documentation of the frequency of occurrence of either type in African Blacks.

The clinical diagnosis of sebaceous carcinoma is often missed or delayed because of non specificity of clinical presentation and mimicry of both benign ocular lesions and malignant cutaneous tumours. This is a documentation of sebaceous carcinoma presentation in a Black African population.

Materials and Method

All diagnosed cases of sebaceous carcinoma over a 14year period from 2000 to 2013 in the Department of Pathology of a Teaching Hospital were retrieved from departmental case records and analyzed. Patients' histology stained slides made from formalin fixed paraffin embedded tissue biopsies were viewed. New slides were also made from archival tissue blocks due to faded stains from initial haematoxylin and eosin stained slides. Immunohistochemical antibody staining was done for epithelial membrane antigen (EMA), S100 protein, CD15 and Ki-67 on fresh sections from tissue blocks of all the cases. Information on patients' bio-data, symptoms duration, and site of affectation, clinical examination findings and diagnosis were accessed from accompanying case cards.

Results

Six males and one female diagnosed with sebaceous carcinoma were studied. During the period, sixty-seven adnexal tumours were

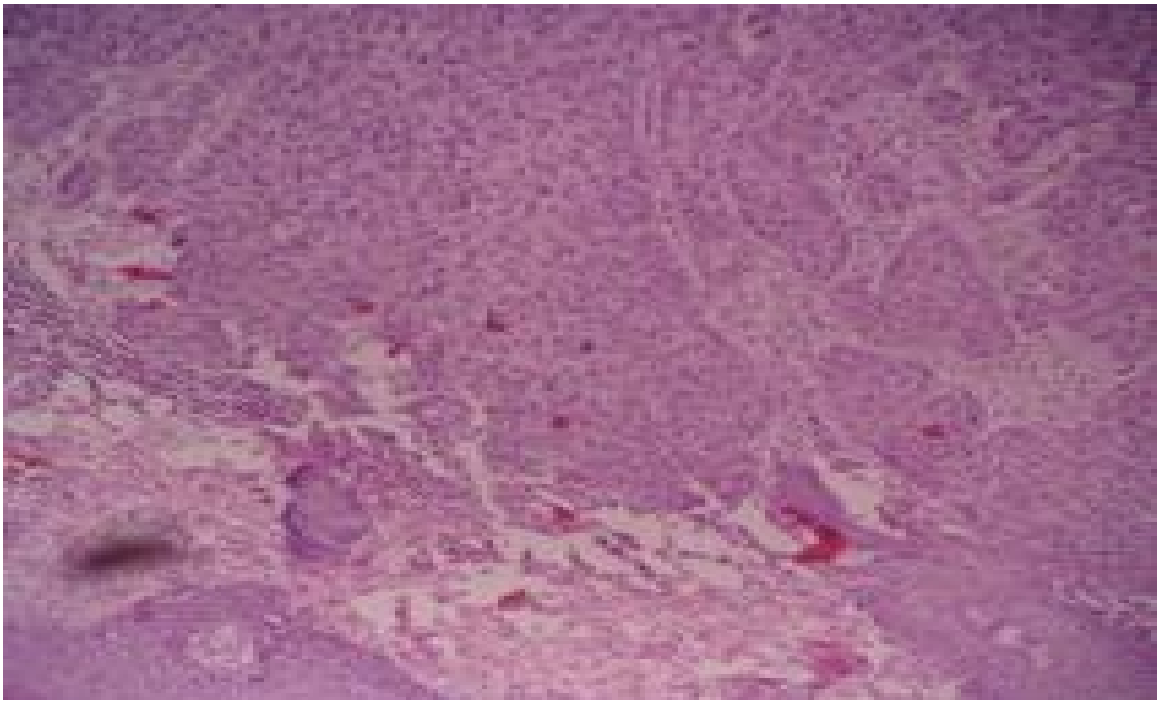

Fig 1 - Lobules of malignant sebaceous glands- H& E, mag x10

Table 1: Clinical details of all seven cases of sebaceous carcinoma

Serial No	Sex	Age(yrs)	Clinical Presentation	Duration	Clinical Diagnosis
1.	Male	55	Right painful axillary mass with fungating ulcer involving the entire axilla.	7years	Sarcoma
2.	Male	43	Right orbital mass with visual loss and destruction of ocular structures.	<1year	MelanomaR/O Lymphoma
3.	Female	50	Bulging left eye mass with history of redness and loss of vision.	6months	Orbital sarcoma
4.	Male	35	Fungating orbital tumour with no identifiable ocular structures. Associated contact bleeding	<1year	Massive orbital tumour ? cause
5.	Male	65	Fungating axillary mass with contact bleeding.	4months	Malignant ulcer
6.	Male	40	Left orbital mass which started as swelling on white part of eye. Lesion was excised twice and rapidly increased in size with associated visual loss and pre-auricular swelling.	10years	Basal cell carcinoma
7.	Male	25	Right conjunctival growth associated with pain and reduced vision. Had surgical excision thrice.	8years	Squamous cell carcinoma

diagnosed in the department and 20 of these were malignant. The remaining thirteen (13) malignant tumours were of eccrine and apocrine sweat gland origin. Also, 6,128 cutaneous lesions were biopsied and sent to our laboratory during the same period. The age range of our seven patients was 25years to 65years and mean age was 44.7years. Two patients had ulcerated axillary masses of 5months and 7years duration each.

The lesions started as painful nodules which progressively increased in size and was associated with contact bleeding. Five patients had ocular affectation and of these, two presented with orbital swelling, fungating orbital mass, destruction of ocular structures and visual loss in affected eye. The only female patient aged 50years presented with 6months history of redness, bulging left eye and visual loss while the last two patients aged 25years and 40years had past histories of recurrent conjunctiva growths which were previously excised. However, the excised growths were not sent for histolopathological diagnosis.

The current lesion in both patients rapidly enlarged and was associated with visual loss and pre-auricular swellings. **(Table 1)** Clinical diagnoses based on individual patient assessment included malignant ulcer, axillary sarcoma, melanoma, lymphoma, basal cell carcinoma and squamous cell carcinoma. Haematoxylin & eosin stained tissue histology sections from all seven patients showed varying sized irregular lobular formations consisting of undifferentiated cells, distinct sebaceous cells with foamy cytoplasm and considerable

nuclear and nucleolar pleomorphism. **(Figures 1 &2)** Pagetoid spread of malignant cells was also seen in the conjunctiva epithelium and eyelid. Only one case was a poorly differentiated tumour. Intracellular vacuolation was demonstrated with oil red O stain. All the

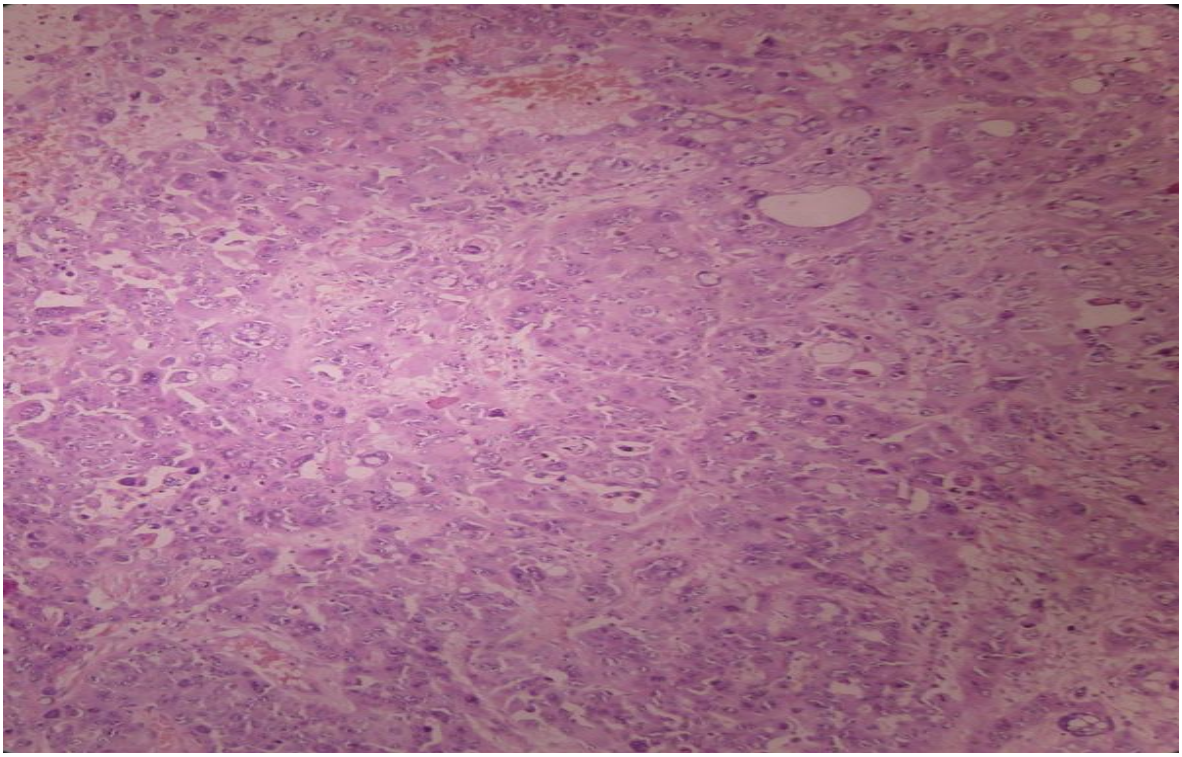

Fig. 2: Lobules of malignant sebaceous glands- H& E, mag x40

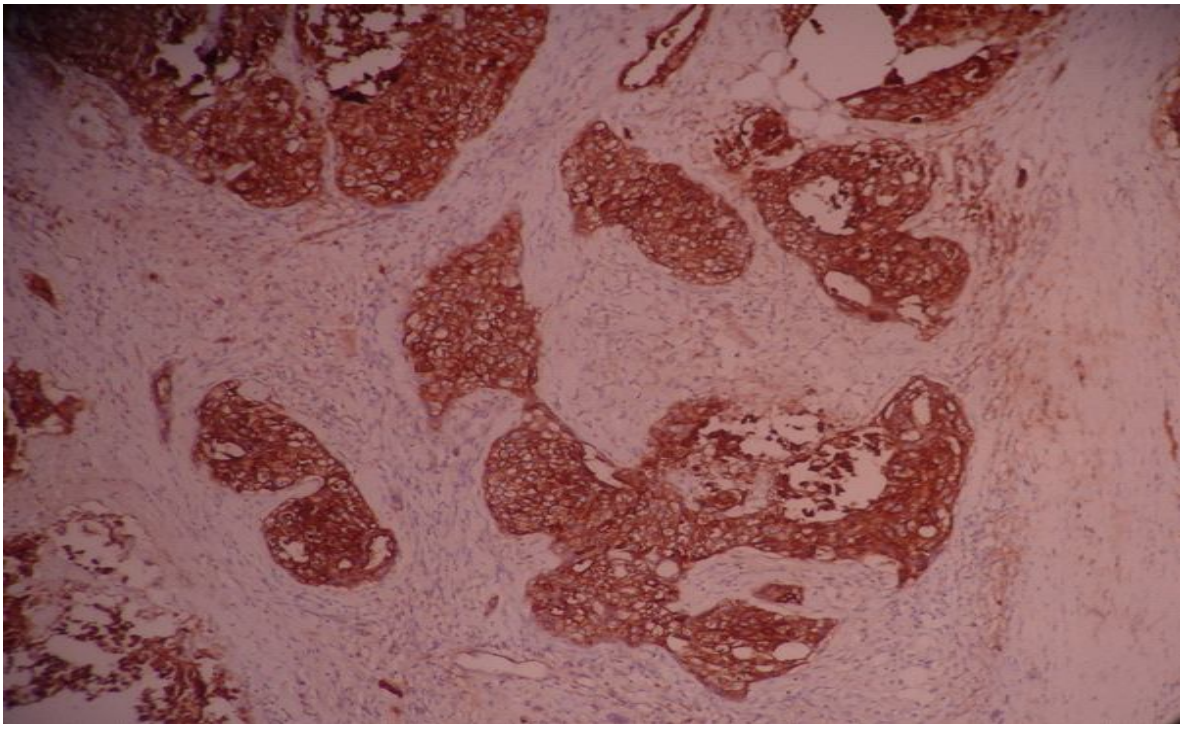

Fig. 3: Epithelial membrane antigen positive staining. Mag x 10

seven cases showed strong immunoreactivity for epithelial membrane antigen (EMA). (**Fig.3**)

43years old Black man with extra-ocular axillary sebaceous carcinoma.[5]

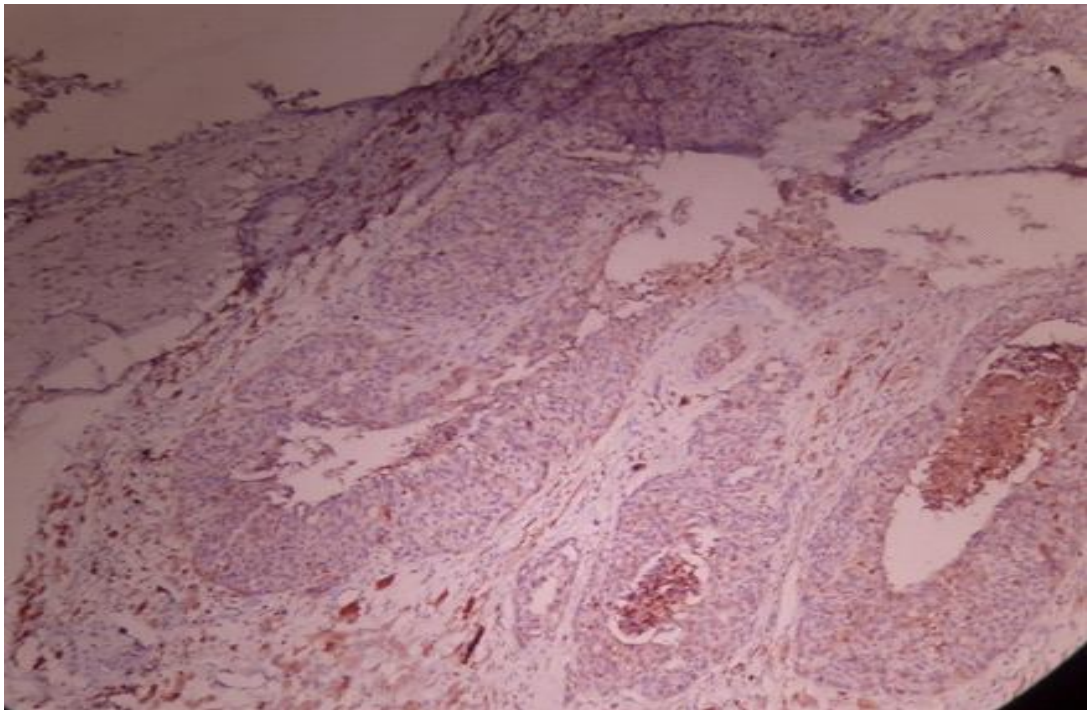

Fig 4.: S100 non reactive staining. Mag x 10

There was no reaction with CD15 and S100 protein (**Fig 4**) while mitosis was demonstrated by Ki-67. No lymph nodes were biopsied.

Discussion

The seven sebaceous carcinoma cases analyzed accounted for 0.1% of all cutaneous lesions diagnosed during the study period while the adnexal tumours accounted for1.1%. These frequency rates are comparable to earlier reported frequency rates for sebaceous carcinoma and adnexal tumours.[14, 24, 26]

Several reports [3, 13-18] have documented that elderly females in the sixth to seventh decades of life are more predisposed to developing sebaceous carcinoma. Six of our seven cases were males and the mean age in our series was 44.7years. The only female in this series was 50years old and only one patient was above sixty years of age. It would appear that sebaceous carcinoma occurs a decade earlier in African Blacks. Moreno *et al* also reported a

Ocular sebaceous carcinoma accounted for 71% of our cases. It is the commonly encountered subtype and represents over 70% of all reported cases and also accounted for 28% of 85 malignant eyelid tumours in one series.[27, 28] Lesions usually involve the eyelid primarily before spreading to other ocular structures and the upper lid is more commonly involved.[29-31]

Clinical presentation could be as flat lesions that spread horizontally in a pagetoid pattern along the eyelids and conjunctiva epithelium or as nodules with multiple foci. All the patients in this series presented with advanced disease, varying degree of ocular structures destruction and visual loss. Conjunctiva involvement rather than eyelid was seen in two patients. Similar conjunctiva affectation with sparing of the eyelids was also documented in a recent report.[32] Other likely clinical presentations include redness of the eye and loss of eyelashes hence the frequent misdiagnosis with benign eye lesions such as chalazion,

blepharoconjunctivitis and cicatricial pemphigoid.[33-36] Recurrent eye lesions as seen in two of our cases should raise the suspicion for a diagnosis of sebaceous carcinoma and further emphasizes the need for excised tissues to be sent for histopathological assessment.

The extra-ocular subtype commonly occurs in the skin of the genitals particularly the vulva and penis, the head, neck and extremities.[6, 8, 10] Other rare sites are the breast, salivary glands and lungs.[30, 37, 38] Clinical presentation at these sites is often as a nodule which frequently ulcerates.[39] Both extra-ocular cases in this series involved the axilla and started as nodules that progressively enlarged and became ulcerated. The myriad of clinical diagnosis also confirms the notoriety of sebaceous carcinoma's mimicry of cutaneous tumours such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and melanoma. Late hospital presentation and advanced disease stage is the typical patient presentation in our setting thus, increasing disease morbidity from the attendant regional and visceral tissue destruction. This also increases the potential for misdiagnosis with the more common cutaneous cancers.

Tissue biopsy is mandatory for accurate diagnosis and histology varies from well to poor tumour differentiation. Immunohistochemical antibody staining aids confirmatory diagnosis especially in poorly differentiated tumours with little recognizable sebaceous issue and also differentiates from other cutaneous tumours. All our cases were immunoreactive to epithelial membrane antigen (EMA). Some sebaceous carcinoma cases have been demonstrated to show variable reactivity to CD 15 however, this was not demonstrable in our cases. Other useful immunohistochemical antibodies are S100 which is usually positive in SCC and negative in sebaceous carcinoma as seen in our cases while both EMA and S100 are negative in BCC.[40, 41]

The treatment of choice is surgical excision with wide excision free margins while adjuvant radiotherapy and chemotherapy have a role in aggressive infiltrative and metastatic disease.[42, 43]

Conclusion

In conclusion, middle aged males were predominantly affected in our setting. The extra-ocular type involved the axilla mainly as fungating masses and over seventy percent were the ocular type with extensive destruction of ocular structures and visual loss. Clinicians and even pathologists should have a high index of suspicion for sebaceous carcinoma in patients presenting with axillary and ocular masses associated with recurrence. This will reduce rate of missed and delayed diagnosis as well as the attendant disease morbidity of late patients' presentation and advanced disease stage.

References

1. Graham RH, McKee PH, McGibbon DH. Sebaceous carcinoma. Clin Exp Dermatol 1984; 9: 466-471.
2. Prioleau PG, Sanya Cruz DJ. Sebaceous carcinoma. J Cutan Pathol. 1984; 11: 396-414.
3. Melette JR. Jr, Amonette RA, Gardner JH, Chesney TM. Carcinoma of sebaceous glands of the head and neck: a report of 4 cases. J Dermatol Surg Oncol. 1981; 7:404-407.
4. Scuderi S, Giaccone M, D'Errico E, Maorenzic MA, Fontanellaa M, Castellano I, et al. Aggressive sebaceous carcinoma of the head. Chir Ital. 2009; 61:401-404.
5. Moreno C, Jacyk WK, Judd MJ, Requena L. Highly aggressive extraocular sebaceous carcinoma. Am J Dermatopathol 2001; 23: 450- 455.
6. Escalonilla P, Grilli R, Cañamero M, Soriano ML, Fariña MC, Manzarbeitia F, et al. Sebaceous carcinoma of the vulva. Am J Dermatopathol. 1999; 21:468-472.
7. Rao NA, Hidayat AA, McLean IW, Zimmerman LE. Sebaceous carcinomas of the ocular adnexa: A clinicopathologic study of 104 cases, with five-year follow-up data. Hum Pathol. 1982; 13:113-122.

8. Kane HD, Squire MA, Kallet HA. Sebaceous carcinoma of the foot. Case presentation and discussion. J Am Podiatry Assoc. 1984; 74:120-124.
9. Yamazawa K, Ishikura H, Matsui H, Seki K, Sekiya S. Sebaceous carcinoma of the uterine cervix: a case report. Int J Gynecol Pathol. 2003; 22:92-94.
10. Wick MR, Goellner JR, Wolfe JT,III, Su WP. Adnexal carcinomas of the skin. II Extraocular sebaceous carcinomas. Cancer. 1985; 56:1163–1172.
11. Ausidio RA, Lodeville O, Quaglivolo V, Clemente C. Sebaceous carcinoma arising from the eyelid and from extra-ocular sites. Tumori.1987; 73:531–535.
12. Akhtar S, Oza KK, Roulier RG. Multiple sebaceous adenomas and extraocular sebaceous carcinoma in a patient with multiple sclerosis: case report and review of literature. J Cutan Med Surg. 2001; 5:490-495.
13. McCulley JP, Shine WE. The meibomian glands and tear films lipids: structure, function and control. Adv Exp Med Biol. 2002; 506: 373-378.
14. Kass LG, Hornblass A. Sebaceous carcinoma of the ocular adnexa. Surv Ophthalmol. 1989; 33:477-490.
15. Dores GM, Curtis RE, Toro JR, Devesa SS, Fraumeni JF. Incidence of cutaneous sebaceous carcinoma and risk of associated neoplasms: insight into Muir-Torre syndrome. Cancer. 2008;113:3372-3381
16. Howrey RP, Lipham WJ, Schultz WH, Buckley EG, Dutton JJ, Klintworth GK, et al. Sebaceous gland carcinoma: a subtle second malignancy following radiation therapy in patients with bilateral retinoblastoma. Cancer. 1998; 83: 767-771.
17. Jensen ML. Extraocular sebaceous carcinoma of the skin with visceral metastases: case report. J Cutan Pathol. 1990; 17: 117-121.
18. Bhavarajua VM, Shamim SE, Naik VR, Shaari S. Sebaceous cell carcinoma of scalp. A rare presentation. Malays J Med Sci. 2007; 14:67-70.
19. Samaila MOA. Malignant Appendage Tumours in Zaria. Sudan J Dermatol 2007; 5:11-14.
20. Margo CE, Mulla ZD. Malignant tumors of the eyelid: a population-based study of non-basal cell and nonsquamous cell malignant neoplasms. Arch Ophthalmol. 1998; 116: 195-198.
21. Nelsen BR, Hamlet KR, Gillard M. sebaceous carcinoma. J Am Acad Dermatol. 1995; 33: 1-15
22. Ghosh SK, Bandyopadhyay D, Gupta S, Chatterjee G, Ghosh A. Rapidly growing extraocular sebaceous carcinoma occurring during pregnancy: A case report. Dermatol Online J. 2008;14:8.
23. Upender K Wali, Abdullah Al-Mujaini. Sebaceous gland carcinoma of the eyelid. 2010; 3: 117-121.
24. Ni C, Kou PK. Meibomian gland carcinoma: A clinico-pathological study of 156 cases with long-period follow up of 100 cases. Jpn J Ophthalmol 1979; 23:388- 401.
25. Khalil MK, Lorenzetti HD. Sebaceous gland carcinoma of the lid. Can J Ophthalmol 1980;15:117-21.
26. Samaila MO. Adnexal skin tumors in Zaria. Ann Afr Med 2008;7:6-10.
27. Abdi U, Tyagi N, Maheshwari V. Tumours of eyelid: a clinicopathologic study. J Indian Med assoc. 1996; 94: 405-409
28. Cieza-Díaz DE, Cano-Martínez N, Barchino-Ortiz L, Longo-Imedio I. Extraocular sebaceous carcinoma: a report of 2 cases. Actas Dermosifiliogr. 2012;103: 919-922.
29. Manonukul J, Kajornvuthidej S. Sebaceous neoplasms in Siriraj Hospital, Mahidol University: a 9-year-retrospective study. J Med Assoc Thai. 2010; 93:978-91.

30. Borczuk AC, Sha KK, Hisler SE, Mann JM, Hajdu SI. Sebaceous carcinoma of the lung: histologic and immunohistochemical characterization of an unusual pulmonary neoplasm: report of a case and review of the literature. Am J Surg Pathol. 2002; 26:795-798.
31. Dinakar D, Babu R, Shivaswamy S. A case of giant advanced sebaceous gland carcinoma. Indian J Surg Oncol. 2013; 4:366-367. doi: 10.1007/s13193-013-0254-7.
32. Pandey K, Singh P, Singh A, Pandey H. Primary sebaceous gland carcinoma of the bulbar conjunctiva without involvement of eyelid: A clinical dilemma. Oman J Ophthalmol 2011; 4
33. Dogru M, Matsuo H, Inoue M, Okubo K, Yamamoto M. Management of eye lid sebaceous carcinomas. Ophthalmologica 1997; 211:40-43.
34. Gloor P, Ansari I, Sinard J. Sebaceous carcinoma presenting as a unilateral papillary conjunctivitis. Am J Ophthalmol. 1999; 127: 458-459.
35. Wolfe JT, III, Yeatts RP, Wick MR, Campbell RJ, Waller RR. Sebaceous carcinoma of the eyelid. Errors in clinical and pathologic diagnosis. Am J Surg Pathol. 1984; 8: 597-606.
36. Granström G, Aldenborg F, Jeppsson PH. Sebaceous carcinoma of the parotid gland: report of a case and review of the literature. J Oral Maxillofac Surg. 1987;45:731-3.
37. Takata T, Ogawa I, Nikai H. Sebaceous carcinoma of the parotid gland. An immunohistochemical and ultrastructural study. Virchows Arch A Pathol Anat Histopathol. 1989; 414:459-464.
38. Ahmed Alzaraa, Imran Ghafoor, Andrew Yates and Alhad Dhebri. Sebaceous carcinoma of the skin of the breast: a case report. Journal of Medical Case Reports 2008, 2:276 doi:10.1186/1752-1947-2-276.
39. Urban FH, Winkelmann RK. Sebaceous malignancy. Arch Dermatol 1961; 84:63.
40. Sinard JH. Immunohistochemical distinction of ocular sebaceous carcinoma from basal cell and squamous cell carcinoma. Arch Ophthalmol 1999;117:776-783.
41. Rutten A, Wick MR, Sangueza OP, Wallace C. Tumours with sebaceous differentiation. In: LeBoit PE, Burg G, Weedon D, Sarasin A (eds). World health Organization's Classification of Tumours. Pathology & Genetics. IARC Press, Lyon (France). 2011, pp160-162.
42. Poonam Joshi, Amit Joshi, Vanita Norohna, Kumar Prabhash, Subhdha Kane, Anil K. D'cruz. Sebaceous carcinoma and systemic chemotherapy. Indian J Med Paediatr Oncol. 2012 ; 33: 239–241. doi: 10.4103/0971-5851.107105.
43. Murthy R, Honavar SG, Burman S, Vemuganti G, Naik MN, Reddy VA. Neoadjuvant chemotherapy in the management of sebaceous gland carcinoma of the eyelid with regional lymph node metastasis. Ophthal Plast Reconstr Surg. 2005; 21:307–9.Department of Head & Neck Surgery, Tata Memorial Hospital, Mumbai, Maharashtra, India