

Poorly Differentiated Pancreatic Adenocarcinoma with Isolated Signet-Ring Cells: A Case Report

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1. Abstract

Isolated signet-ring cells within pancreatic adenocarcinoma represent an extremely rare histological variant, typically associated with poor differentiation and an unfavorable prognosis. We describe the case of a woman diagnosed with a locally advanced pancreatic neoplasm. The diagnosis was established via lymph node biopsy and immunohistochemical analysis. This report highlights the diagnostic challenges of rare pancreatic cancer subtypes and emphasizes the importance of a multidisciplinary strategy and tailored therapeutic approach.

2. Introduction

Among gastrointestinal cancers, pancreatic ductal adenocarcinoma stands out for its aggressive clinical course and high mortality. Because it is usually diagnosed at an advanced stage and responds poorly to therapy, its long-term survival rates remain extremely low [1,2]. Clinical signs are often vague, such as abdominal discomfort, weight loss, or asthenia [3]. Histologically, Pancreatic ductal adenocarcinoma (PDAC) typically presents with glandular structures and various levels of differentiation [4]. The presence of isolated signet-ring cells-mucin-filled tumor cells with peripherally displaced nuclei—is exceedingly rare in pancreatic tissue [5]. These cells are more commonly observed in gastric or colorectal mucinous carcinomas and raise concern for metastatic disease [6]. We report a case of PDAC with isolated signet-ring cells, diagnosed through lymph node biopsy and immunohistochemistry after inconclusive initial sampling and negative upper/lower endoscopy.

3. Case Presentation

A 54-year-old woman with a history of type 2 diabetes presented with persistent epigastric pain evolving over several months, along with anorexia, fatigue, and 26 kg weight loss. There was no vomiting, jaundice, or gastrointestinal bleeding. Clinical evaluation found a stable, alert patient with a BMI of 22.2 kg/m². The abdomen was tender in the epigastric area, without palpable mass or lymphadenopathy. Contrast-enhanced abdominal CT revealed a hypodense mass centered on the pancreatic head, infiltrating the mesenteric vessels and portal vein, with two nonspecific right-sided pulmonary micronodules (Figure 1). Initial endoscopic ultrasound-guided biopsy was non-diagnostic. A second biopsy of deep lymph nodes showed malignant cells with signet-ring morphology. Histology revealed poorly differentiated carcinoma. Immunohistochemistry showed CK7+ (30%), AE1/AE3++ and Ki-67 at 25%, with negative CK20, synaptophysin, and chromogranin A—favoring pancreatic origin. Upper endoscopy and colonoscopy were unremarkable. The patient was referred for systemic chemotherapy.

4. Discussion

PDAC is the most frequent pancreatic malignancy, representing >90% of cases [1]. Its global incidence is rising, ranking as the seventh leading cause of cancer-related death [2]. Prognosis remains poor due to late-stage diagnosis and resistance to therapy [3]. Recognized risk factors include

diabetes, smoking, obesity, chronic pancreatitis, and familial history [4]. Frequent mutations involve KRAS, TP53, CDKN2A, and SMAD4 [5]. Poorly differentiated PDACs are uncommon but portend a worse prognosis [6]. The presence of isolated signet-ring cells in pancreatic tumors is extremely rare [7]. When present, it is critical to rule out non-pancreatic primary sources via histology and immunostaining [8]. In this case, the clinical presentation was typical, but the signet-ring pattern made diagnosis challenging. Repeat biopsy and IHC were essential for confirmation [9]. CT imaging helped establish local vascular invasion and unresectability [10]. Biopsy of lymph nodes rather than the tumor was decisive. Literature confirms the value of repeating biopsies when results are inconclusive [11]. IHC profile (The tumor showed strong expression of cytokeratin 7 and a high proliferation index (Ki-67), while markers such as CK20 and neuroendocrine antigens were absent—supporting pancreatic ductal origin) is consistent with primary PDAC [8,12]. Similar patterns were described in rare cases reported by Yamaguchi et al. [13]. Basturk et al. also observed signet-ring features in a subset of poorly differentiated PDACs, linked to poor outcomes [6]. Adsay et al. highlighted the limited chemotherapy sensitivity of these tumors [14]. In recent studies, Damjanov et al. described the aggressive molecular and histologic profile of these variants [15]. Shah et al. emphasized the importance of IHC to avoid misdiagnosis [16]. Zhang et al. discussed their rarity and diagnostic complexity [17], while Belghiti et al. explored their developmental origins [18]. In patients deemed inoperable, combination chemotherapy—most commonly modified FOLFIRINOX—is currently the recommended initial approach offers better outcomes in fit patients [19]. In poorly differentiated tumors, responses are limited, and clinical trials may be considered [20]. Prognosis remains grim, with Patients with advanced disease typically have a short life expectancy, often limited to

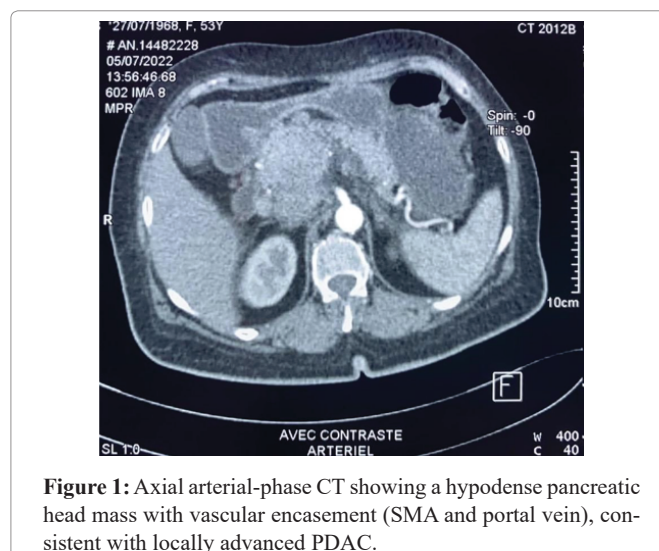


Figure 1: Axial arterial-phase CT showing a hypodense pancreatic head mass with vascular encasement (SMA and portal vein), consistent with locally advanced PDAC.

a few months despite treatment [21]. Tumor biology, microenvironment, and genetics influence response and outcomes [22-24].

5. Conclusion

This case illustrates an unusual presentation of PDAC with isolated signet-ring cells and poor differentiation. Diagnostic confirmation required repeated biopsy and thorough IHC analysis. Given its aggressive nature, multidisciplinary and personalized care is essential, along with careful exclusion of other primary tumors.

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