International Journal of Research in Medical Sciences
Vijayan P et al. Int J Res Med Sci. 2015 Aug;3(8):1889-1894
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20150297

Research Article

Spectrum of malignant skin adnexal tumors – a single institution study of 17 cases with clinicopathological correlation

Poornima Vijayan[1]*, Ramadas Nayak[2], Laila M. Ilias[1], Anupama Ponniah[1]

[1]Department of Pathology, MES Medical College, Malappuram district, Kerala, India
[2]Department of Pathology, Yenapoya Medical College, Mangalore, Karnataka, India

Received: 27 May 2015
Accepted: 05 July 2015

***Correspondence:**
Dr. Poornima Vijayan,
E-mail: poornima_vij@yahoo.co.in

ABSTRACT

Background: Skin adnexal tumors are a rare, assorted group of tumors with differentiation towards hair follicle, sebaceous glands or sweat glands. A vast majority of them are benign. But for every benign adnexal tumor, a malignant counterpart exists. Many histological subtypes of these malignant tumors been described, but only in short series or individual case reports. So, not much is known about their incidence or prognosis simply because of the limited number of cases available for analysis. This study was undertaken to contribute towards this less traversed area of dermatopathology.
Methods: In the present study, a total of 60 cases with a histopathological diagnosis of skin adnexal tumors were studied. The slides and blocks were retrieved from the archives and were reviewed and were reclassified and subtyped as per WHO classification of skin tumors, 2006.
Results: Among the 60 cases of adnexal tumors documented and reviewed over the four year study period, 17 cases of malignant adnexal tumors were encountered. Of these, 10 (58%) were tumors with eccrine or apocrine differentiation, 5 (29%) were of follicular differentiation and two (12%) were of sebaceous differentiation. Mammary paget disease (MPD) was the most frequent malignant tumor encountered both overall and among the tumors with eccrine and apocrine differentiation. Other tumors encountered in their order of frequency were Malignant proliferating trichelemmal tumor, apocrine carcinoma, sebaceous carcinoma and extramammary paget disease, trichelemmal carcinoma and eccrine carcinoma. These tumors were evaluated with regard to their age, site, gender distribution, clinical characters and histopathological features.
Conclusion: Malignant adnexal tumors are extremely rare with indistinct clinical characteristics. They are locally aggressive, and have the potential for nodal involvement and distant metastasis, with a poor clinical outcome. A high index of suspicion is necessary to establish a diagnosis in most cases.

Keywords: Malignant adnexal skin tumors, Eccrine, Apocrine, Sebaceous, Trichelemmal

INTRODUCTION

Adnexal skin tumors aptly termed "troublesome tumors" by Cotton D,[1] pose a major diagnostic difficulty to both the surgeon and the pathologist. The bewildering array of differentiation they display and the ever-expanding list of entities add further to the confusion.[2] Tumors of the pilosebaceous apparatus can occur as single-lineage neoplasms or may manifest as complex proliferations with multilineal differentiation patterns. Eccrine and apocrine neoplasms present a bewildering array of morphologies, which often defy precise classification.[3]

A large majority of skin adnexal tumors are benign and for most part complete excision is curative. A malignant counterpart of almost every Skin adnexal tumors has been

described. These tumors are rare, locally aggressive, and have the potential for nodal involvement and distant metastasis, with a poor clinical outcome. Therefore, establishing a diagnosis of malignancy in skin adnexal tumors is important for therapeutic and prognostic purposes.[4]

Many studies have been published on benign adnexal tumors but studies on their malignant counterpart remain far and few. Though, it is true that many short series and case reports of individual and composite malignant adnexal tumors have been reported in the western literature, however, the fact remains that for many adnexal carcinomas there are simple insufficient numbers reported to develop much of an idea simply regarding their prognosis.[2] This study was undertaken so as to make an attempt to make a contribution to this less traversed area of dermatopathology.

METHODS

The present study was conducted retrospectively over a period of five years, 2007 – 2012 in the Department of Pathology at a tertiary centre in Karnataka, South India. During this five year period, all excision biopsy specimens which had a diagnosis of skin adnexal origin was included in this study. This included both benign and malignant adnexal tumors of the skin. A total of 60 cases were retrieved and studied. The clinical details were obtained from the hospital records and the requisition form that was received in the department of pathology. The slides and blocks were retrieved from the archives and multiple serial sections were taken for each biopsy and stained with routine haematoxylin and eosin stain. The slides were reviewed and were reclassified and subtyped as per WHO classification of skin tumors, 2006.[2]

RESULTS

The present study is a comprehensive analysis of collective adnexal tumors of skin wherein 60 cases with histopathological diagnosis of skin adnexal tumors were studied retrospectively during a 5 year period. All cases were reviewed and 17 cases of malignant adnexal skin tumors were documented. These tumors have been classified according to WHO classification[2] and analyzed with regard to their age, sex, site, clinical presentation as well as their various histomorphologic patterns. Table 1 depicts the various malignant adnexal tumors encountered in our study and their distribution according to their differentiation.

Table 1: Malignant adnexal tumors.

Tumors	Males	Females	Total
Tumors with follicular differentiation			
Trichelemmal Carcinoma	1	1	2
Malignant profilerating trichelemmal tumor	1	2	3
Tumors with sebaceous differentiation			
Sebaceous Carcinoma	-	2	2
Tumors with eccrine and apocrine differentiation			
Eccrine carcinoma	1		1
Mammary paget disease	-	4	4
Apocrine carcinoma		3	3
Extramammary paget Disease	1	1	2
Total	**4**	**13**	**17**

During the five year study period, a total of 60 cases of skin adnexal tumors were reviewed, out of which 43 (71%) were benign and 17 (29%) were malignant. Out of the 17 malignant cases, tumors with eccrine and apocrine differentiation constituted 58% (10), 5 (29%) were of follicular differentiation and two (12%) were of sebaceous differentiation.

Pagets disease of the breast was the most common malignant adnexal tumor constituting 4 cases, followed by 3 cases of apocrine carcinoma and malignant proliferating trichelemmal tumor. Two cases each of trichelemmal carcinoma, sebaceous carcinoma and extramammary pagets disease were encountered and one case of eccrine carcinoma was also noted in our study.

In most cases of malignant adnexal tumors in our study, the age of incidence was the 6th and 7th decades, except one case of eccrine carcinoma in a 45 year old male. A definite female preponderance was noted in our study.

Clinically, seven cases were correctly diagnosed as malignant adnexal tumor. Two malignant proliferating trichelemmal tumors were diagnosed as squamous cell carcinomas. Patients presented with recurrence in 2 cases of malignant proliferating trichelemmal tumor and one case of sebaceous carcinoma. All three cases of Apocrine carcinoma presented as axillary nodules. Tumor size was >5 cm in 8 tumors. Ulceration was noted in 2 cases of MPTT and one case of sebaceous carcinoma. All cases of Mammary Paget disease and extramammary pagets disease presented as eczematous and erythematous lesions. All 4 cases of MPD was associated with underlying invasive ductal carcinoma breast and one was associated with an in-situ component also. Neither cases of EMPD was associated with an internal malignancy. All tumors in our study were solitary lesions. Two cases of recurrent MPTT (Figure 1) and one case of recurrent trichelemmal carcinoma were treated with radical neck dissection (Figure 2 & 3) and lymphnode metastasis was noted in two cases (Figure 4 & 5). The salient clinical and histopathological features of the malignant tumors encountered in our study are enumerated in Tables 2 & 3.

Table 2: Salient clinical features of malignant adnexal skin tumors.

Clinical features	Number of cases	Percentage
Number of lesions		
Solitary	17	100%
Multiple	-	-
Size of lesion		
<2cm	4	23%
2-5cm	5	29%
>5cm	8	47%
Other features		
Tenderness	8	47%
Erythema/Eczema	6	35%
Ulceration	5	29%
Loss of circumscription	8	47%
Recurrence	3	17%
Asymmetry	7	41
Infiltrative borders	7	41%
Regional Lymphadenopathy	3	17%

Table 3: Salient histopathological features of malignant adnexal skin tumors.

Histopathology	Number of cases	Percentage
Atypia	17	100%
Atypical Mitosis	17	100%
Pleomorphism	17	100%
Infiltrative borders	15	88%
Vascular invasion	10	58%
Lymphatic invasion	5	29%
Perineural invasion	4	23%
Lymph node metastasis	3	17%
Necrosis	7	41%
Lobular architecture	4	23%
Sheeting pattern	5	29%
Infiltrating cords and trabeculae	0	0%
Papillary pattern	1	5%
Glandular pattern	1	5%
Pagetoid pattern	6	35%

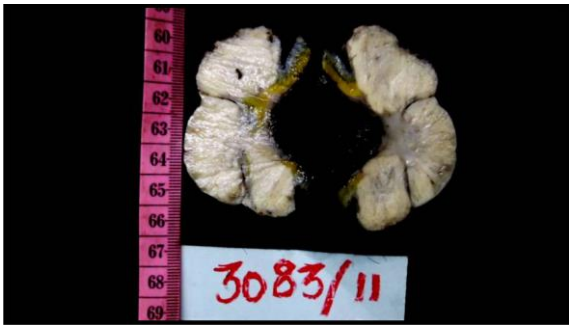

Figure 1: Recurrent malignant proliferating trichelemmal tumors over scalp in 65/ female.

Figure 2: Radical neck dissection specimen in a case of recurrent malignant proliferating trichelemmal tumor.

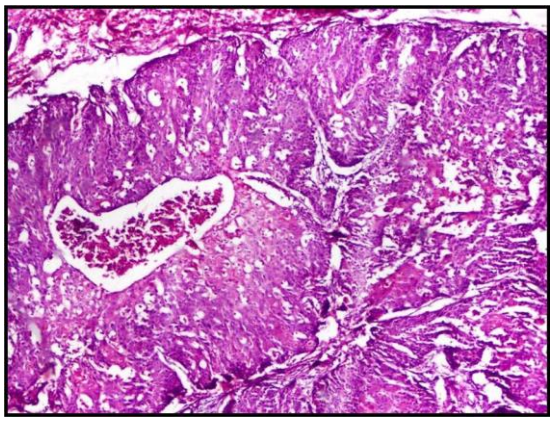

Figure 3: Lobules of pleomorphic tumor cells with mitosis and necrosis, a case of malignant proliferating trichelemmal tumor (H&E, 10x).

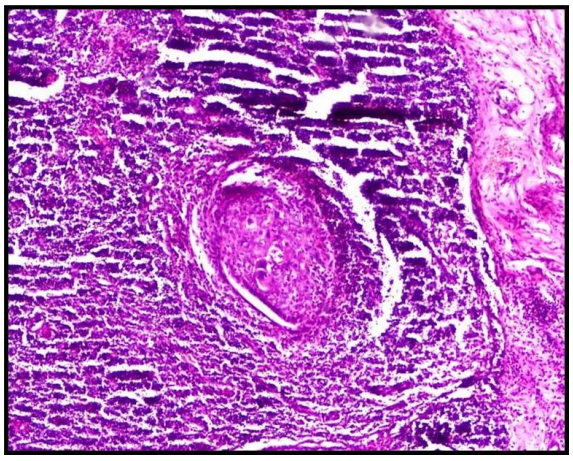

Figure 4: Lymph node deposits in malignant proliferating trichelemmal tumor (H&E, 10x).

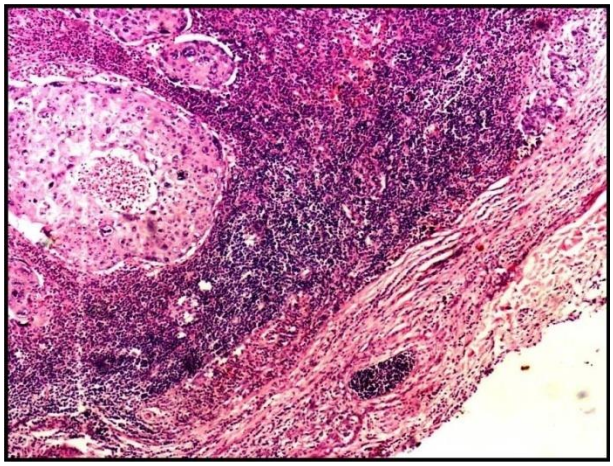

Figure 5: Lymph node deposits in Trichelemmal carcinoma (H&E, 10x).

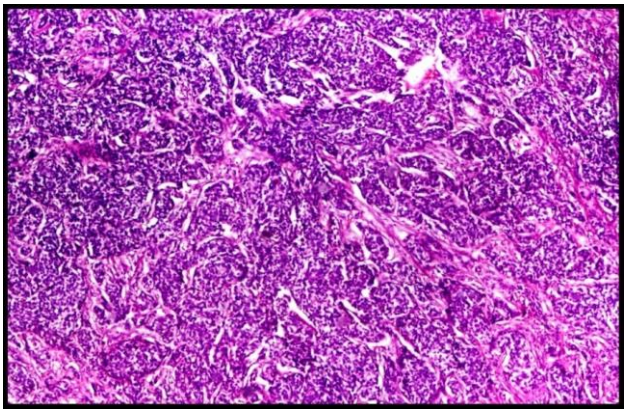

Figure 6: Sheeting pattern of pleomorphic tumor cells in a case of recurrent ocular sebaceous carcinoma (H&E, 4x).

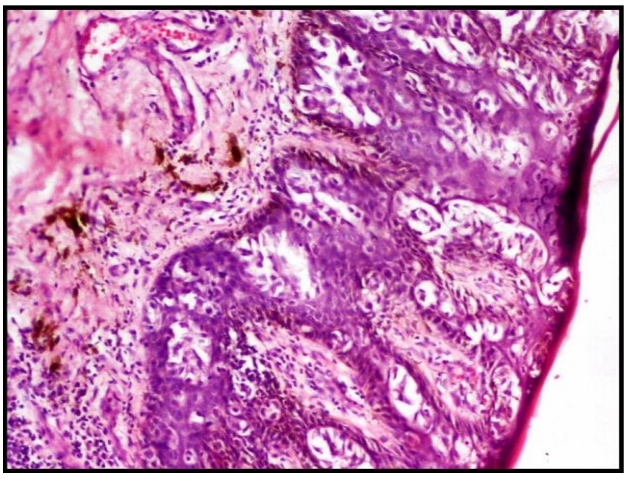

Figure 7: Large neoplastic cells with abundant pale cytoplasm and prominent nucleoli in clusters within the epidermis, Paget disease of breast (H&E, 10x).

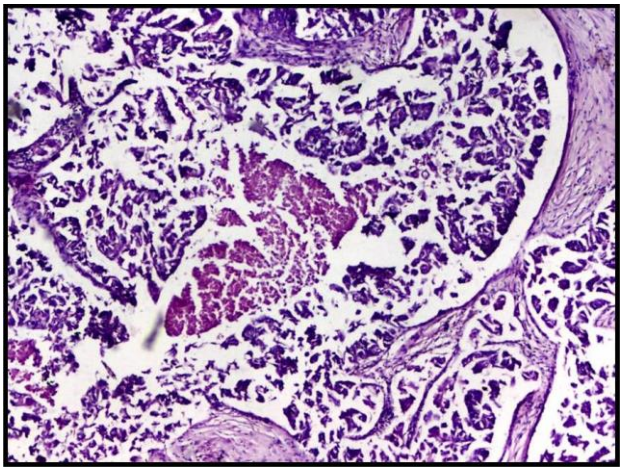

Figure 8: Underlying invasive ductal carcinoma in a 65/female with mammary paget disease (H&E, 10x).

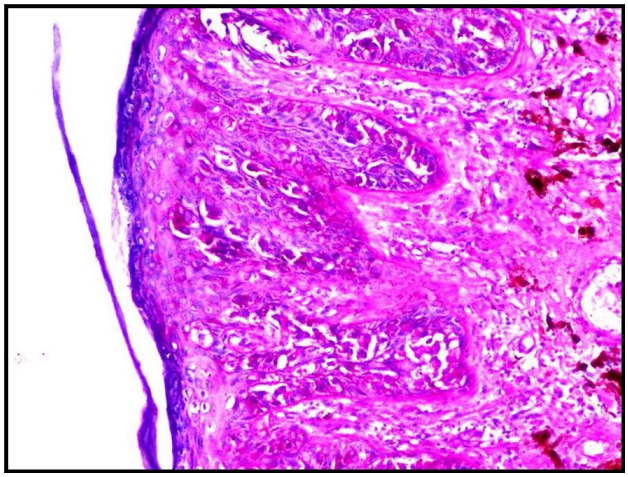

Figure 9: PAS positive neoplastic cells in a case of scrotal Extramammary paget disease (PAS, 10x).

DISCUSSION

Skin adnexal epithelial neoplasms are an assorted group of tumors that show differentiation towards pilosebaceous, eccrine or apocrine structures. Often, they show evidence of more than one lineage within a single tumor. This is said to be because of their common embryogenesis.[4,5] Many studies have shown that a vast majority of the adnexal skin tumors are benign and if excised completely are curative.

A malignant counterpart of almost every skin adnexal tumors has been described. The complex nomenclature, the evergrowing list of entities and different classification systems by different authors have made subtyping these rare tumors an intimidating task to even the experienced pathologist, especially because they are so uncommonly met with. In the present study, we have followed the WHO classification of skin tumors, 2006.[1]

Atypia, more nuclear than cellularity, is regarded as the most important histologic trait favouring malignancy.

This term refers to nuclei that are larger, darker, variably sized, irregularly outlined, have coarse chromatin, nucleoli and abnormal mitoses. All these are subjective, especially when they are present focally or to a mild degree.[6] A set of silhouette features at scanner magnification was described by Dr. Ackerman to differentiate benign from malignant skin adnexal tumors.[7] The other criteria for malignancy include poor circumscription, presence of nuclear atypia and mitotic activity, predominantly solid cell islands, infiltrative growth pattern and angio-lymphatic permeation.[8] All our cases were assessed using these parameters.

The 2006 WHO classification for skin tumors sub classifies Paget disease of breast and extramammary paget disease under malignant skin adnexal tumors with apocrine and eccrine differentiation.[1] In 1874, Sir James Paget first described few cases of eczematous lesions of the nipple and areola and noted that mammary cancer developed in all patients within two years. MPD occurs almost exclusively in women. And they almost always are associated with an underlying carcinoma breast as it is said to represent retrograde extension of the underlying tumor into the epidermis. Cases without underlying carcinoma do exist, but are exceptional. MPD involves the nipple and areola and can extend to the adjacent skin in advanced cases. The etiology implicated in both carcinoma breast and MPD is the same.[9] All four of our cases were women in the 6th decades. All four cases showed underlying invasive carcinoma breast with an additional in-situ component in one case (Figure 7 & 8).

EMPD affects apocrine gland bearing areas of the skin, mainly female and male genital areas. Vulva is the most common site of involvement. They represent an apocrine adenocarcinoma in situ that has a high recurrence rate and may invade the dermis and acquire metastatic potential. In a small subset of cases, they may represent the skin manifestation of an underlying internal malignancy.[9] Two cases were documented in our study, one involved the scrotum in a male patient and the other was seen over the perianal region in a female patient. Both the patients were in their 60's. In neither of our patients, underlying malignancy was detected (Figure 9).

Mammary Paget disease (MPD) and Extramammary Paget disease (EMPD) are intraepidermal adenocarcinomas characterized by large atypical and pale staining cells with prominent nucleoli scattered throughout the epidermis as single cells or in small clusters. All our cases showed similar histologic features. The tumor cells have a propensity to track along the skin appendages. This feature was noted in one case of MPD.

Apocrine carcinoma is a rare malignant sweat gland tumor with apocrine differentiation with no sex or racial predeliction. Most common site is the axilla followed by anogenital region. Variants of apocrine carcinoma have been described on the ear (ceruminous carcinoma) and the eyelid (Moll gland carcinoma).[9] All three patients in this study were female and all of them presented with solitary nodules in the axilla.

Histopathologically, apocrine carcinomas are deep dermal based lesions with variable growth patterns. The tumor cells have abundant eosinophilic cytoplasm, vesicular nucleiand prominent nucleoli. The key feature is the presence of decapacitation secretion in the form of apical snouts. All three of our cases showed this feature.[9]

The malignant proliferating pilar tumor can arise from pre-existing pilar tumor and can be low or high grade in character, and in either manifests infiltration of the dermis and subcutaneous tissue by irregularly shaped and irregularly sized nests of malignant cells in high-grade neoplasms and of proplastic atypical cells in low-grade neoplasms. Striking stromal desmoplasia, numerous and atypical mitotic figures can also be seen in high grade tumors.[3] These features were seen in all 3 of our cases. Two of them presented with recurrence and showed regional lymph node deposits (Figure 3 & 4).

Sebaceous carcinomas can be ocular or extra-ocular, both being aggressive and lethal malignant neoplasms. Ocular sebaceous carcinomas are much more common than their extra-ocular counterparts. It usually is seen in elderly individuals with a definite female predilection. They classically present as a solitary painless papule or nodule over the margin of the upper eyelid. Both our cases were elderly females presenting with solitary nodules over the eyelid. One case was a recurrent case and presented with ulceration. Depending on the degree of differentiation, the identification of sebaceous origin becomes problematic. Low grade tumors show multi-vesicular cytoplasm indenting the nucleus and a lobular growth pattern. High-grade tumors show scant cytoplasmic vacuolation with more prominent nucleoli, atypical mitoses, abundant necrosis, infiltrative patterns of growth with stromal desmoplasia and invasion of adjacent structures. The main differential diagnosis include clear cell epithelial neoplasms, in particular, clear cell squamous cell carcinoma and clear cell BCC. Immunohistochemically, sebaceous carcinomas decorate strongly with EMA. In contrast, squamous cell carcinomas decorate weakly and BCCs are negative with this marker.[9] In our study, one was a low grade sebaceous carcinoma and the other was a high grade carcinoma (Figure 6).

Other malignant adnexal tumors recorded in our study were one case each of trichelemmal carcinoma and one case of eccrine carcinoma.

CONCLUSION

To conclude, malignant tumors of this group are extremely rare with no discrete clinical characters, a high index of suspicion is required to diagnose them. Large size, asymmetry, irregular borders, ulceration and recurrence are some clinical features that should arouse

suspicion of malignancy. Histopathological features of malignancy include loss of circumscription, nuclear atypia, mitosis, pleomorphism, sheeting pattern, infiltrative growth pattern, necrosis and lymphovascular invasion. A thorough knowledge about the histomorphological features is necessary for subtyping these tumors based on their differentiation. Surgery with wide excision margin and sometimes even local lymph node resection may be necessary in these patients.

ACKNOWLEDGEMENTS

I wholeheartedly thank Dr. Radha Pai, our H.O.D. and all my professors of KMC, Mangalore who have always encouraged me throughout my tenure.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Cotton D. Troublesome tumors 1: Adnexal tumors of the skin. J Clin Pathol.1991;44:543–8.
2. LeBoit P, Burg G, Weedon D, Sarasin A. Pathology and genetics of skin tumors.Lyon: IARC Press; 2006.
3. Crowson AN, Margo CM, Mihm MC. Malignant adnexal neoplasms. Mod Pathol. 2006;19:93-126.
4. Alsaad KO, Obaidat NA, Ghazarian D. Skin adnexal neoplasms-part I: an approach to tumors of the pilosebaceous unit. J Clin Pathol. 2007:60;129-44.
5. Alsaad KO, Obaidat NA, Ghazarian D. Skin adnexal neoplasms-part 2: An approach to tumors of cutaneous sweat glands. J Clin Pathol. 2007;60:145–59.
6. Tirumalae R, Roopa MO. Benign vs. Malignant Skin Adnexal Neoplasms: How Useful are Silhouettes? Indian J Dermatol. 2013;58(1):30–3.
7. Ackerman AB. Differentiation of benign from malignant neoplasms by silhouette. Am J Dermatopathol. 1989;11:297–300.
8. Vaideeswar P, Madhiwale CV, Deshpande JR. Malignant hidradenoma: A rare sweat gland tumor. J Postgrad Med. 1999;45:56-7.
9. Requena L, Kutzner H, Hurt MA, Santa Cruz DJ, Mehregan AH, Mengesha YM, et al. Appendageal tumors – Malignant tumors with apocrine and eccrine differentiation. In: LeBoit PE, Burg G, Weedon D, Sarasin A, editors. Pathology and genetics of skin tumors. World Health organization classification of tumors. Lyon, France: IARC Press; 2006. p.127.

Cite this article as: Vijayan P, Nayak R, Ilias LM, Ponniah A. Spectrum of malignant skin adnexal tumors – a single institution study of 17 cases with clinicopathological correlation. Int J Res Med Sci 2015;3(8):1889-94.