

Unusual Pancreatic Metastasis of Solid Subtype Adenoid Cystic

Carcinoma: Reappraisal of MYB and CD117 Immunostaining Utility in

Liquid-Based Cytology

Short running title: Pancreatic Metastasis of Solid-Growth ACC: MYB and CD117 in Cytology

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Conflict of Interest

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Data Availability

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

Ethics Approval

Ethical approval was not required for single-case presentation. Written informed consent was obtained, and the investigation was conducted in accordance with the Declaration of Helsinki (1975).

Author Contributions

Keita Jinnouchi contributed to the diagnosis, immunocytochemical analysis, manuscript writing, and figure preparation. Yuki Teramoto contributed to the diagnosis, manuscript writing, and figure preparation and served as the corresponding author. Miho Saeki, Masahiro Hirata, and Hironori Haga contributed to the diagnosis and manuscript review.

Two-liner

36 This article describes a rare case of pancreatic metastasis of adenoid cystic carcinoma diagnosed by
37 fine-needle aspiration cytology. Immunocytochemical staining for MYB and CD117 provided critical
38 diagnostic support, highlighting the utility of liquid-based cytology in rare metastatic tumors.

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Introduction

Pancreatic metastases are uncommon and often mimic primary pancreatic tumors, complicating diagnosis. Common metastatic origins include renal cell carcinoma, lung carcinoma, and melanoma [1, 2]. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is essential for distinguishing secondary pancreatic tumors and guiding clinical management [2].

Adenoid cystic carcinoma (ACC) of the salivary glands exhibits a propensity for distant metastasis, primarily to the lungs, bones, liver, and brain [3]. However, pancreatic involvement is exceedingly rare, with only 3 cases reported [4–6]. Cytological diagnosis of ACC metastases is particularly challenging due to its variable morphology, and to date, only one cytological case [5] of pancreatic ACC metastasis has been documented a decade ago, emphasizing its rarity. Given these diagnostic challenges, a comprehensive approach incorporating cytomorphology and immunocytochemistry is crucial.

We present a case of ACC with pancreatic metastasis, emphasizing the diagnostic utility of liquid-based cytology (LBC) and MYB/CD117 immunostaining in EUS-FNA specimens. This report highlights the value of these adjunct techniques in accurate cytological diagnosis, underscoring the need for a multidisciplinary approach.

Case Presentation

An 80-year-old male with no significant medical history presented with tongue numbness three years prior. Imaging revealed a 2.5 cm mass in the left sublingual gland, which was surgically resected with left neck dissection. Histologically, the tumor exhibited classic ACC patterns (tubular, cribriform, and "Swiss cheese") but was dominated by solid sheets and nests of basaloid tumor cells (Figure 1A, B). Immunohistochemistry confirmed ACC with high-grade transformation, showing diffuse MYB positivity. Cervical lymph node metastases were present (pT2 pN3b), and the patient underwent postoperative radiotherapy (60 Gy in 30

fractions). He was regularly monitored with imaging studies.

Three years postoperatively, abdominal computed tomography (CT) detected an 18 mm hypovascular tumor in the pancreatic body. EUS-FNA was performed for diagnostic confirmation. Rapid On-Site Evaluation (ROSE) was conducted during the procedure, confirming sufficient tumor cell sampling. Cytological samples were processed using the ThinPrep® system (Hologic, Marlborough, MA, USA). In addition, air-dried smears were prepared at the time of FNA for Giemsa staining. Papanicolaou-stained ThinPrep® smears showed uniform basaloid cells with high nuclear-to-cytoplasmic ratios and indistinct nucleoli, forming predominantly cohesive clusters, with occasional solitary cells (Figure 2A). Giemsa staining of the air-dried smears revealed a metachromatic stromal mucin background (Figure 2B). Key ACC features, such as hyaline globules and cribriform or tubular structures, were absent. Immunocytochemistry was performed on ethanol-fixed LBC slides. CD117 staining (VENTANA ULTRA PLUS system, Roche; A4502, 1:200 dilution) showed cytoplasmic and membranous positivity in approximately 50% of tumor cells (Figure 2C), while MYB staining (Leica BOND III, Abcam EP769Y, 1:100 dilution) demonstrated strong nuclear positivity in approximately 20% of tumor cells (Figure 2D). Based on these findings, the lesion was diagnosed as pancreatic metastasis of ACC.

Subsequently, the patient underwent distal pancreatectomy. Histopathological examination of the resected pancreatic tumor confirmed solid-pattern ACC, with the tumor measuring 1.7 cm in greatest dimension. The tumor was predominantly (>95%) composed of solid basaloid nests, although a minor component (<5%) exhibiting tubular structures was present.

Discussion

ACC is a rare malignancy characterized by indolent but persistent growth, perineural invasion, and late distant metastases. Pancreatic metastases from ACC are exceedingly rare, with only three cases documented

[4–6]. The reported cases involved pancreatic head and tail lesions (5.6–6.6 cm) developing 2 to 15 years post-diagnosis, often discovered incidentally or presenting with nonspecific symptoms such as abdominal pain or jaundice. Given ACC’s potential for late metastatic spread, awareness of this entity in pancreatic lesions is critical.

Cytological diagnosis of ACC is inherently difficult, particularly in metastatic settings. The solid basaloid subtype, as observed in our case, poses additional challenges due to its resemblance to other malignancies. This subtype is characterized by basaloid cells arranged in solid sheets or nests, typically exhibiting small to medium size, scant cytoplasm, and hyperchromatic nuclei with mild to severe atypia. The nuclear arrangement often displays a vertical orientation towards the periphery of the cell clusters, with dispersed naked nuclei sometimes present. One of the hallmark features of ACC, including the solid subtype, is the presence of extracellular matrix globules. These globules, which may be hyaline or magenta, are not exclusive to ACC but are highly suggestive when seen in conjunction with characteristic cellular features. However, the solid subtype may exhibit fewer hyaline globules than other ACC subtypes, making the diagnosis more challenging [7]. The diagnostic difficulty is further reflected in the high false-negative rate reported in ACC fine-needle aspiration cytology, with one study by the College of American Pathologists documenting a 36.4% false-negative rate [8]. In the present case, however, the cytological features—including relatively mild nuclear atypia and the presence of basaloid cells—were not typical of primary pancreatic adenocarcinoma, which generally exhibits marked nuclear pleomorphism and irregular nuclear contours. These cytological findings, together with the patient’s known history of ACC, led us to prioritize pancreatic metastasis of ACC in the differential diagnosis. Since the last cytological report of pancreatic ACC metastasis over a decade ago, no additional cytological cases have been documented. However, a recent histology-based case report has been published [6], underscoring the continued rarity of cytologically diagnosed cases and the necessity for improved cytodiagnostic strategies.

MYB and CD117 are critical immunomarkers in ACC diagnosis. MYB is a key molecular driver of ACC,

frequently associated with *MYB::NFIB* gene fusion [9]. However, its diagnostic specificity is limited, as MYB expression has been reported in pancreatic adenocarcinomas [10]. CD117, frequently expressed in ACC, serves as a valuable adjunct marker since it is rarely expressed in pancreatic adenocarcinoma. While not entirely exclusive to ACC, CD117's co-expression with MYB strengthens diagnostic confidence, particularly when classic histological features are absent.

LBC provides superior cell preservation and standardized sample preparation compared to conventional smears, enhancing the reliability of immunocytochemical assessment. In our institution, when the aspirated material is expected to be limited, as in this case, liquid-based cytology specimens are preferentially prepared to allow subsequent immunocytochemical staining. Although LBC immunocytochemistry does not enable control tissues to be stained on the same slide, antibody performance is routinely validated against known positive control materials to ensure diagnostic reliability. This case underscores the value of integrating MYB and CD117 immunostaining in LBC samples for diagnosing pancreatic metastases of ACC, reinforcing the role of cytology in minimally invasive precision diagnostics.

Conclusion

Pancreatic metastasis of ACC is rare, and cytological diagnosis is challenging due to its varied morphological presentation. This case highlights the diagnostic value of MYB and CD117 immunostaining in LBC-prepared FNA samples, providing a robust approach for distinguishing metastatic ACC from primary pancreatic neoplasms. Given the absence of reported cytological cases in over a decade, this report underscores the need for continued awareness and refinement of cytodiagnostic methods for ACC metastases. Additionally, the subsequent histopathological confirmation following distal pancreatectomy validated the accuracy of the cytological diagnosis, reinforcing the importance of a multimodal diagnostic approach.

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Figure legends

FIGURE 1. Histopathological findings of the primary sublingual gland tumor

A. Tumor exhibits a cribriform and tubular pattern, representing the characteristic histological features of adenoid cystic carcinoma (Hematoxylin-Eosin, $\times 100$)

B. Basaloid tumor cells infiltrate in large solid nests, demonstrating an invasive growth pattern (Hematoxylin-Eosin, $\times 100$)

FIGURE 2. Cytological and immunocytochemical findings of the pancreatic metastasis

A. Cytology reveals uniform basaloid cells with high nuclear-to-cytoplasmic ratios and indistinct nucleoli, forming tightly cohesive clusters (Papanicolaou stain, $\times 400$)

B. Giemsa staining demonstrates a metachromatic stromal mucin background (Giemsa stain, $\times 200$)

C. Immunocytochemistry shows CD117 positivity in the cell membrane and cytoplasm (CD117, DAB, $\times 1000$)

D. MYB immunostaining demonstrates strong nuclear positivity (MYB, DAB, $\times 1000$)