Ocular Oncology and Pathology

Research Article

Ocul Oncol Pathol 2024;10:1–8
DOI: 10.1159/000535169

Received: August 2, 2023
Accepted: November 8, 2023
Published online: December 10, 2023

Periocular Sebaceous Carcinoma: A Case Audit from the National Specialist Ophthalmic Pathology Service in Liverpool from 2009 to 2022 to Assess the Diagnostic Utility of PRAME Expression

Amizatul Aini Salleh[a, b, c] Yamini Krishna[a, b] Sarah E. Coupland[a, b]

[a]Liverpool Ocular Oncology Research Group, Department of Molecular and Clinical Cancer Medicine, ISMIB, University of Liverpool, Liverpool, UK; [b]Liverpool Clinical Laboratories, Department of Cellular Pathology, Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK; [c]Department of Pathology, Hospital Serdang, Serdang, Malaysia

Keywords
Periocular sebaceous carcinoma · Histomorphological features · Immunohistochemistry · Preferentially expressed antigen in melanoma · Adipophilin

Abstract
Introduction: Periocular sebaceous carcinoma (PSC) remains a common diagnostic pitfall both clinically and histomorphologically. PRAME (preferentially expressed antigen in melanoma) has been studied in the various neoplasms as proposed as diagnostic and therapeutic markers. PRAME is expressed in normal sebaceous units and in some sebaceous lesions; however, its utility in sebaceous carcinoma diagnosis has not yet been extensively investigated. We conducted a 13-year retrospective review of the patients diagnosed with PSC at the National Specialist Ophthalmic Pathology Service in Liverpool. Herein, we report the histomorphological and immunohistochemical (IHC) features of these tumors, particularly PRAME expression in this cohort. ***Methods:*** Thirty-one PSC cases diagnosed between 2009 and 2022 were retrieved from the histopathology archives. Twenty cases diagnosed as invasive PSC and 11 cases with in situ PSC were included. The hematoxylin and eosin (H&E) slides and previously performed IHC slides were reviewed; clinical information data were obtained. Cases with an adequate tissue were also stained for PRAME (preferentially expressed antigen in melanoma) and adipophilin (if not already performed). ***Results:*** In total, there were 24 females and 7 males diagnosed with PSC, ranging from 55 to 90 years (median, 78 years). The types of specimens received were 11 conjunctival mapping biopsies, 19 excisions/wedge resections, and 1 orbital exenteration. The eyelid was the commonest site involved (n = 24), followed by eyelid with conjunctiva (3), and conjunctiva alone (4). All patients presented with the clinical suspicion of malignancy. Histologically, 11 invasive PSC (55%) exhibited poorly differentiated morphology, composed of predominantly atypical basaloid cells with minimal sebocytic differentiation; 9 cases (45%) were moderately differentiated with noticeable finely multivacuolated cytoplasm; and 3 (15%) showed associated comedo necrosis. Most invasive PSC showed moderate-to-brisk mitotic activities. Of those cases with available immunostains (n = 31), 25 (80.6%) expressed adipophilin; 18 (58.1%) Ber-EP4; 14 (45.2%) epithelial membrane antigen (EMA); and 5 (16.1%) both androgen receptor and perforin positivity. PRAME expression was seen in normal sebaceous glands; however, only (5/19; 26%) of invasive PSC showed focal weak-to-moderate PRAME positivity, and mostly in moderately differentiated tumors. None of the in situ PSCs

karger@karger.com
www.karger.com/oop

Correspondence to:
Sarah E. Coupland, s.e.coupland@liverpool.ac.uk

were PRAME-positive. ***Conclusions:*** Most PSCs are moderate-to-poorly differentiated. Although PRAME is expressed in normal sebaceous units, it appears less useful as diagnostic marker for PSC, especially in poorly differentiated tumors. In difficult cases, panels of IHC studies (adipophilin, Ber-EP4, and EMA) achieve a definitive diagnosis.

Introduction

Sebaceous carcinoma (SC) is a malignant sebaceous gland tumor and generally classified into periocular and non-ocular SC [1–3]. Periocular sebaceous carcinoma (PSC) is rare, accounting for 1–4% of eyelid tumors [1, 4, 5]. However, its prevalence varies geographically, from 1% to 5.5% in the USA to as high as 28–60% in Asian-Indian populations [1, 5]. It behaves aggressively and is associated with high morbidity and mortality [3, 6]. The gold standard for diagnosis is tissue biopsy; however, in the periocular region only small tissue samples are obtained, leading to diagnostic issues [7, 8]. PSC may also mimic other skin tumors histomorphologically, leading to potential misinterpretation and difficulty in reaching an accurate diagnosis [3, 9, 10]. Typically, a panel of immunohistochemical (IHC) markers is required to secure the diagnosis. This typically includes adipophilin, which detects intracellular lipid droplet in sebaceous lesions [9]. Although adipophilin has been considered a useful marker in diagnosing SC, there are certain limitations and challenges associated with its interpretation in some cases, as it can exhibit various staining patterns and it is also expressed in some clear-cell neoplasms, including trichilemmomas and hidradenomas [1, 5, 6, 10–12]. Recently, "preferentially expressed antigen in melanoma" (PRAME), a diagnostic, immunotherapeutic target and prognostic marker in melanocytic lesions [6, 8, 11–13], was found to be expressed in normal sebaceous glands [6, 8, 11]. Two recent studies showed PRAME is useful as diagnostic IHC marker for sebaceous lesions [8, 11]. The purpose of the study was to review the histomorphological and IHC findings on PSC in our institution and to evaluate the expression of PRAME compared to adipophilin.

Materials and Methods

Cases

Thirty-one cases of PSC diagnosed between 2009 and 2022 were retrieved from the pathology archives. In total, 20/31 cases of invasive SC and 11/31 cases of PSC in situ were included. The H&E-stained sections and the previously performed IHC slides were reviewed, and the clinical information data were obtained.

Histological features of PSC aid their degree of sebocytic differentiation such that PSC can be classified into 3 categories: well, moderately, or poorly differentiated based on the WHO grading system [14]. Samples with either an inadequate tissue or non-availability of paraffin blocks were excluded. A total of 19/31 with adequate tissues were stained with PRAME and adipophilin (see below).

IHC Staining Technique and Interpretation

Paraffin-embedded tissue sections were cut (3–5 μm thick), dried, deparaffinized, and rehydrated using standard procedures. A commercial antibody to PRAME (clone QR 005 AnatoPath Cat CSH/17 0 2 PR 29513) is ready to use antibody by using Roche Ultraview AP detection system on the Benchmark Ultra staining platform. As described previously, the tissue was also stained with adipophilin (clone PLIN2/ADFP/Adipophilin Rabbit anti-Human Polyclonal Antibody), dilution: 1:500, by using Dako/Agilent Autostainer Link 48 platform [12]. All slides were evaluated by three pathologists (A.A.S., S.E.C., and Y.K.).

Interpretation

PRAME expression was evaluated according to the previous study by Donnell et al. [11]. Only cytoplasmic and perinuclear staining was considered positive. For the purposes of sebaceous differentiation, nuclear expression of PRAME was considered as negative/nondiagnostic. Normal sebaceous glands are used as internal controls. In the evaluation of immunoreactivity for PRAME, both the percentage of positive tumor cells and the intensity of staining were considered. The extent of staining is scored based on the percentage of positive cells as follows: score 0 = no staining observed; score 1 = less than 5% of cells showing positive staining or minimal staining observed; score 2 = 5–50% of cells showing positive staining or focal staining observed; and score 3 = more than 50% of cells showing positive staining or diffuse staining observed. The staining intensity is scored based on the strength of immunoreactivity as follows: score 0 = negative staining; score 1 = weak staining intensity; score 2 = moderate staining intensity; and score 3 = strong intensity staining. To determine a composite score for each case, the scores for the tumor positivity and intensity of staining are added together. A composite score of 4–6 is considered positive, indicating significant immunoreactivity, while a composite score of 0–3 is considered negative, indicating minimal or no immunoreactivity. Assessment of PRAME positivity is summarized in Table 1.

Adipophilin expression was evaluated based on vesicular or membranous staining of intracytoplasmic lipid droplet positivity. Granular positivity is considered negative/nondiagnostic. Percentages of PRAME and adipophilin expression were calculated.

Statistical Analysis

The only statistical analyses that were applicable in this study were descriptive analyses.

Results

In total, there were 24 females and 7 males diagnosed with PSC, ranging from 55 to 90 years (median, 78 years). The types of specimens received were 11/31; 65% conjunctival

Table 1. PRAME immunostaining and assessment of positivity (according to the scheme of Donnell et al. [11])

IHC	Interpretation
PRAME*	• Cytoplasmic and perinuclear staining • Composite score (4–6 or positive) • Composite score (0–3 or negative) • For the purposes of sebaceous differentiation, nuclear expression of PRAME was considered negative/nondiagnostic • Normal sebaceous glands are used as internal control
0	No staining at all
1+	1–25% of tumor cells
2+	26–50% of the tumor cells
3+	51–75% of the tumor cells
4+	76–100% or diffuse
Intensity score	
Mild	1
Moderate	2
Strong	3
Adipophilin	Vesicular or membranous staining of intracytoplasmic lipid droplet positivity

Table 2. Clinicopathological data and initial IHC stains of the examined cases

Age	Gender	Location	Specimen	Diagnosis	Initial IHC profile
90	F	Left upper lid	Conjunctival mapping biopsies	SC in situ	EMA+, Ber-Ep4−, S100p−, CEA−, melan A−, and CD15−
64	F	Right upper eyelid	Right upper eyelid and conjunctival mapping biopsies	Invasive SC	EMA+, perforin +
76	F	Right lower lid	Right eyelid wedge excision and conjunctiva mapping biopsies	Invasive SC with in situ	EMA+, perforin +, adipophilin+
79	F	Right tarsal conjunctiva	Conjunctiva biopsy	SC in situ with focal microinvasion	Ber-EP4+
78	F	Eyelid	Eyelid wedge resection and conjunctiva mapping biopsies	Invasive SC	EMA+, perforin +, adipophilin+
77	F	Right lower lid	Biopsy	Invasive SC with in situ	Ber-EP4+, EMA+, adipophilin+, perforin +
78	F	Conjunctiva	Conjunctival mapping biopsies	SC in situ	H&E
82	F	Conjunctiva	Conjunctival mapping biopsies	SC in situ	EMA+, Ber-EP4+, adipophilin, perforin +
65	M	Left upper lid	Eyelid wedge resection and conjunctiva mapping biopsies	Invasive SC	H&E
90	M	Right lower lid margin	Biopsies	SC in situ	Ber-EP4+, adipophilin+, EMA +
68	M	Right lower lid	Excisional biopsy	Invasive SC	EMA+, Ber-Ep4+, adipophilin+
59	F	Right upper lid	Wedge excision	Invasive SC	EMA+, adipophilin+
55	M	Upper lid	Excision	Invasive SC	Ber-EP4+, adipophilin+, EMA +
81	M	Right upper lid		SC in situ	Adipophilin+, Ber-EP4+

Table 2 (continued)

Age	Gender	Location	Specimen	Diagnosis	Initial IHC profile
83	M	Lower lid	Exenteration and Conjunctival mapping biopsies Lower lid wedge excision and conjunctival mapping biopsies	SC in situ	Ber-EP4+, adipophilin+
56	M	Right upper lid	Eyelid wedge resection	Invasive SC	Ber-EP4+, AR+, adipophilin+
87	F	Left eyelid tarsal and conjunctival lesion	Eyelid resection	Invasive SC with in situ component	Ber-EP4+, adipophilin+
78	F	Left upper lid	Shave excision biopsy	Invasive SC	Adipophilin+
64	F	Upper eyelid	Eyelid wedge resection and conjunctival mapping biopsies	SC in situ	Adipophilin+, AR +
71	F	Left upper eyelid	Left upper lid wedge biopsy and left upper lid tarsal conjunctiva	SC in situ	Adipophilin+
61	F	Left lower lid	Lower lid excision biopsy and conjunctival mapping	Invasive SC	EMA, Ber-EP4, adipophilin+. CAM 5.2–, AR–
78	M	Left upper lid	Lid biopsy and conjunctival mapping biopsies	Invasive SC	Adipophilin+
86	F	Excision	Right lower eyelid	Invasive SC	EMA+, Ber-EP4+, adipophilin+, AR focal +
77	M	Conjunctiva	Conjunctival mapping biopsies	SC in situ	Adipophilin+, EMA +, Ber-EP4–
68	M	Left eyelid	Excision	Invasive SC	EMA+, adipophilin+
88	F	Eyelid	Conjunctival mapping biopsies	SC in situ	Ber-EP4+, adipophilin+
58	F	Left upper lid	Conjunctival mapping biopsies	Invasive SC with in situ	AR+, adipophilin+
82	M	Right lower lid	Eyelid and conjunctival mapping biopsies	Invasive SC	EMA+, Ber-EP4, +
69	F	Left upper lid	Excision	Invasive SC	EMA, Ber-EP4+, adipophilin+
86	M	Right lower lid	Excision	Invasive SC	EMA+, Ber-EP4+, adipophilin, AR +
85	M	Eyelid	Excision	Invasive SC	EMA+, Ber-EP4+, adipophilin+

SC, sebaceous carcinoma; EMA, epithelial membrane antigen; CEA, carcinoembryonic antigen; AR, androgen receptor; +, positive; –, negative.

Table 3. Morphological features of PSC

Morphological features	Findings
PSC in situ	Variable surface epithelial erosion, dense chronic inflammation in the stroma
Invasive SC	None of the cases show well-differentiated morphology
Moderately differentiated	Arranged in lobules with noticeable intracytoplasmic vacuoles
Poorly differentiated	Prominent basaloid cells, lack of intracytoplasmic vacuoles, central comedo necrosis
Other histological findings	Multifocal intraepithelial (pagetoid) extension Most PSCs show moderate-to-brisk mitotic activity Central pseudo-cystic formation in the tumor

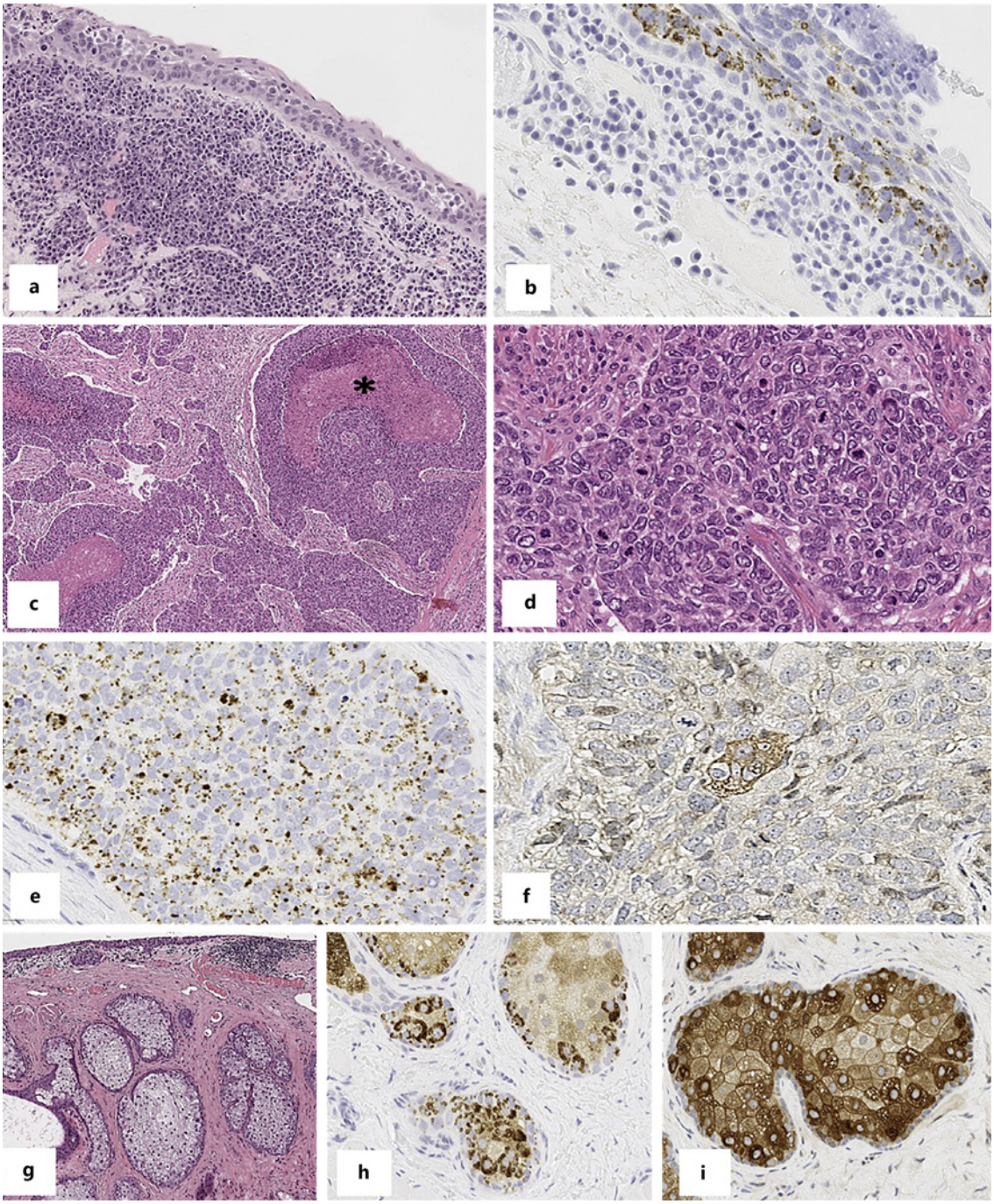

Fig. 1. SC. **a** SC in situ (H&E. ×200). **b** Adipophilin-positive in SC in situ. Invasive SC with central comedo necrosis (*) (**c**) and brisk mitotic activity (H&E. ×400) (**d**). **e** Adipophilin positive in poorly differentiated invasive SC. **f** PRAME with cytoplasmic and perinuclear positivity invasive SC. **g** Normal sebaceous glands (H&E. ×200). **h** Adipophilin-positive sebaceous glands (×200). **i** PRAME with cytoplasmic positivity in normal sebaceous glands.

mapping biopsies and 19 excisions/wedge resections and 1/31; 4% orbital exenteration. The eyelid was the commonest site involved (24), followed by eyelid with conjunctiva (3), and conjunctiva alone (4). All patients presented with eyelid swellings, and most of the cases were presented with clinical suspicion of malignancy. Histologically, 11 tumors (55%)

Table 4. PRAME positivity in PSC

Composite score	PRAME expression composite score	
	4–6 or positive	0–3 or negative
SC in situ, *n* (%)	0/10 (0)	10/10 (100)
Invasive SC, *n* (%)	5/9 (56)	4/9 (44)
Moderately differentiated, *n* (%)	4/5 (80)	1/5 (20)
Poorly differentiated, *n* (%)	1/4 (25)	3/4 (75)

Table 5. Comparison of PRAME and adipophilin expression in PSC

Antibody	PRAME	Adipophilin
Positive, *n* (%)	5/19 (26)	18/19 (95)
Negative, *n* (%)	14/19 (74)	1/19 (5)

exhibited poorly differentiated morphology, composed of predominantly basaloid cells with minimal sebocytic differentiation; 9 cases (45%) were moderately differentiated with noticeable finely multivacuolated cytoplasm; 3 (15%) showed associated central comedo necrosis. Other histological features included central pseudo-cystic formation within the tumor nests (10%). Most invasive PSCs showed moderate-to-brisk mitotic activity. All PSC in situ (11/11, 100%) exhibited a variable surface erosion and dense chronic inflammation within the stroma.

The cases that had immunohistochemistry were 25 (80.6%) positive for adipophilin, 18 (58.1%) Ber-EP4-positive, 14 (45.2%) epithelial membrane antigen (EMA)-positive, and 5 (16.1%) are positive for androgen receptor and perforin, respectively. The clinical information and IHCs are summarized in (Table 2). The morphological features are summarized in (Table 3).

PRAME Immunostaining

In total, 5/19 (26%) cases of invasive PSC were positive for PRAME (Table 3). The reactivity of PRAME staining was focal and patchy with only weak-to-moderate intensity (Fig. 1). Of the 5 PRAME-positive cases, 4 were moderately differentiated tumors, and 1 case was poorly differentiated tumor. None of the PSC in situ cases showed PRAME immunoreactivity (Table 4).

Adipophilin Immunostaining

In total, 18/19 sebaceous lesions (95%) were adipophilin-positive. All invasive PSC cases (9/9; 100%) were positive for adipophilin, while 9 cases of PSC in situ (9/10; 90%) were positive for this marker (Table 5). The intensity staining was moderate-to-strong distinct vesicular and membranous staining of intracytoplasmic lipid droplet positivity (Fig. 1).

Discussion

SC is a malignant sebaceous neoplasm that can occur at any site but most commonly in the head and neck region, particularly at the periocular location [3, 4, 6, 14]. Extraocular SC is encountered in the skin of the head and neck, followed by the trunk, genital regions, and extremities [3, 4, 6, 14]. PSC, particularly at the eyelid, develops de novo and can be uncommonly associated with the other sebaceous lesions or associated with Muir-Torre syndrome [3, 15]. There are several studies suggesting that mutation of the tumor suppressor protein P53 contributes the underlying pathogenesis of the SC [3, 4, 14]. Typically, middle-aged or elderly patients with a median age at diagnosis of 73 years are affected [1]. Diverse presentations of PSC can lead to mimic inflammatory and non-neoplastic conditions [10]. The most typical clinical manifestation of SC is a painless, slowly growing subcutaneous pink to yellowish nodule [13]. In periocular lesions, patients can present with chalazion, blepharitis, cicatricial pemphigoid, or conjunctivitis [4, 7].

Histological features of SC are based on the degree of differentiation, with SC being classified into well-, moderately, or poorly differentiated tumors [3, 4, 7]. Sebocytic differentiation is defined as bubbly multivesicular cytoplasmic clearing with or without nuclear scalloping [10]. The commonly recognized histological patterns of infiltrative growth include lobular, papillary, and trabecular [14]. In this study, we found that most PSCs are moderate-to-poorly differentiated morphology. Histomorphological clues supporting the diagnosis of PSC include the presence of intracytoplasmic vacuoles with a "foamy" appearance and multifocal intraepithelial tumoral extension [1, 2, 4, 5, 10, 14]. This foamy appearance is due to the lipids within the neoplastic cells' cytoplasm. In the past, this used to be highlighted in

frozen sections using Oil red O [3]. Recent IHC panels – including adipophilin, EMA, Ber-EP4, and androgen receptor – applied on fixed tissue enable easier confirmation of the diagnosis [2, 4, 5, 14, 16]. It was recently proposed that PRAME could be added to this diagnostic panel [8, 11]. Donnell et al. [11] suggested in a pilot study that PRAME was 100% positive in sebaceous neoplasms, compared with controls (tumor mimickers), and that most sebaceous lesions showed at least weak intensity staining.

In our study, however, we observed that PRAME highlighted strong cytoplasmic positivity in normal mature sebaceous glands, but low expression was observed in PSC, especially in poorly differentiated tumors. Most of the positive tumors show focal staining scores 1–3 and mild-to-moderate intensity. None of the PSC in situ was positive for PRAME. In contrast, adipophilin was convincing strong and diffuse positivity in 100% of PSC and 90% of SC in situ. Our findings are in concordance with the recent paper by Cazzato et al. [6] who also reported lack of PRAME expression in SC. These authors observed that PRAME is highly expressed in well- and moderately differentiated SC but almost completely absent in poorly differentiated tumors. A study by Ng et al. [8] also demonstrates that PRAME is more useful in identification of sebaceous differentiation but less specific for sebaceomas and SCs.

Conclusions

Although PRAME shows positivity within normal sebaceous units, it appears to be less useful diagnostic marker for PSC, especially in poorly differentiated tumors. We found that adipophilin when combined with the morphology was our "go-to" reliable marker in the IHC panel for PSC. In difficult cases or small biopsies, we would recommend a panel comprising adipophilin, Ber-EP4, and EMA to achieve the diagnosis.

Acknowledgments

The Liverpool Clinical Laboratories aided in the additional immunostaining of some of the cases.

Statement of Ethics

The Liverpool University Hospitals NHS Foundation Trust (LUHFT) approved and hosted this audit study. The study was performed in compliance with the tenets of the Declaration of Helsinki. Written informed consent was not required as this was an audit study (registration No.: 12086), which was approved by the Clinical Audit Group at LUHFT, who are responsible for governance and ethics of all clinical audits across the organization.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

Funding Sources

A.A.S.' Ophthalmic Pathology Fellowship at the Liverpool National Specialist Ophthalmic Pathology Service was supported by the Ministry of Health Malaysia. The funders had no role in the preparation, review, or approval of the manuscript.

Author Contributions

A.A.S., Y.K., and S.E.C. were involved in the study concept and design, provided data acquisition, all interpreted the data, performed development of methodology and writing, reviewing, revision, and approved the final manuscript. AAS provided analysis.

Data Availability Statement

All data analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Knackstedt T, Samie FH. Sebaceous carcinoma: a review of the scientific literature. Curr Treat Options Oncol. 2017;18(8):47.
2 Park SK, Park J, Kim HU, Yun SK. Sebaceous carcinoma: clinicopathologic analysis of 29 cases in a tertiary hospital in korea. J Korean Med Sci. 2017;32(8):1351–9.
3 Shields JA, Demirci H, Marr BP, Eagle RC Jr, Shields CL. Sebaceous carcinoma of the ocular region: a review. Surv Ophthalmol. 2005;50(2):103–22.
4 Grossniklaus HE, Eberhart CG, Kivelä TT. WHO classification of tumours of the eye. 4th ed. IARC Publications. Vol. 12.
5 Kaliki S, Ayyar A, Dave TV, Ali MJ, Mishra DK, Naik MN. Sebaceous gland carcinoma of the eyelid: clinicopathological features and outcome in Asian Indians. Eye. 2015;29(7):958–63.
6 Cazzato G, Colagrande A, Ingravallo G, Lettini T, Filoni A, Ambrogio F, et al. PRAME immuno-expression in cutaneous sebaceous carcinoma: a single institutional experience. J Clin Med. 2022;11(23):6936.
7 Helmi HA, Alsarhani W, Alkatan HM, Al-Rikabi AC, Al-Faky YH. Sebaceous gland carcinoma with misleading clinical appearance: a case report of an eyelid lesion. Am J Case Rep. 2020;21:e925134.

8 Ng JKM, Choi PCL, Chow C, Li JJX, Chan AWS, Cheung CMT, et al. PRAME immunostain expression in sebaceous lesions, cutaneous carcinomas and adnexal structures. Pathology. 2022;54(6):721–8.
9 Milman T, Schear MJ, Eagle RC Jr. Diagnostic utility of adipophilin immunostain in periocular carcinomas. Ophthalmology. 2014; 121(4):964–71.
10 Mittal R, Araujo I, Czanner G, Coupland SE. Perforin expression in eyelid sebaceous carcinomas: a useful and specific immunomarker for the differential diagnosis of eyelid carcinomas. Acta Ophthalmol. 2016; 94(5):e325–30.
11 Donnell SA, LeBlanc RE, Yan S, Parra O, Momtahen S, Sriharan A, et al. Comparison of adipophilin and recently introduced PReferentially expressed Antigen in MElanoma immunohistochemistry in the assessment of sebaceous neoplasms: a pilot study. J Cutan Pathol. 2021;48(10):1252–61.
12 Matareed M, Maranou E, Koskela SA, Mehmood A, Kalirai H, Coupland SE, et al. Novel prognostication biomarker adipophilin reveals a metabolic shift in uveal melanoma and new therapeutic opportunities. J Pathol. 2023;260(2):203–21.
13 O'Connor MK, Dai H, Fraga GR. PRAME immunohistochemistry for melanoma diagnosis: a STARD-compliant diagnostic accuracy study. J Cutan Pathol. 2022;49(9): 780–6.
14 Elder DE, Massi D, Scolyer RA, Willemze R. WHO classification of skin tumours. 4th ed. IARC Publications. Vol. 12.
15 Tetzlaff MT. Immunohistochemical markers informing the diagnosis of sebaceous carcinoma and its distinction from its mimics: adipophilin and factor XIIIa to the rescue? J Cutan Pathol. 2018;45(1): 29–32.
16 Wali UK, Al-Mujaini A. Sebaceous gland carcinoma of the eyelid. Oman J Ophthalmol. 2010;3(3):117–21.