Primary mucinous carcinoma of the scalp

Axel De Greef ,[1] Lucie Landen,[2] Hugues Fierens,[2] Marie Baeck[1]

[1]Dermatology Department, Cliniques universitaires Saint-Luc, Brussels, Belgium
[2]Department of Dermatology, Clinique Saint Jean, Brussels, Belgium

Correspondence to
Dr Axel De Greef;
axel.degreef@saintluc.uclouvain.be

Accepted 30 October 2024

SUMMARY

Mucinous carcinoma of the skin is a rare, low-grade malignancy often clinically misdiagnosed as a benign lesion. This tumour mostly grows locally and has minimal potential for lymphatic or distant metastasis. Commonly affected sites include the periorbital region, particularly the eyelid, and the scalp. Surgical resection is the preferred treatment. However, recurrences are frequent when resection margins are less than 1 cm. Differential diagnosis with mucinous skin metastases can be challenging. We report a patient with an occipital scalp tumour initially considered benign and left untreated for 10 years. After an initial resection, the tumour recurred, requiring a second resection with adequate margins.

BACKGROUND

Mucinous carcinoma is a rare form of skin cancer characterised by slow growth pattern and a low likelihood for lymphatic or haematogenous spread.[1] Its indolent nature often leads to neglect or misdiagnosis as a benign condition, resulting in delayed treatment.

CASE PRESENTATION

An immunocompetent white Caucasian woman in her 80s presented a 5 cm polylobular subcutaneous painless occipital mass of the scalp, which had slowly grown over 10 years. The patient had a history of curative surgeries for stage T3N0M1 sigmoid colon adenocarcinoma (without mucoid differentiation) and liver metastases, with a 7-year remission. Clinical examination revealed an elastic skin-adherent tumour with no suspicious lymph nodes in the head and neck area. Clinical examination of the breast was unremarkable. The tumour was undetected on 18-fluorodeoxyglucose positron emission tomography/CT (18F-FDG-PET/CT) conducted during the evaluation for her colon adenocarcinoma. Because of its indolent evolution, the scalp lesion was presumed benign, and resection was performed under local anaesthesia and conscious sedation, without frozen section analysis. Pathology revealed a low-grade mucinous carcinoma with invaded margins. Primary mucinous adenocarcinoma arising elsewhere with secondary skin metastasis was excluded by thoracoabdominal CT scans, 18F-FDG-PET/CT and serum tumour markers carcinoembryonic antigen (CEA), cancer antigen (CA) 125, CA 19–9 and CA 15–3. Given the patient's age and the indolent behaviour of the tumour, clinical surveillance was recommended. However, 4 years later, the tumour recurred, measuring 3×2×2 cm (figure 1). A wide excision with 1 cm margins was performed under general anaesthesia.

Histological analysis showed a well-delimited tumour centred in the hypodermis, extending into the superficial dermis, displacing surrounding structures (figure 2). There was no in situ contingent. Deep resection margin was positive. The tumour displayed an abundant mucinous stroma (positive for Alcian blue staining), compartmentalised by connective septa (figure 3). Small cell clusters comprising a few dozen cells with little polymorphism were present. Tumour cells were arranged in aggregates or fine trabeculae. Cytoplasm was eosinophilic, with slightly enlarged nuclei and cells had an ovoid chromatic nucleus without nucleolus. Tumour cells stained intensely with antibodies against cytokeratin (CK) 7 (figure 4) and Guanine-Adenine-Thymine-Adenine (GATA)-binding protein 3 (GATA 3) (figure 5). Immunostainings for caudal-related homeobox transcription factor 2 (CDX2) and insulinoma-associated protein 1 (INSM1) were both negative (figure 6). Cells displayed heterogeneous positivity for keratin-associated protein 5–7 and cluster of differentiation (CD) 10 antibody. There was no staining with antibodies against CK 20, p63, S100 protein and epithelial membrane antigen (EMA). 2% cells stained with Ki-67 antibody, reflecting a low mitotic index. This profile was consistent with a primary mucinous carcinoma of the skin (PCMS).

OUTCOME AND FOLLOW-UP

At 1-year follow-up postsecond resection, the patient showed no signs of local recurrence.

DISCUSSION

PMCS is a rare low-grade malignancy occurring in 1 per 150 000 capita annually, first described in 1952 by Lennox *et al*.[1] There is no sex predominance according to the latest WHO skin tumour classification[2] and the median age of onset is 63 years.[3] A SEER population-based cancer registry study comprising 411 patients reported that the incidence was twice as high in blacks compared with other American ethnicities.[4] Although predominantly arising in the head and neck as in our patient, PMCS may occasionally involve the buttocks, axillae, vulva or limbs. In 40%–50% of cases, the tumour develops in the periorbital region, particularly the lower eyelid.[3 5] PMCS usually presents as a subcutaneous solid mass measuring 1–8 cm, covered by translucent grey or blue-coloured skin. Cystic and ulcerated forms have been described.[6]

Clinical misdiagnosis with benign skin tumours and delays of several years prior to treatment are common as demonstrated in this observation. Differential clinical and/or histopathological diagnosis includes cutaneous lymphoma, metastatic carcinoma, epidermoid cyst, pilomatrixoma and

Check for updates

© BMJ Publishing Group Limited 2024. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: De Greef A, Landen L, Fierens H, *et al*. *BMJ Case Rep* 2024;**17**:e260991. doi:10.1136/bcr-2024-260991

BMJ Case Rep: first published as 10.1136/bcr-2024-260991 on 4 December 2024. Downloaded from http://casereports.bmj.com/ on January 13, 2025 at Universite Catholique de Louvain. Protected by copyright.

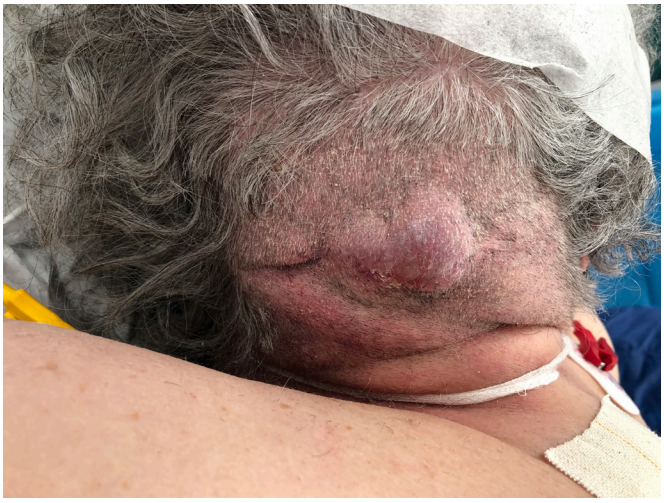

Figure 1 Preoperative view of the occipital tumour. Patient in prone position.

lipoma.[7 8] Biopsy is warranted to confirm the diagnosis. 18F-FDG-PET/CT may be useful in attesting the malignant nature of primary and metastatic tumours.[9] However, in our patient, 18F-FDG-PET/CT remained negative. Lack of FDG uptake can be expected in low-grade malignancy (low mitotic index) and low malignant cell density/mucoid component ratio as in mucinous skin carcinoma.[10] Nevertheless, it is important to consider additional imaging modalities, such as mammography, ultrasound, breast MRI, and head and neck CT-scan, as these can be useful in ruling out primary tumours in other locations that may not be detected by 18F-FDG-PET/CT alone.

The cell line of origin of PMCS, eccrine or apocrine, is still debated. An eccrine sweat gland origin is supported by the presence of cells resembling the dark cells of eccrine glands.[11] Apocrine origin from the sebaceous gland-hair follicle units is supported by several findings. Vesicle shedding from the luminal pole of tumour cells lining tubules is like that observed in apocrine cells. The similarity to apocrine mammary colloid carcinoma and the presence of plasmacytoid cells found exclusively in apocrine-differentiated neoplasms are further arguments in favour of an apocrine origin.[12] Recently, a neuroendocrine histogenesis has been hypothesised because the majority of PMCS specimens stain for INSM1, a sensitive marker for neuroendocrine cells.[13 14] Immunohistochemistry for CDX2 can also help to differentiate

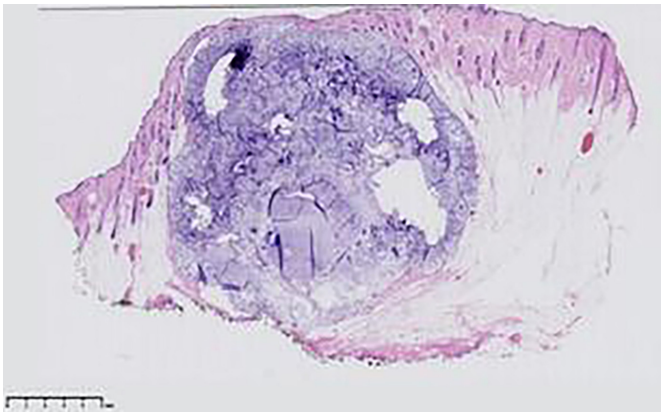

Figure 2 Low magnification of the excised specimen showing a well-delimited tumour circumscribed by a thin connective tissue capsule (H&E staining). Deep resection margin was positive.

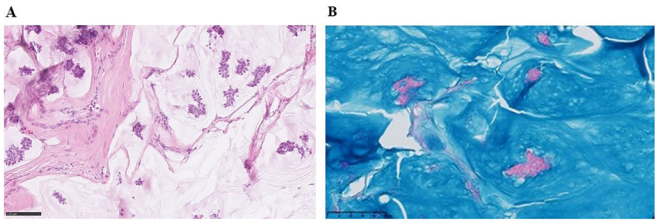

Figure 3 Small cell clusters of a few dozen cells, with little polymorphism are present. Tumour cells are arranged in aggregates or fine trabeculae (H&E staining, 20× magnification) (A). Abundant mucinous stroma (Alcian blue staining positive, 20× magnification) compartmented by connective septa (B).

PMCS from mucinous skin metastases. In this case, clusters of cells were negative for both markers, going against a digestive origin (CDX2 negative) and against a neuroendocrine differentiation (INSM1 negative). Although S100 is not typically expressed in PMCS, it is a useful marker to exclude melanocytic lesions, as well as neural and myoepithelial tumours, which can have mucinous components.[15] EMA is an epithelial marker expressed in a wide variety of epithelial-derived tumours, including many adenocarcinomas. The negativity of EMA staining in this case helped to support the diagnosis of a low-grade mucinous carcinoma with minimal or absent epithelial differentiation, which is consistent with PMCS.[15]

Gross examination of the cut section of the tumour reveals characteristic honeycomb spaces filled with gelatinous material. Histologically, PMCS is composed of Periodic Acid-Schiff (PAS)-positive sialomucin lakes separated by thin fibrous septae. Nests of tumour cells, sometimes organised in duct-like structures reminiscent of skin glands, are found floating in the mucus. Tumour cells are round or cuboidal with abundant cytoplasm, small central nuclei, minimal nuclear atypia and rare mitoses. This contrasts with skin metastases from mucinous tumours, in which nuclear pleomorphism and mitotic figures are prominent. Other characteristics that may help to differentiate PMSC from mucinous metastases are the thickness of fibrous septa, the cell-to-mucin ratio and the clear presence of an in situ component which is exclusively found in primary tumours.[16] On the contrary, dirty necrosis is a finding commonly encountered in mucinous metastasis of intestinal origin.[16] When exposed to Alcian blue or PAS and diastase, mucin of gastrointestinal and salivary gland tumours commonly does not stain whereas mucin within PMCS stains.

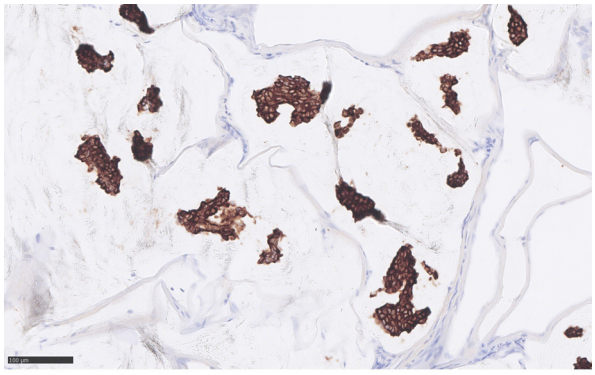

Figure 4 Intense staining of tumorous cells with CK 7 antibody (20× magnification). *CK 7*, cytokeratin 7.

BMJ Case Rep: first published as 10.1136/bcr-2024-260991 on 4 December 2024. Downloaded from http://casereports.bmj.com/ on January 13, 2025 at Universite Catholique de Louvain. Protected by copyright.

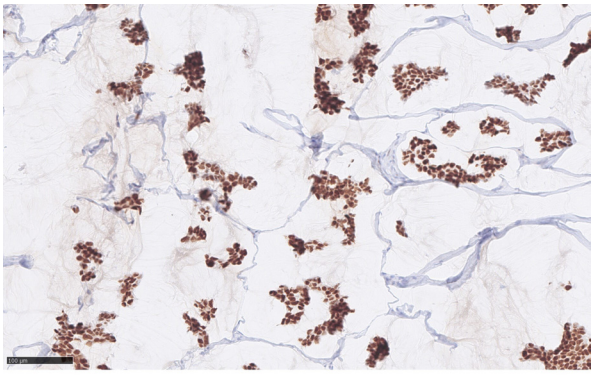

Figure 5 Intense staining of tumorous cells with GATA 3 antibody (20× magnification). *GATA 3*, Guanine-Adenine-Thymine-Adenine (GATA)-binding protein 3.

It is important to distinguish between PMCS and the more common skin metastasis arising from adenocarcinomas in other organs. This is particularly true in patients with a history of adenocarcinoma of other origin as in the present case. Mucinous adenocarcinomas most commonly arise in the breast, gastrointestinal (GI) tract, salivary glands, lacrimal glands, nose, paranasal sinuses, bronchi, renal pelvis and ovary.[12] Besides PMSC, CK 7 is also expressed in adenocarcinoma of lung, breast, thyroid, endometrium, cervix, ovary, salivary gland, upper GI tract and urinary epithelium. It is generally not expressed in colorectal carcinoma. CK 20 is expressed in colorectal and urinary epithelial tumours but not in PMCS. GATA 3 is expressed in mammary and urothelial carcinomas but also in sweat gland tumours. Furthermore, PMSC are commonly oestrogen and progesterone receptor positive.[17]

PMCS are slow-growing, with local recurrence in 30% of cases, preventable by wide (≥1 cm) surgical margins. Involvement of regional lymph nodes is reported in less than 10% of cases. Distant metastases are even less frequent, ranging from 3% to 6%.[3 5] Young age, non-Asian ethnicity, positive surgical margins, tumour size >1.5 cm and tumour location on the trunk are associated with a higher risk of postsurgical recurrence and metastasis after treatment.[5] There is no significant differences in cancer-specific mortality according to sex, age, race, primary site, histological tumour grade, tumour size, tumour stage or treatment.[4] PMCS is not linked to an increased risk of developing other malignancies.[4]

Although PMCS does not invade the overlying epidermis, it adheres to the skin, precluding attempts at enucleation, which would likely lead to recurrence. Radical treatment consists of conventional surgical excision with 1 cm margins. In superficial tumours, where such margins are difficult to achieve because of anatomical or cosmetic constraints, such as eyelid tumours, Mohs surgery may be indicated and even appears to be associated with a lower risk of recurrence and metastases.[5] Radiotherapy and chemotherapy have not proved to be useful in the treatment of PMCS, being considered only in advanced or disseminated disease. In hormone receptor-positive tumours, aromatase inhibitors have recently been used as adjuvant therapy following resection.[17] Regular surveillance is recommended to detect recurrences at an early stage. One patient with metastases 10 years after resection has been reported.[18]

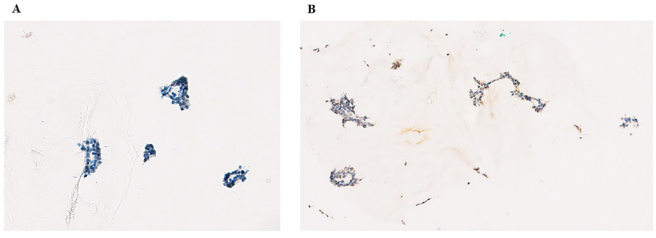

Figure 6 Negative staining of CDX2 (A) and INSM1 (B) (20× magnification). *CDX2*, caudal-related homeobox transcription factor 2; *INSM1*, insulinoma-associated protein 1.

In conclusion, this case confirms that PMCS are usually indolent and develop locally, often leading to long delays in diagnosis, but also emphasises the importance of adequate surgical margins.

The particularities of this case are the differential diagnosis with skin metastasis, given the patient's history of colon adenocarcinoma with liver metastases, and the negativity of the 18F-FDG-PET/CT scan in contrast with cases previously reported in the literature.

Learning points

- Primary mucinous skin carcinoma is a rare low-grade malignancy frequently misdiagnosed as a benign lesion.
- Clinical awareness of primary mucinous skin carcinoma and the use of skin biopsy for diagnosis are crucial for enabling early surgical resection with adequate margins.
- Differentiating primary mucinous carcinoma from mucinous skin metastases is essential due to their significantly different treatments and prognoses.

Acknowledgements We thank Mariana Andrade (M.D.), who provided editorial assistance.

Contributors ADG and LL contributed equally as first authors. ADG: drafting of the text, sourcing and editing of clinical images, critical revision for important intellectual content. LL: drafting of the text, sourcing and editing of clinical images, investigation results. HF: critical revision for important intellectual content. MB: critical revision for important intellectual content. The following authors gave final approval of the manuscript: LL, ADG, HF, MB. LL and ADG are the guarantors.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

ORCID iD
Axel De Greef http://orcid.org/0000-0003-0713-8283

REFERENCES

1 Breiting L, Dahlstrøm K, Christensen L, *et al*. Primary mucinous carcinoma of the skin. *Am J Dermatopathol* 2007;29:595–6.
2 Kazakov D, Calonje J, Pulitzer M, *et al*. Mucinous carcinoma. In: *WHO classification of Tumors online*. 2023.
3 Snow SN, Reizner GT. Mucinous eccrine carcinoma of the eyelid. *Cancer* 1992;70:2099–104.
4 Rismiller KP, Crowe DR, Knackstedt TJ. Prognostic Factors, Treatment, and Survival in Primary Cutaneous Mucinous Carcinoma: A SEER Database Analysis. *Dermatol Surg* 2020;46:1141–7.
5 Kamalpour L, Brindise RT, Nodzenski M, *et al*. Primary cutaneous mucinous carcinoma: a systematic review and meta-analysis of outcomes after surgery. *JAMA Dermatol* 2014;150:380–4.
6 Kelly BC, Koay J, Driscoll MS, *et al*. Report of a case: primary mucinous carcinoma of the skin. *Dermatol Online J* 2008;14:4.

BMJ Case Rep: first published as 10.1136/bcr-2024-260991 on 4 December 2024. Downloaded from http://casereports.bmj.com/ on January 13, 2025 at Universite Catholique de Louvain. Protected by copyright.

7 Saito Y, Ota K, Sumita Y. Primary mucinous carcinoma of the skin arising from the upper eyelid: A case report and literature review. *JPRAS Open* 2020;25:18–23.
8 Soror NN, Lutaya I, Shah P, *et al*. A Rare Case of Primary Adenocarcinoma of the Eyelid. *Case Present Rev Lit Cureus* 2021;13:e16580.
9 Kitamura S, Hata H, Inamura Y, *et al*. Positron emission tomography-computed tomography can be useful in the early detection of metastases in primary mucinous carcinoma of the skin on the head and neck. *Br J Dermatol* 2015;173:1263–5.
10 Berger KL, Nicholson SA, Dehdashti F, *et al*. FDG PET evaluation of mucinous neoplasms: correlation of FDG uptake with histopathologic features. *AJR Am J Roentgenol* 2000;174:1005–8.
11 Yamamoto O, Nakayama K, Asahi M. Sweat gland carcinoma with mucinous and infiltrating duct-like patterns. *J Cutan Pathol* 1992;19:334–9.
12 Requena L, Kiryu H, Ackerman AB. *Neoplasms with Apocrine Differentiation*. Philadelphia: Lippincott-Raven, 1998:907–47.
13 Levett K, Taylor B, Krishnan B, *et al*. Recurrent Neuroendocrine Primary Cutaneous Mucinous Carcinoma of the Scalp After Complete Excision. *Am J Dermatopathol* 2023;45:123–6.
14 Adkins KE, Busam K, Pulitzer M. Cutaneous Neuroendocrine Mucinous Carcinomas Are Low-grade But May Be Associated With Other Cancers. *Am J Surg Pathol* 2023;47:1186–91.
15 Miettinen M. Immunohistochemistry of soft tissue tumours - review with emphasis on 10 markers. *Histopathology* 2014;64:101–18.
16 Kazakov DV, Suster S, LeBoit PE, *et al*. Mucinous carcinoma of the skin, primary, and secondary: a clinicopathologic study of 63 cases with emphasis on the morphologic spectrum of primary cutaneous forms: homologies with mucinous lesions in the breast. *Am J Surg Pathol* 2005;29:764–82.
17 Miyachi H, Hashimoto H, Suehiro K, *et al*. Aromatase inhibitor for the treatment of primary mucinous carcinoma of the skin with distant metastasis. *JAAD Case Rep* 2018;4:235–8.
18 Miyasaka M, Tanaka R, Hirabayashi K, *et al*. Primary mucinous carcinoma of the skin: a case of metastasis after 10 years of disease-free interval. *Eur J Plast Surg* 2009;32:189–93.

Copyright 2023 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit
https://www.bmj.com/company/products-services/rights-and-licensing/permissions/
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:
- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

Customer Service
If you have any further queries about your subscription, please contact our customer services team on +44 (0) 207111 1105 or via email at support@bmj.com.

Visit casereports.bmj.com for more articles like this and to become a Fellow

BMJ Case Rep: first published as 10.1136/bcr-2024-260991 on 4 December 2024. Downloaded from http://casereports.bmj.com/ on January 13, 2025 at Universite Catholique de Louvain. Protected by copyright.