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CASE REPORT

Primary Cutaneous Mucinous Carcinoma of the Left Zygomatic Region: A Case Report

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Abstract: We describe a case involving a 50-year-old male with who presented with a facial lesion on the left cheek of zygomatic region for 7 years. The diagnosis of primary cutaneous mucinous carcinoma (PCMC) was established through immunohistochemistry and histopathology. And the patient underwent wide excision of the tumor, has no evidence of recurrence after 15 months of follow-up.

Keywords: primary cutaneous mucinous carcinoma, immunohistochemistry, histopathology

Introduction

Primary cutaneous mucinous carcinoma (PCMC) is a rare adnexal tumour of the skin. It is a slow-growing tumour that rarely metastasizes.[1] The incidence rate is approximately 0.07 per million, and it has characteristic histopathology. Standard practice is to remove it surgically, with wide local excision of a 1- to 2-cm margin.[2] There are increasing reports of Mohs micrographic surgery as a tissue sparing technique that allows complete margin control of these rare neoplasia.[3] In this report, we present a case of HCMC diagnosed by immunohistochemistry and histopathology, where the patient opted for surgical enlarged resection of the tumour due to financial reasons, and is currently being followed up for 15 months postoperatively without recurrence.

Case Presentation

A 50-year-old male patient presented with a facial lesion located on the left cheek in the zygomatic region persisting for 7 years. The lesion initially appeared as a small yellow papule without any identifiable cause. The patient sought medical attention at a local hospital 7 years ago, where it was diagnosed as an "epidermal cyst", but it remained untreated. Over the past 3 years, the skin lesion gradually increased in size, reaching the dimensions of a lentil (approximately the size of a chickpea). The lesion would occasionally become irritated, leading to surface erosions and crusting. Seeking for further evaluation and treatment, the patient visited our hospital. His medical history was unremarkable for chronic illnesses, infectious diseases, drug or food allergies, and there were no significant findings in his personal or family history.

Specialist Examination: upon examination, a half-round, gelatinous-like nodule with a clear border was observed on the left cheek. The lesion exhibited a smooth surface, felt firm to the touch, and had a crusted top, with no noticeable discharge. The patient reported no subjective symptoms associated with the lesion (see Figure 1A and B).

Laboratory texts: Blood routine, urine routine, stool routine, electrocardiogram (ECG), and chest X-ray showed no significant abnormalities.

Pathological Examination: Histopathological examination revealed a tumor located in the dermis and subcutaneous tissue. The tumor exhibited nodular growth with relatively clear borders. Within the tumor, abundant basophilic mucin

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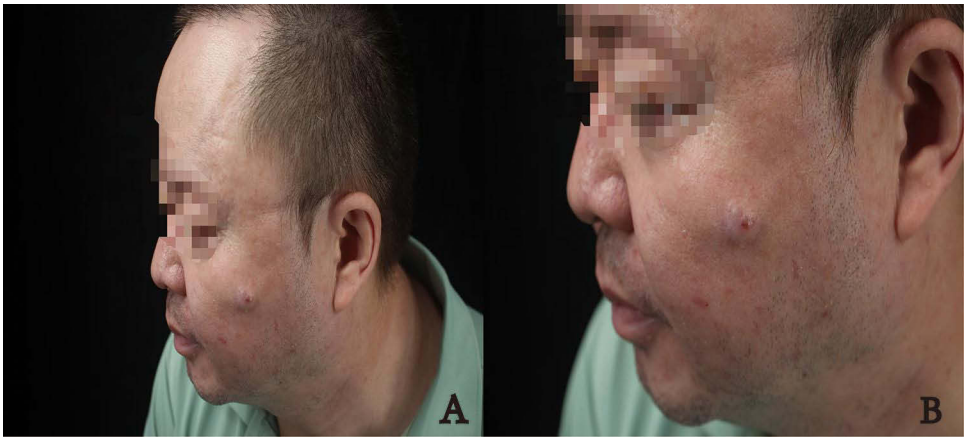


Figure 1 (**A** and **B**) On the left cheek of zygomatic region, there is a semi-circular, gelatinous-like nodule, raised on the skin. The surface is smooth, touched hard, with a crusted top, and the border is well-defined, without any noticeable discharge.

pools were present, separated by fine fibrous septa into multiple compartments. Floating within the mucin lakes were island-like clusters of epithelial cells, some forming glandular or incomplete tubular structures. The tumor cells showed mild atypia, indistinct cell boundaries, acidophilic cytoplasm, occasional intracytoplasmic mucin vacuoles, increased nuclear-to-cytoplasmic ratio, fine chromatin, and rare mitotic figures (Figure 2A and B).

Immunohistochemistry: The tumor was positive for alcian blue staining (AB), recombinant cytokeratin 7 (CK7), epithelial membrane antigen(EMA), and weakly positive for androgen receptor (AR). Negative markers includes recombinant cytokeratin 20(CK20), a member of p53 family, is frequently overexpressed in squamous cell carcinoma (P63), Calponin, thyroid transcription factor-1 (TTF1), caudal-related homeobox transcription factor 2 (CDX2), estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2(HER2), gross cystic disease fluid protein 15(GCDFP15), syntaxin(Syn), glycoprotein hormones alpha chain(CgA), and KI-67 (PROLIFERATION MARKER) approximately 5% (Figure 3A–H). The explanations of various immunohistochemical stains and their uses see in Table 1.

Based on the clinical presentation, histopathology, and immunohistochemistry, he was diagnosed with primary cutaneous mucinous adenocarcinoma(PCMC). Mohs micrographic surgery is a tissue sparing technique that allows complete margin control of these rare neoplasia. But the patient opted for surgical enlarged resection of the tumour due to financial reasons, during the surgical procedure, the patient was positioned laterally, allowing for full exposure of the left

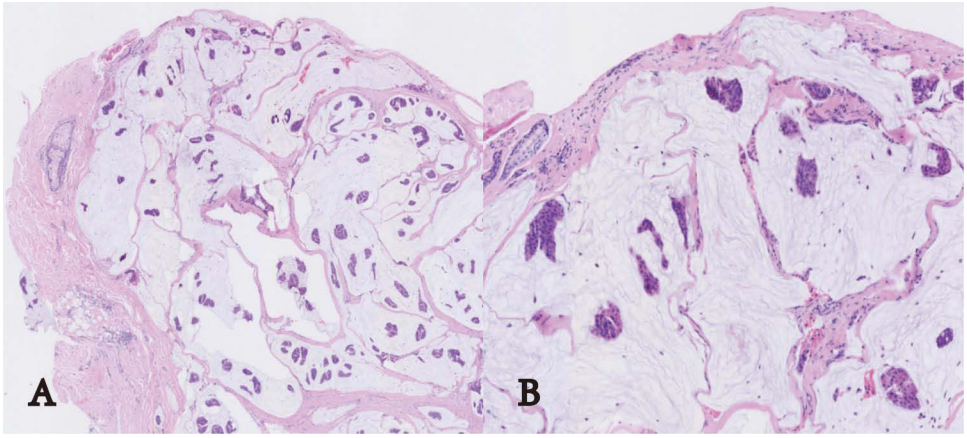
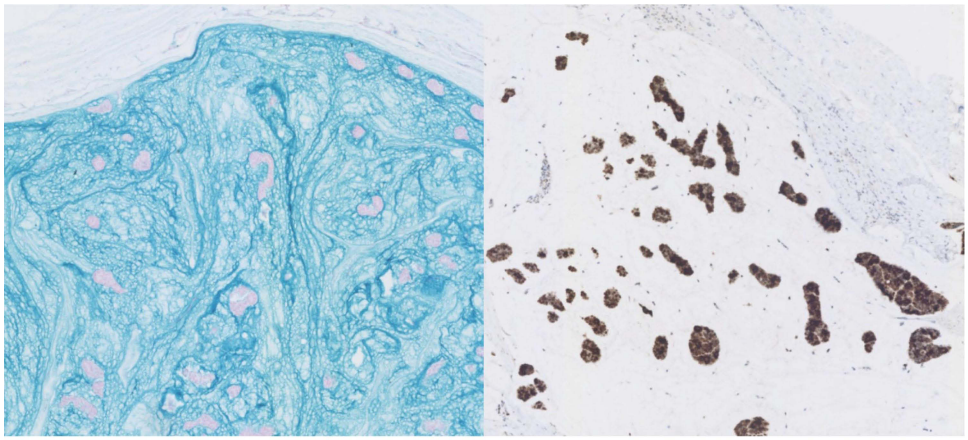


Figure 2 (**A**) The tumor is located in the dermis and subcutaneous tissue, exhibiting nodular growth with relatively clear borders. Within the tumor, large mucin pools are visible, separated by fine fibrous septa into multiple compartments (magnification ×10). (**B**) The tumor cells show mild atypia, with indistinct cell boundaries, acidophilic cytoplasm, and occasional intracytoplasmic mucin vacuoles. The nuclear-to-cytoplasmic ratio is increased (magnification ×40).

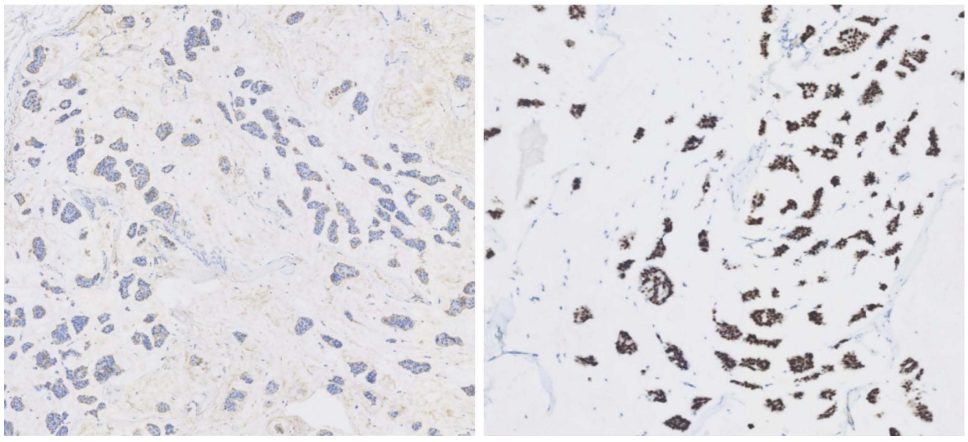
facial operative area, which was then sterilized with iodophor and routinely taped. The edges of the lesion were marked with melphalan, followed by local infiltration anesthesia using a 2% lidocaine injection. An incision was made along the marked line down to the subcutaneous fat layer, and the lesion was completely excised. Bipolar electrocoagulation was employed to effectively control hemorrhage. The subcutaneous fat layer adjacent to the trauma margin was separated from the surrounding tissue, after which the subcutaneous tissues were sutured using a 5–0 absorbable suture. The skin was then closed with a 6–0 silk suture, and the area was covered with oil gauze and a compression bandage. The operation proceeded smoothly with minimal intraoperative bleeding. The patient was monitored for 15 months post-operation, during which no recurrence was observed.

Discussion

Mucinous carcinoma is a relatively rare malignant tumor characterized by the presence of abundant mucin pools containing varying-sized cell islands. The most common origins of mucinous carcinoma include skin appendages, breast tissue, and the digestive tract. Additionally, specific mucinous carcinomas can originate from the bladder, lungs, and other sites.[4] Primary cutaneous mucinous carcinoma (PCMC), also known as gelatinous cystadenocarcinoma, is an exceptionally rare low-grade malignant tumor originating from sweat glands in the skin. It predominantly affects middle-aged to elderly male patients on the head and face. Clinically, PCMC presents as slow-growing, painless, soft nodules or cysts with colors ranging from flesh-colored to red or gray-blue.[5] Although there is some debate about whether PCMC



(A)、AB(+) (B)、CK7(+)



(C)、EMA(+) (D)、ER(+)

Figure 3 Continued.

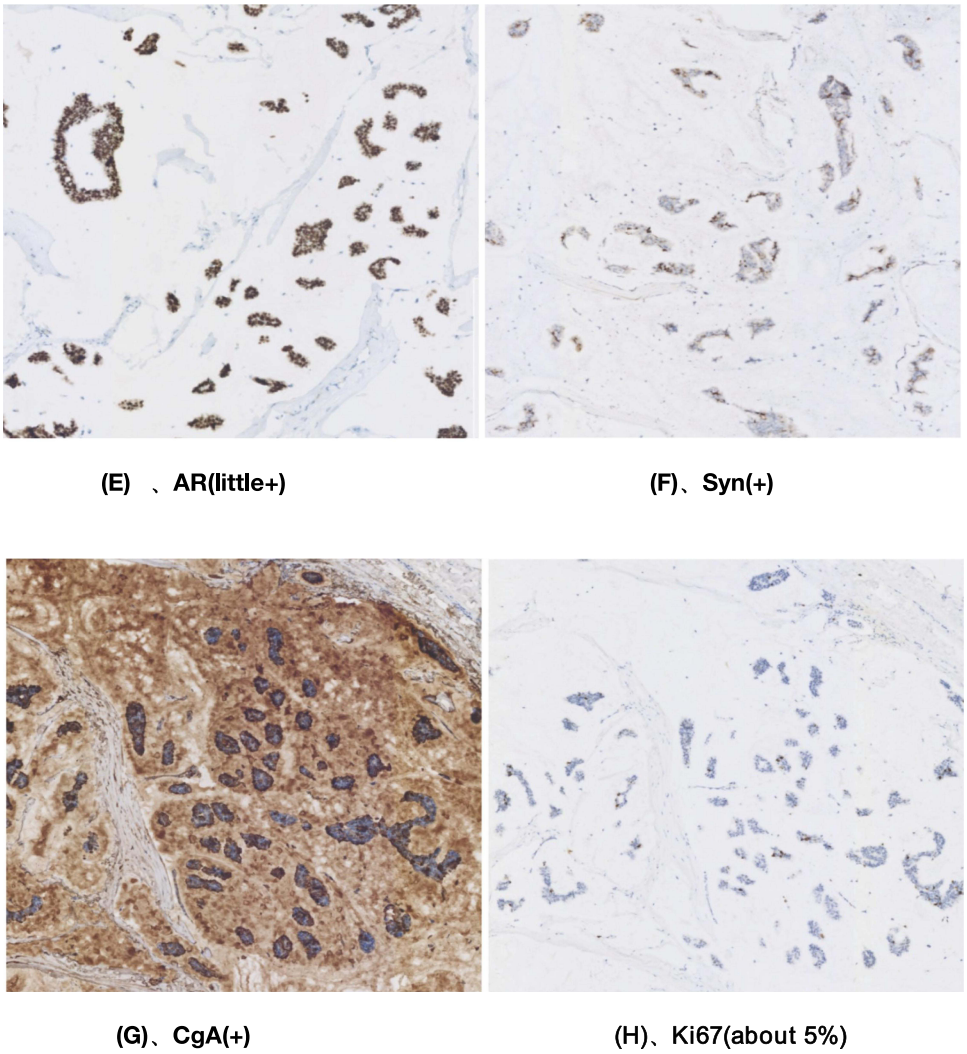


Figure 3 (**A**–**H**) Immunohistochemistry: AB+, CK7+, EMA+, ER+, PR+, weakly AR+, Syn+, CgA+, Ki67 approximately 5%.

originates from eccrine or apocrine glands, most experts believe that this tumor arises from eccrine sweat glands. Locally, it can exhibit invasive growth. Surgical excision and mohs micrographic surgery are the primary treatment, resulting in a favorable prognosis and low metastatic rates, although local recurrence remains a challenge.[6] In this case, the patient's course extended over 7 years, with the initial skin lesion starting as a papule and gradually enlarging to the size of a chickpea. We used surgical enlarged resection of the tumour due to financial reasons, and it is currently being followed up for 15 months postoperatively without recurrence.

PCMC must be distinguished from secondary mucinous carcinomas originating from the breast, digestive tract, and other specific sites, such as the bladder and lungs. The differentiation primarily relies on clinical presentation, pathological examination, and immunohistochemistry. PCMC predominantly occurs in the head and face, including the eyelids. Pathologically, the tumor is mainly located in the dermis or subcutaneous tissue. It features abundant basophilic mucin pools, with islands of epithelial-like cells floating within. Some areas may exhibit glandular lumina or incomplete tubular structures. PCMC often demonstrates morphological continuity with skin appendages, such as hair follicles or sweat glands in consecutive sections. The presence of myoepithelial cells further assists in determining whether the tumor is of cutaneous origin.[7] Immunohistochemistry (IHC) findings in PCMC include positive expression of cytokeratin spectrum antibodies (AE1/AE3), epithelial membrane antigen (EMA), and carcinoembryonic antigen (CEA), with a low Ki-67 index. Additionally, androgen receptor (AR), estrogen receptor (ER), and progesterone receptor

Table 1 Various Immunohistochemical Stains

Immunohistochemical Stain	The Role of Immunohistochemical Stain
Alcian blue staining	Alcian Blue, also known as Aisin Blue, is a copper-titanium anthocyanine-conjugated dye. This cationic dye specifically binds to anionic groups, such as carboxyl groups and sulfates in tissues, resulting in the formation of insoluble complexes. The pH of the dye is instrumental in differentiating between classes of mucus substances. For instance, at pH 2.5, mucus substances containing carboxyl groups, such as proteoglycans, hyaluronic acid, and epithelial acidic mucins, can be detected. Conversely, at pH 1.0, mucus substances with sulfates, including sulphated mucus substances, can be identified.
CK7	CK7 is a significant member of the cytokeratin family, primarily associated with migratory and glandular epithelia. It is positively expressed in the lung, ovary, breast ductal epithelium, endometrium, and mesothelial cells, while typically showing negative expression in adenocarcinomas of gastrointestinal origin. Notably, CK7 is generally absent from normal colonic and rectal mucosa.
Epithelial membrane antigen, EMA	EMA is a transmembrane glycoprotein with a relative molecular mass of 400,000, prepared by isolating and purifying the membrane glycoproteins of lactolipids secreted by mammary epithelial cells. It is widely distributed in the membrane structures of various epithelial cells, with positively expressed particles localized in both the cell membranes and cytoplasm. The labeling profiles of EMA are broadly similar to those of cytokeratins; however, its expression is not as pronounced as that of cytokeratins in keratinized epithelia. In contrast, EMA labeling is more prominent than that of cytokeratins in the adeno-epithelial cells of viscera. EMA is extensively utilized in the diagnosis and differential diagnosis of epithelial tumors, serving as a marker for epithelial cells and epithelial differentiation.
Chromogranin, CgA	CgA is a member of the chromogranin or secretogranin family and serves as a principal component of secretory granules in neuroendocrine cells. It is regarded as a relatively specific biomarker for neuroendocrine cells due to its widespread expression within the neuroendocrine system.
Synaptophysin, Syn	Syn is a specific protein that plays a crucial role in synaptic remodeling, as well as in nerve repair and regeneration. It is utilized in both the diagnosis and differential diagnosis of pheochromocytoma, ganglion cell neuroma, and paraganglioma.
Androgen receptor, AR	Positive androgen receptor (AR) expression is proportional to the degree of tissue differentiation in prostate cancer and is primarily utilized for the detection of prostate cancer and the guidance of clinical treatment.
Estrogen receptor, ER	Estrogen receptor (ER) belongs to the steroid hormone nuclear receptor family. AR positivity is observed in approximately 60–90% of ER-positive patients. Research indicates that AR-positive breast cancer patients tend to have a better prognosis compared to their AR-negative counterparts. However, AR is not yet widely implemented in clinical practice.
Ki-67	The Ki-67 antigen is a nuclear antigen expressed in proliferating cells. Due to its short half-life, it serves as a valuable indicator of apoptotic and proliferative activity. Ki-67 is expressed by all cells in the active phases of the cell cycle and has been found to correlate with tumor recurrence, grading, and staging. Additionally, the Ki-67 index can be utilized as a scale for determining the grade of tumor growth.

(PR) may show positivity. These features support the tumor's origin from eccrine sweat glands. However, in some cases, IHC results may suggest differentiation toward apocrine glands or even originate from large sweat glands. Furthermore, previous studies have indicated that the presence of myoepithelial cell components (such as P63 and CK5/6) around the tumor can aid in diagnosing primary cancer.[8] In this case, the patient's positive P63 expression further supports the diagnosis of PCMC. Metastatic mucinous carcinomas originating from the breast are more common in elderly female patients, often occurring in proximity to the breast. Immunohistochemical staining results for both PCMC and metastatic breast mucinous carcinoma are similar, making differentiation challenging. However, a thorough systemic examination to identify deep-seated breast tumors provides strong evidence for distinguishing between them. Mucinous carcinomas originating from the digestive tract are typically found in primary foci such as the rectum and colon. Pathologically, these tumors exhibit abundant cellular debris, resulting in a phenomenon known as dirty necrosis, which aids in differentiation. Immunohistochemical staining for mucinous carcinomas originating from the digestive tract usually shows positive staining for cytokeratin CK-20 and CDX-2, whereas primary mucinous carcinomas are typically negative for these markers.[9] Additionally, negative expression of TTF1, PSA, and CA125 helps exclude mucinous carcinomas originating

from the thyroid, lungs, prostate, ovaries, and other sites that may metastasize to the skin. The integration of these findings with a systemic evaluation enhances the diagnostic accuracy.

In this case, the patient is an elderly male presenting with a facial nodule. Histopathology and immunohistochemistry results indicated the following: AB+ (positive), CK7+ (positive), CK20- (negative), EMA+ (positive), P63- (negative), Calponin- (negative), TTF1- (negative), CDX2- (negative), ER+ (positive), PR+ (positive), AR weakly positive, HER2- (negative), GCDFP15- (negative), Syn+ (positive), CgA+ (positive), and Ki67 approximately 5%. Systemic examinations of the heart, lungs, digestive tract, prostate, and thyroid revealed no abnormalities, effectively ruling out metastatic mucinous carcinomas from the breast, gastrointestinal tract, lungs, and prostate. The final diagnosis was PCMC. The current treatment for this condition primarily involves local surgical excision, with wide removal of the surrounding tissue to prevent recurrence, and mohs micrographic surgery. In this case, the patient underwent local excision of the skin lesion because of economic reasons, and follow-up observations have shown no tumor recurrence. The patient is currently still under surveillance.

Ethics Statement

The patient provided written informed consent to publish not only the details of the case but also any accompanying images. The informed consent form clearly states that the institution has agreed to publish relevant information about this case.

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Disclosure

The authors report no conflicts of interest in this work.

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