

Signet Ring Basal Cell Carcinoma: An Extraordinary Case

Özben Yalçın, Buse Akı, Seden Atike Arsoy

University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital, Clinic of Pathology, İstanbul, Turkey

Abstract

Basal cell carcinomas are slow-growing, locally aggressive tumors arising from the interfollicular epidermis and/or hair follicle. Here, a 74-year-old man presented with an irregular nodule 2.5x2 cm in size on the left ala of the nose for 3 years. On light microscopy the signet ring cell configuration was observed among neoplastic cells focally (in some areas). The most prominent feature was cells containing large eosinophilic, pink, eccentric intracytoplasmic inclusions that compress the nuclei to the cell border. The cell inclusions did not stain with periodic acid schiff and alcian blue pH 2.5. The tumor cells were positive for Ber-EP4 but negative for S-100.

Keywords: Signet ring cell, basal cell carcinoma, dermatopathology

INTRODUCTION

Basal cell carcinomas (BCCs) are slow-growing, locally aggressive tumors originating from interfollicular epidermis and/or hair follicle (1). It is the most common malignancy in fair skinned populations worldwide and has many histological variants including nodular, superficial, basosquamous, infiltrating etc. (1). Although there is no specific statistical ratio regarding its prevalence in the literature, we know that signet ring cell BCC is a very rare variant of BCC that tumor cells contain large, pink, eosinophilic, eccentric intracytoplasmic inclusions that crescentically compress nuclei to the cell border (2).

CASE PRESENTATION

A 74-year-old man presented with an irregular nodule 2.5x2 cm in size on the left ala of nose for 3 years. The patient was evaluated as fitzpatrick type 3 on physical examination. The lesion was diagnosed as BCC by incisional biopsy and then a wide excision was performed.

Histopathological and Immunohistochemical Findings

On light microscopy the tumor consists of islands of basaloid cells with peripheral palisading, clefts separating

neoplastic epithelium and intervening fibroblastic stroma (retraction artefact) (Figure 1). Signet ring cell configuration was observed among neoplastic cells focally. The most prominent feature was cells containing large eosinophilic, pink, eccentric intracytoplasmic inclusions, which compress the nuclei in a few lobules (Figure 2A-C). The cell inclusions did not stain with periodic acid schiff (PAS) (Figure 3) and alcian blue pH 2.5 (Figure 4). Tumor cells were positive for Ber-EP4 (Figure 5) but negative for S-100 except for some

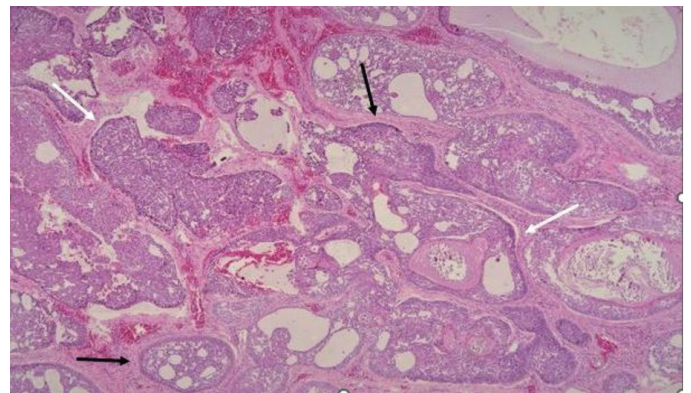


Figure 1. Peripheral palisading basaloid cells (black arrows), clefts separating neoplastic epithelium and intervening fibroblastic stroma (white arrows), hematoxylin and eosin, X40



Address for Correspondence: Buse Akı, University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital, Clinic of Pathology, İstanbul, Turkey

Phone: +90 543 581 11 20 **E-mail:** busseyildirim@gmail.com **ORCID ID:** orcid.org/0000-0002-1539-9427

Cite this article as: Yalçın Ö, Akı B, Arsoy SA. Signet Ring Basal Cell Carcinoma: An Extraordinary Case. Eur Arch Med Res 2022;38(3):230-232

©Copyright 2022 by the University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital
European Archives of Medical Research published by Galenos Publishing House.

Received: 08.09.2022

Accepted: 08.09.2022

cells corresponding to Langerhans cells, which are scattered within tumor islands (Figure 6).

DISCUSSION

Although BCC is the most common cutaneous malignancy, signet ring cell BCCs are rare in routine and our case was not a pure signet ring cell variant as well. At this point, the overall pattern of the

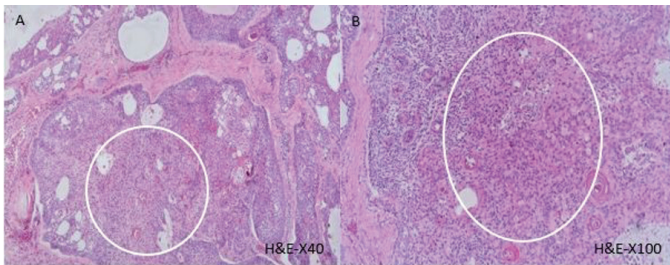


Figure 2. A, B) Signet ring cell configuration among neoplastic cells focally (white circles)

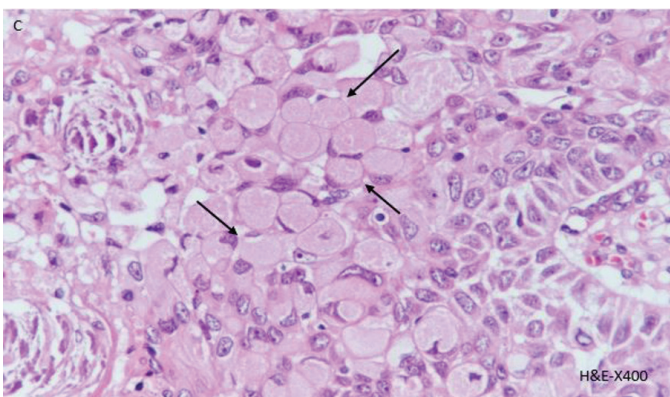


Figure 2. C) The cells containing large, pink, eccentric intracytoplasmic inclusions that compress the nuclei (black arrows)

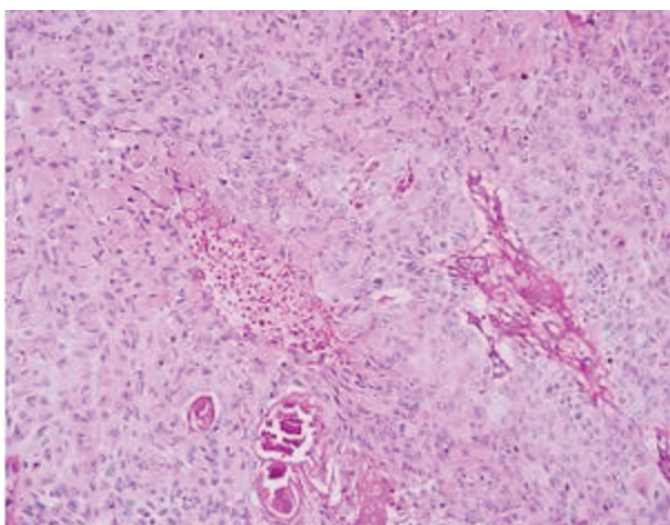


Figure 3. Signet ring tumor cells are negative for PAS, x100
PAS: Periodic acid schiff

neoplasm becomes the most important diagnostic criterion for histological evaluation (3). Although the characteristic features are well-known of BCC, pathologists may consider metastasis of an adenocarcinoma when observing signet ring cells in a skin

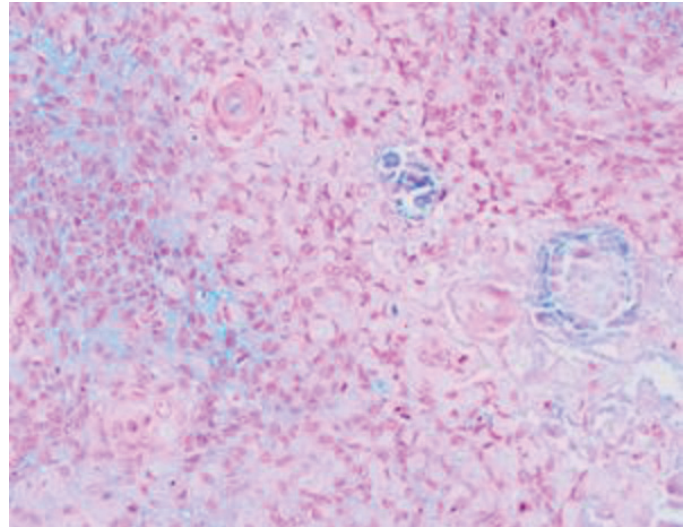


Figure 4. Signet ring tumor cells are negative for Alcian blue pH 2,5, X200

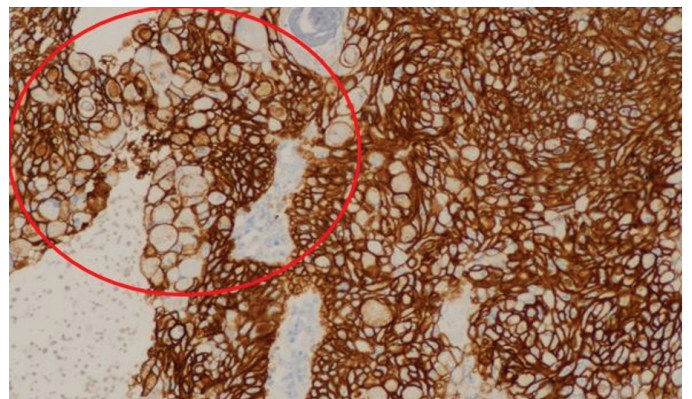


Figure 5. Tumor cells were positive for Ber-EP4. Signet ring cell group also positive for Ber-EP4 (red circle), X100

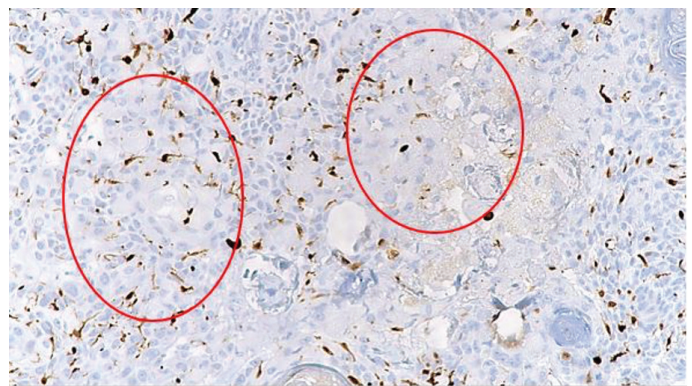


Figure 6. Tumor cells are negative for S-100 except for some cells corresponding to Langerhans cells which are scattered within tumor islands, X200

neoplasm. Nuclear pleomorphism, hyperchromatism, mitotic activity, a type of infiltration (e.g. diffuse pattern supports metastasis), and clinical correlation could help to distinction between metastasis and BCC (4). In cutaneous metastases of visceral adenocarcinomas, there is nuclear displacement because of cytoplasmic musin deposition, which giving signet ring shape to the cell. Therefore, neoplastic cells are stained with PAS and D-PAS (3). In metastatic lesions, typically there is a diffuse dermal infiltrate. Additionally the overlying epidermis is intact and there is an underlying spared zone of uninvolved dermis which is called grenz zone (5). Also the neoplastic cells are generally positive for carcinoembryonic antigen (3). Primary cutaneous signet ring cell neoplasms can also be seen like trichilemmal carcinoma, signet ring cell lymphoma, signaling ring cell squamous cell carcinoma (SCC), sebaceous carcinoma, signet ring melanoma except for metastatic adenocarcinomas (5). In trichilemmal carcinoma, there are foci of keratinization, PAS-positive tumor cells, lobular architecture composed of large atypical cells with clear cytoplasm and prominent nucleoli. This neoplasm is usually deeply seated with no connection to the epidermis and there is no normal pilar structures (6). In signet ring cell lymphomas, tumor cells may have abundant clear or vacuolated cytoplasm that giving shape to cell signet ring appearance mostly because of the abnormal membrane recycling or secretion of immunoglobulin and either B or T-cell markers are positive immunohistochemically (7,8).

In signet ring cell SCCs are negative for BREP4 and CD10 (9). In sebaceous carcinomas are characterized by lobular formations of sebaceous and undifferentiated basaloid cells. Also, the sebaceous cells show foamy, microvesicular cytoplasm instead of a signet ring shape (6). Sebaceous carcinoma shows immunoreactivity for CKPAN, EMA, adipophilin and perilipin (10). Signet ring melanoma stain for melanocyte markers such as HBM-45, Melan-A, and S-100.

To sum up, signet ring cells are uncharacteristic of any particular primary or secondary cutaneous neoplasm. We attach great importance to histomorphology in the differential diagnosis since BCC has well-known diagnostic criteria such as peripheral palisading, retraction artefact, tumor nests. We report this case due to the limited number of studies in the literature about signet ring cell BCC.

CONCLUSION

This case report and similar studies could make it easier to recognize this tumor. Further studies including more cases

would be necessary to clarify the clinical behavior and nature of signaling ring cell BCCs.

Ethics

Informed Consent: Patient consent could not be received from the patient due to the retrospective design of the study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ö.Y., B.A., S.A.A., Concept: Ö.Y., B.A., S.A.A., Design: Ö.Y., B.A., S.A.A., Data Collection or Processing: Ö.Y., B.A., S.A.A., Analysis or Interpretation: Ö.Y., B.A., S.A.A., Literature Search: Ö.Y., B.A., S.A.A., Writing: Ö.Y., B.A., S.A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. *Br J Dermatol* 2012;166:1069-80.
2. White GM, Barr RJ, Liao SY. Signet ring cell basal cell carcinoma. *Am J Dermatopathol* 1991;13:288-92.
3. Aroni K, Lazaris AC, Nikolaou I, Saetta A, Kavantzias N, Davaris PS. Signet ring basal cell carcinoma. A case study emphasizing the differential diagnosis of neoplasms with signet ring cell formation. *Pathol Res Pract* 2001;197:853-6. Erratum in: *Pathol Res Pract* 2002;198:64.
4. Lowe L, Rapini RP. Newer variants and simulants of basal cell carcinoma. *J Dermatol Surg Oncol* 1991;17:641-8.
5. Bastian BC, Kutzner H, Yen Ts, LeBoit PE. Signet-ring cell formation in cutaneous neoplasms. *J Am Acad Dermatol* 1999;41:606-13.
6. Cohen RE, Zaim MT. Signet-ring clear-cell basal cell carcinoma. *J Cutan Pathol* 1988;15:183-7.
7. Zhang S, Sun J, Fang Y, Nassiri M, Liu L, Zhou J, et al. Signet-ring cell lymphoma: clinicopathologic, immunohistochemical, and fluorescence in situ hybridization studies of 7 cases. *Ann Diagn Pathol* 2017;26:38-42.
8. Moran CA, Suster S, Abbondanzo SL. Cutaneous B-cell lymphoma with signet ring-cell morphology: a clinicopathologic and immunohistochemical study of three cases. *Am J Dermatopathol* 2001;23:181-4.
9. El Demellawy D, Onuma K, Alowami S. Signet ring squamous cell carcinoma--the forgotten variant: case report and review of the literature. *J Cutan Pathol* 2011;38:306-8.
10. Ostler DA, Prieto VG, Reed JA, Deavers MT, Lazar AJ, Ivan D. Adipophilin expression in sebaceous tumors and other cutaneous lesions with clear cell histology: an immunohistochemical study of 117 cases. *Mod Pathol* 2010;23:567-73.