

## CASE REPORT

## Sebaceoma associated with seborrheic keratosis

ANGEL FERNANDEZ-FLORES<sup>1-3)</sup>, JOSÉ ANTONIO MANJÓN<sup>4)</sup>

<sup>1)</sup>Department of Cellular Pathology, Hospital El Bierzo, Ponferrada, Spain

<sup>2)</sup>CellCOM-SB Group, Institute for Biomedical Research of A Coruña (INIBIC), University of A Coruña (UDC), A Coruña, Spain

<sup>3)</sup>Department of Cellular Pathology, Hospital de la Reina, Ponferrada, Spain

<sup>4)</sup>Department of Dermatology, Hospital El Bierzo, Ponferrada, Spain

### Abstract

Sebaceoma associated with seborrheic keratosis has only been described once in the literature. Herein, we present an additional case in a 69-year-old woman who complained of a multicolored plaque on the left breast. Dermatoscopy showed a central orange lesion with orange globules suggestive of dilated glands. The periphery of the lesion was brown and gray, with some more pigmented zones. The histopathological study demonstrated a seborrheic keratosis in the peripheral areas, whereas the central part of the lesion was a sebaceoma. We performed an immunohistochemical study with antibodies against MSH6, MSH2, MLH1, and PMS2, which demonstrated preserved nuclear expression of the mismatch repair proteins, therefore ruling out Muir–Torre syndrome.

**Keywords:** sebaceoma, sebaceous adenoma, Muir–Torre syndrome, seborrheic keratosis with sebaceous differentiation, sebomatrichoma.

### Introduction

Sebaceoma associated with seborrheic keratosis is very rare. We are aware of only one previous report, in which the authors described a plaque on the left cheek of a 60-year-old woman [1]. Although the lesion showed the typical configuration of a seborrheic keratosis in the periphery, the central parts of the plaque had the morphology of a typical sebaceoma.

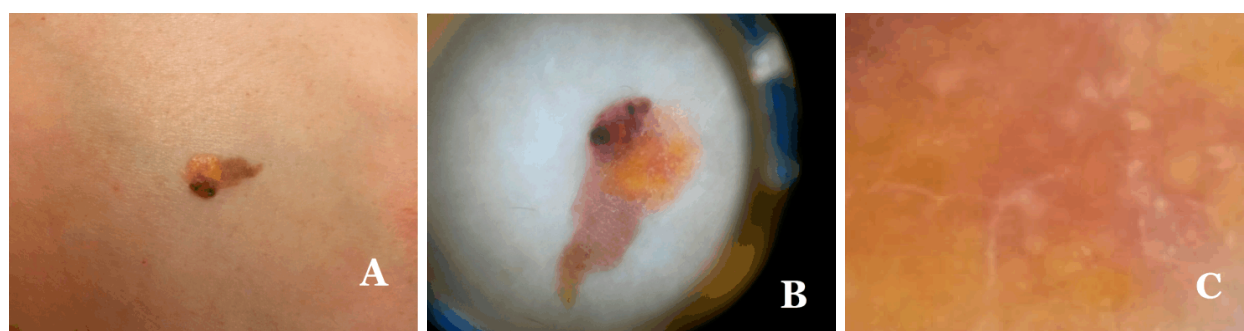
Herein, we present a similar case of sebaceoma associated with seborrheic keratosis, the second one in the literature, to the best of our knowledge. Because sebaceoma has the strongest association with internal malignancy among the sebaceous neoplasias [2], clinical differentiation from benign seborrheic keratosis is essential.

### Case presentation

A 69-year-old woman presented to the dermatology consultancy complaining of a lesion on her left breast.

The lesion was a multicolored plaque 14 mm in diameter (Figure 1A). The peripheral area showed a light gray-brown color. In one pole of the lesion, a darker, more pigmented area raised suspicion of basal cell carcinoma. The center of the lesion had a yellowish-orange color (Figure 1B).

Dermatoscopy revealed orange globules suggestive of dilated glands in the central zones of the lesion (Figure 1C). Focally, the plaque showed a dark reddish hemorrhagic appearance.



**Figure 1 – (A) Multicolored plaque on the left breast. Four distinct areas could be seen. (B) Dermoscopic examination of the lesion. (C) In the yellow areas, there were roundish globules suggesting dilated sebaceous glands.**

The lesion was widely sectioned, and the different areas were examined under the microscope.

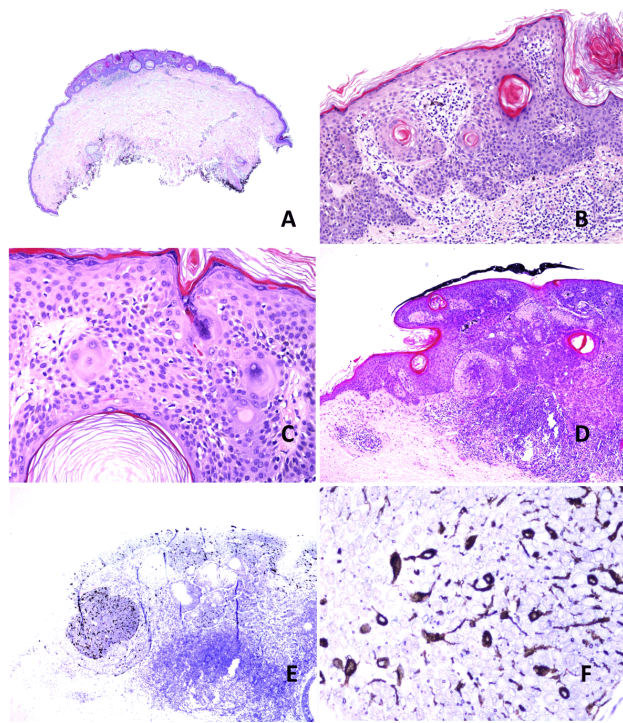
The peripheral areas showed the typical features of seborrheic keratosis, with an exophytic symmetric silhouette and horny pseudocysts (Figure 2A). Basaloid cells were the most common in these areas (Figure 2B). A second

cellular component identified was composed of squamoid cells, including some squamous eddies (Figure 2C).

In the more pigmented area – the one resembling basal cell carcinoma under dermatoscopy – the histopathological features were those of a moderately pigmented seborrheic keratosis (Figure 2D) overlying the peripheral parts of the

sebaceous tumor and accompanied by lichenoid inflammatory lymphohistiocytic infiltrate. In such areas, the seborrheic keratosis was colonized by many dendritic melanocytes (Figure 2, E and F).

The morphology of the orange-yellowish areas was different. The silhouette was that of a benign tumor mainly composed of dilated structures (Figure 3A). Such structures were of two types. Some were dilated secretory parts of sebaceous glands (Figure 3B), showing a sebaceous lining composed of mature sebaceous cells, as well as intermediate mature and immature sebocytes (Figure 3, C and D). Others



**Figure 2** – (A) Low-power view of the peripheral zones of the lesion, with morphology of a typical seborrheic keratosis with an exophytic symmetric silhouette and horny pseudocysts. The predominant type of cell in these areas was the basaloid cell. (B) A second cellular component were squamoid cells, including some squamous eddies. (C) In the most pigmented and troubling areas of the lesion, the morphology was still that of seborrheic keratosis, but pigment was abundant. (D) In such areas, the seborrheic keratosis was overlying the sebaceous tumor accompanied by lichenoid inflammatory lymphohistiocytic infiltrate. (E and F) The seborrheic keratosis was colonized by many dendritic melanocytes. HE staining:  $\times 20$  (A);  $\times 100$  (B);  $\times 200$  (C and D). Melan-A/Giemsa staining:  $\times 20$  (E);  $\times 200$  (F).

## Discussion

To the best of our knowledge, sebaceoma associated with seborrheic keratosis has only been described once in the literature, by Betti *et al.* [1].

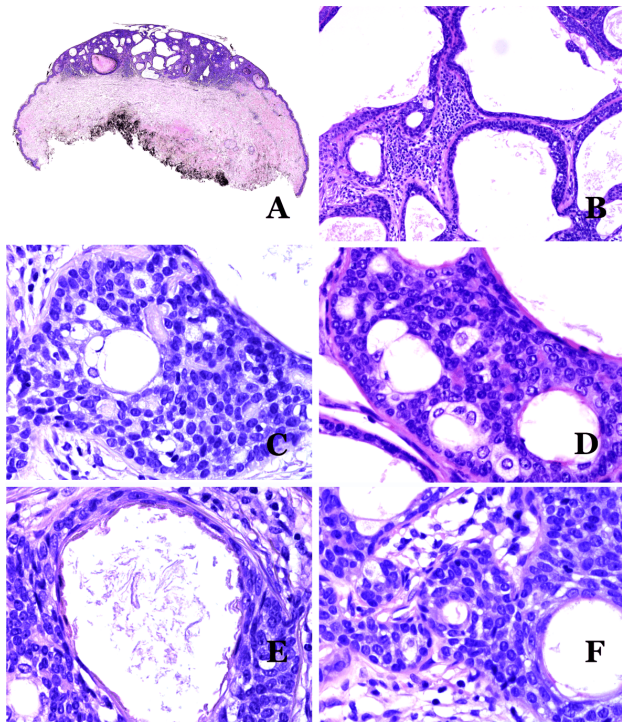
Rothko *et al.* published a case of a 48-year-old man with six lesions, some of which showed a morphology compatible with seborrheic keratosis, whereas the others were compatible with sebomatrixomas [3]. None of these lesions exhibited coexistence of seborrheic keratosis and sebomatrixoma.

Requena *et al.* published two cases of pigmented ambiguous lesions, for which they offered two feasible

were sebaceous ducts, with a characteristic corrugated squamous lining and granular content (Figure 3E). Some similar, although very small ducts were also seen (Figure 3F).

The lesion was diagnosed as sebaceoma coexisting with peripheral seborrheic keratosis.

We performed an immunohistochemical study with antibodies for MutS protein homolog 6 (MSH6), MutS protein homolog 2 (MSH2), MutL protein homolog 1 (MLH1), and postmeiotic segregation increased 2 (PMS2). Nuclear expression of all of these was preserved in the sebaceoma.



**Figure 3** – Morphology of the orange zones of the lesion. (A) The low-power view shows the silhouette of a benign tumor mainly composed of dilated structures. Such structures were of two types: Some were the dilated secretory parts of sebaceous glands (B) with mature sebaceous cells and intermediate mature sebocytes and immature sebocytes (C and D). (E) The second dilated structures were sebaceous ducts, with a characteristic corrugated squamous lining and granular content. (F) Some similar, although very small, ducts were also seen. HE staining:  $\times 20$  (A);  $\times 100$  (B);  $\times 200$  (C–F).

diagnostic interpretations: either pigmented and nested sebomatrixoma or seborrheic keratosis with sebaceous differentiation [4]. At no point in their report did the authors suggest that seborrheic keratosis might coexist with a sebomatrixoma in the same lesion.

Misago *et al.* published a review of 30 cases of sebaceomas and related neoplasias with sebaceous differentiation [5]. One of their cases (their Figure No. 5) showed a mostly endophytic neoplasia with infundibular hyperplasia, squamoid and basaloid cells, and seborrheic keratosis-like features intermingled with sebaceoma features. Unlike in our case, the seborrheic keratosis com-

ponent and the sebaceoma component were not sharply demarcated from each other. The authors diagnosed this lesion as a sebaceoma, seborrheic keratosis type.

Very recently, Misago *et al.* presented a 31-year-old woman with a yellowish flat plaque diagnosed as apocrine poromas with sebaceous differentiation [6]. The lesion was intraepidermal, and a seborrheic keratosis component was excluded by immunohistochemical staining.

In conclusion, the case by Betti *et al.* is the only one, apart from ours, showing two sharply demarcated components of seborrheic keratosis in the periphery and a sebaceous neoplasia in the central areas [1].

Some authors suggested that the case by Betti *et al.* might also be a seborrheic keratosis with sebaceous differentiation [7]. However, the latter mainly showed mature sebocytes, with multivacuolated cytoplasm and an indented nucleus. In contrast, sebaceous adenoma shows a larger number of immature sebocytes. In their report, Betti *et al.* stated that in some sections, they found immature sebocytes [1]. In our case, there were plenty of these, and they also coexisted with plenty of sebocytes in intermediate stages of maturation.

Distinguishing between a seborrheic keratosis with sebaceous differentiation and a sebaceoma in the context of a seborrheic keratosis is not a trivial task. Seborrheic keratosis – even with sebaceous differentiation – is not related to Muir–Torre syndrome. In contrast, in a study by Morales-Burgos *et al.* on MSH2 and MLH1 expression in Muir–Torre syndrome-related and sporadic sebaceous neoplasias, the authors found sebaceomas to have the strongest association with the patient's history for internal malignancy [2].

Mismatch repair protein defects in sebaceous lesions can easily be investigated by immunohistochemistry for four main DNA repair proteins: MSH6, MSH2, MLH1, and PMS2. Some studies remark that the use of only three of these (MSH6, MLH1, and PMS2) is probably enough to detect most Muir–Torre associated cases [8, 9]; however, because some additional MSH6 and PMS2 mutations can be partially compensated for by other mismatch repair (MMR) proteins, the use of all four markers seems to be the ideal protocol for an optimal screening [8, 10].

## Conclusions

In summary, we present the second case of sebaceoma associated with seborrheic keratosis and emphasize the importance of distinguishing such a lesion from a trivial seborrheic keratosis, as well as the value of studying the expression of mismatch repair proteins in the sebaceous component.

## Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

## References

- [1] Betti R, Inselvini E, Vergani R, Moneghini L, Crosti C. Sebaceoma arising in association with seborrheic keratosis. *Am J Dermatopathol*, 2001, 23(1):58–61.
- [2] Morales-Burgos A, Sánchez JL, Figueroa LD, De Jesús-Monge WE, Cruz-Correa MR, González-Keelan C, Nazario CM. MSH-2 and MLH-1 protein expression in Muir Torre syndrome-related and sporadic sebaceous neoplasms. *P R Health Sci J*, 2008, 27(4):322–327.
- [3] Rothko K, Farmer ER, Zeligman I. Superficial epithelioma with sebaceous differentiation. *Arch Dermatol*, 1980, 116(3):329–331.
- [4] Requena L, Kuztner H, Fariña MC. Pigmented and nested sebomatricoma or seborrheic keratosis with sebaceous differentiation? *Am J Dermatopathol*, 1998, 20(4):383–388.
- [5] Misago N, Mihara I, Ansai S, Narisawa Y. Sebaceoma and related neoplasms with sebaceous differentiation: a clinicopathologic study of 30 cases. *Am J Dermatopathol*, 2002, 24(4):294–304.
- [6] Misago N, Inoue T, Toda S. Intraepidermal benign sebaceous neoplasm: apocrine poroma (hidroacanthoma simplex type) with extensive sebaceous differentiation with sebaceoma-like features. *J Cutan Pathol*, 2016, 43(2):171–176.
- [7] Requena L, Requena C. Queratosis seborreica con diferenciación sebácea. In: Requena L (ed). *Neoplasias anexas cutáneas*. Aula Médica, Madrid, 2004, 449–453.
- [8] Chhibber V, Dresser K, Mahalingam M. MSH-6: extending the reliability of immunohistochemistry as a screening tool in Muir–Torre syndrome. *Mod Pathol*, 2008, 21(2):159–164.
- [9] van Puijenbroek M, Middeldorp A, Tops CM, van Eijk R, van der Klift HM, Vasen HF, Wijnen JT, Hes FJ, Oosting J, van Wezel T, Morreau H. Genome-wide copy neutral LOH is infrequent in familial and sporadic microsatellite unstable carcinomas. *Fam Cancer*, 2008, 7(4):319–330.
- [10] Shia J. Immunohistochemistry *versus* microsatellite instability testing for screening colorectal cancer patients at risk for hereditary nonpolyposis colorectal cancer syndrome. Part I. The utility of immunohistochemistry. *J Mol Diagn*, 2008, 10(4):293–300.

## Corresponding author

Angel Fernandez-Flores, MD, PhD, Servicio de Anatomía Patológica, Hospital El Bierzo, Medicos sin Fronteras 7, 24411 Ponferrada, Spain; Phone 0034987454200, Fax 0034987412540, e-mail: dermatopathonline@gmail.com

Received: March 6, 2017

Accepted: July 2, 2017