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Case report of a rare carcinosarcoma of the ampulla of Vater with a monoclonal histologic variant

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Abstract

Carcinosarcoma of the ampulla of Vater is exceedingly rare, with only three prior well-documented cases. It behaves more aggressively than conventional ampullary adenocarcinoma, and surgical resection with a pancreaticoduodenectomy with regional lymphadenectomy remains the primary treatment when feasible. This 62-year-old female with prior cholecystectomy presented with progressive jaundice and fatigue. Workup revealed a cholestatic pattern and a mass at the pancreatic uncinate process causing distal biliary obstruction. Endoscopic biopsy confirmed invasive adenocarcinoma with intact mismatch repair proteins. She underwent pancreaticoduodenectomy, revealing a 6.2×5.8×3.9 cm ampullary mass invading the duodenal muscularis propria and extending into the pancreas. Histology demonstrated biphasic morphology with malignant epithelial and sarcomatoid components, consistent with carcinosarcoma. The postoperative course was initially uneventful; however, the patient re-presented with metastatic disease and expired shortly on comfort-focused care. This case report highlights the importance of tumor immunohistochemistry to identify a potential future therapeutic target.

Introduction

Carcinosarcoma of the ampulla of Vater are aggressive biphasic neoplasms comprised of both malignant epithelial (carcinomatous) and mesenchymal (sarcomatous) parts [1]. The pathophysiology and histogenesis of these tumors remain debated [1,2]. Earlier studies suggest the two independent neoplasms; however, accumulating molecular evidence supports a different theory where the sarcomatoid component arises from the carcinomatous component through an epithelial to mesenchymal transition [1,2]. The location of carcinosarcomas of the hepatobiliary tract carry a poor prognosis. In the largest analysis reviewing 131 cases of carcinosarcoma of the hepatobiliary tract, the overall 1-, 3-, and 5-year survival rates were 44%, 29.3%, and 27% respectively.[3] Authors found that advanced stage was the most significant prognostic factor [3].

The current literature documents only three isolated reports of carcinosarcoma of the ampulla of Vater [2,4,5]. The first reported case in 1997 describes the tumor composed of intermixed carcinomatous elements (adenocarcinoma plus squamous cell carcinoma) and sarcomatous elements [4]. Their immunohistochemistry showed focal cytokeratin reactivity in the sarcomatoid element, with positive staining for desmin and actin in the adjacent tissue [4]. The second case report in 1999 detailed tubular adenocarcinoma and sarcomatoid spindle cells and authors hypothesized that the sarcomatoid element arose from the adenocarcinoma via metaplastic transformation because both components stained positive for keratin and CA19-9 [2]. Lastly, the third ampullary carcinosarcoma was a 67-year-old male with mixed osteosarcomatous, small cell neuroendocrine, and adenocarcinoma components, the first case with this combination documented [5].

Because of the rarity, no population data exists. Our case report documents the fourth case of carcinosarcoma of the ampulla of Vater and focuses on the similarities and differences in the immunohistochemistry and pathology to prior cases.

Case introduction

A 62-year-old woman (BMI 16.8) with no past medical history and a prior surgical history of laparoscopic cholecystectomy in the summer of 2023 presented in early 2024 with progressive jaundice and fatigue.

Workup

Outpatient liver function tests revealed a total bilirubin of 7.8 mg/dL, alkaline phosphatase in the 240s U/L, AST in the 60s U/L, and ALT in the 130s U/L, consistent with a cholestatic pattern. An abdominal ultrasound demonstrated a dilated Common Bile Duct (CBD) measuring 14 mm. Subsequent contrast-enhanced CT scan of the abdomen revealed a mass at the level of the pancreas/uncinate process, causing distal biliary obstruction (Figures 1 and 2).

The patient underwent Endoscopic Retrograde Cholangiopancreatography (ERCP) with biliary stent placement a week later to relieve obstruction. Biopsies taken from the ampullary region during the procedure revealed invasive adenocarcinoma. Immunohistochemical analysis demonstrated intact mismatch repair proteins (MLH1, MSH2, MSH6, PMS2).

Initial hospital admission

The next month, the patient underwent a pancreaticoduodenectomy (Whipple procedure) (Figure 3). The postoperative course was uneventful. She was extubated uneventfully, ambulated by POD 3, and had return of bowel function by POD 5. She tolerated a regular diet and was discharged home in stable condition on POD 7.

Pathology

Final surgical pathology revealed a 6.2×5.8×3.9 cm malignant biphasic neoplasm in the ampulla of Vater. The tumor demonstrated invasion into the duodenal submucosa and muscularis propria, extending 0.5 cm into the pancreatic parenchyma. All resection margins were negative for invasive carcinoma. Twenty-four regional lymph nodes were resected, all negative for metastatic disease.

Immunohistochemistry

Microscopically, the tumor consisted of two distinct components. The epithelial component displayed variable morphology, including intestinal-type malignant glandular formation, areas with squamoid features, and sheets of cells with hyperchromatic nuclei and eosinophilic cytoplasm. The mesenchymal component was composed of stellate and highly pleomorphic cells within a myxoid background, with occasional multinucleated giant cells, hyperchromatic nuclei, and frequent mitotic figures as well as extensive necrosis. Immunohistochemical staining demonstrated positivity for CAM5.2, AE1/AE3, and CDX2; focal positivity for synaptophysin and p40 (each <30%); and negativity for desmin and myogenin. These findings support carcinosarcoma of the ampulla of Vater diagnosis.

Postoperative outcome

The patient represented to the hospital two months following her Whipple with complaints of shortness of breath. CT imaging at that time demonstrated findings consistent with metastatic disease. A therapeutic thoracentesis was performed for symptomatic right pleural effusion, and cytologic evaluation of the pleural fluid revealed reactive mesothelial and mixed inflammatory cells without evidence of malignancy. A few days following her hospital admission, the patient and her family met with the palliative care team. They declined hospice services but elected to pursue comfort-focused care. The patient was discharged home and passed away shortly thereafter.

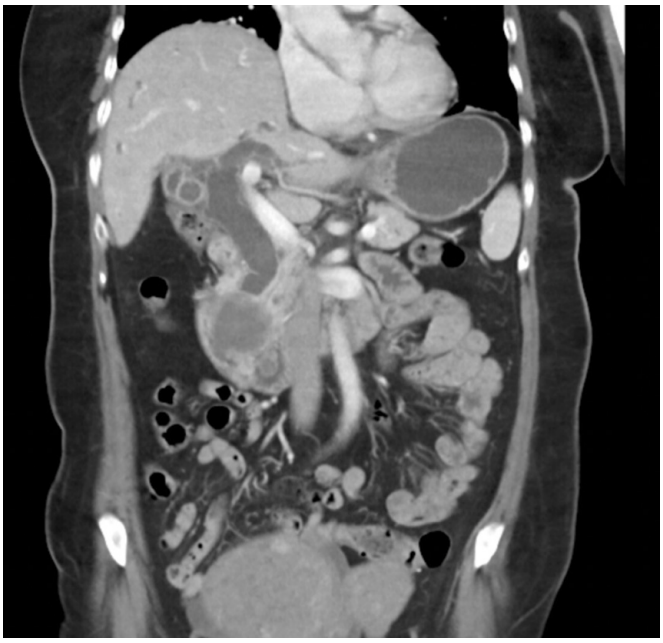


Figure 1: Coronal section of patient demonstrating the carcinosarcoma of the Ampulla of Vater abutting the pancreatic head with dilatation of the common bile duct and pancreatic duct proximally.

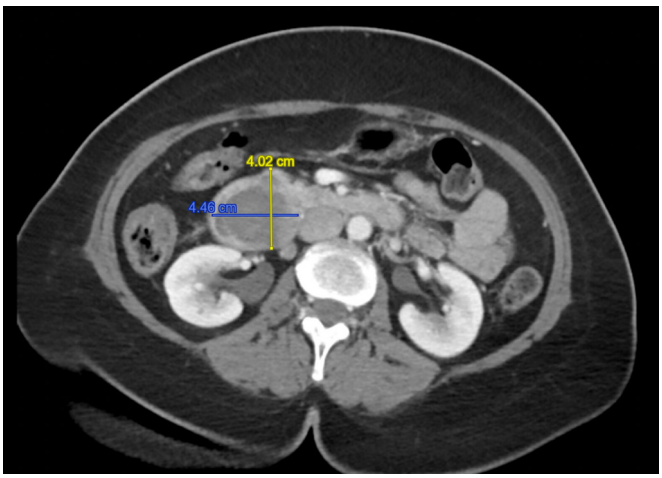


Figure 2: Axial cross section demonstrating the heterogeneity of the neoplasm and initial size of the mass when identified.

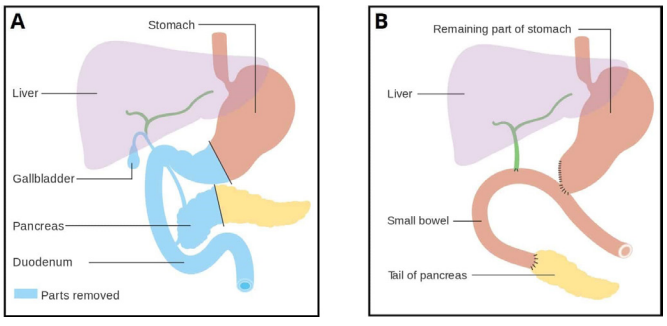


Figure 3: Illustration of a pancreaticoduodenectomy. Depiction of the patient's anatomy prior to and after surgery [12].

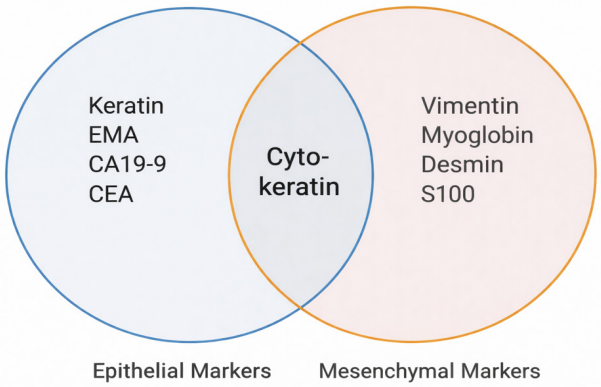


Figure 4: Venn diagram of epithelial and mesenchymal immunohistochemical markers. Our ampulla of Vater carcinosarcoma had cyto-keratin in both the epithelial (left) and mesenchymal (right) components [13].

Discussion

The most common IHC finding in carcinosarcomas of the ampulla of Vater demonstrate dual epithelial and mesenchymal differentiation [2,4,5]. With such an exceedingly rare biphasic neoplasm with no optimal treatment, understanding the immunohistochemistry and pathology is next clinical step to help physicians diagnose and treat carcinosarcoma of the ampulla of Vater [1-5].

Carcinomatous components typically follow a pattern that is positive for cytokeratins, CEA, and epithelial markers such as CA19-9 [5,6]. In contrast, sarcomatous components are positive for vimentin, desmin, smooth muscle actin, and myoglobin [5,6]. This distinction is important because co-expression of vimentin and or cytokeratin has been used as evidence to support the epithelial to mesenchymal metaplastic transition theory [2,6,7]. A comprehensive review of pancreatic biphasic carcinosarcoma concluded that most are monoclonal in origin and appear to arise from the carcinoma element [8]. In our case study, the tumor immunohistochemical staining showed positivity for synaptophysin and p40, which are expected in the carcinomatous component. However, it also expressed positivity for CAM5.2 and AE1/AE3 in the sarcomatous component, which are cytokeratins [9]. These findings parallel the immunohistochemistry of the first case report where the tumor shows focal cytokeratin reactivity in the sarcomatous element (Figure 4). We describe another case supporting the theory that the sarcomatous tissue may arise from the other biphasic epithelial tissue (Figure 4). This is important because finding a therapeutic target directed at these cytokeratins or may affect the growth of both elements in these biphasic neoplasms.

To date, there are no FDA approved immunologic therapies that directly target cytokeratins as an antigen in clinical practice [10,11]. The closest FDA approved therapies target epithelial surface antigens including EpCAM (catumaxomab), Trop-2 (sacituzumab), Nectin-4 (enfortumab), and tissue factor (tisotumab) [10,11]. However, a key distinction is that these antibodies target transmembrane glycoproteins on the cell surface and not the intracellular intermediate filament cytokeratins detected by CAM5.2 and AE1/AE3 on IHC that would be required for our biphasic tumor [11]. For now, we argue that immunohistochemical staining is an important diagnostic tool and future case reports illustrating the IHC patterns can add to the emerging spectrum of carcinosarcoma of the ampulla of Vater.

A large limitation is the paucity of evidence surrounding carcinosarcomas of the ampulla of Vater, periampullary duodenal region, and related biliary tract carcinosarcoma reports. As only the fourth case report on ampullary carcinosarcoma, there is no long-term outcome data and the spectrum of IHC remain too few to draw any conclusions from. A future review comparing the similarities and differences in IHC from all biphasic carcinosarcomas of the hepatobiliary and periampullary tract would better elucidate patterns.

Conclusion

Carcinosarcoma of the ampulla of Vater is an exceedingly rare biphasic malignant tumor of both carcinomatous and sarcomatous components with early metastasis, poor 5-year survival, and no optimal treatment. Our patient's pathology is consistent with earlier reports that the tumors may be of monoclonal origin on immunohistochemistry because all previous case reports demonstrate focal intermediate cytokeratin positivity within both components. By understanding the spectrum of histologic variants, the goal is to diagnose these neoplasms earlier and potentially identify novel molecular therapeutic targets.

Author declarations

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Conflict of interest: The authors declare no conflicts of interest.

Consent to participate: Consent was not obtained due to patient deceased prior to initiation.

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12. Figure created by the author using Microsoft Copilot. Pancreaticoduodenectomy (Whipple procedure) schematic. 2026.

13. Microsoft Copilot. Venn diagram of epithelial and mesenchymal immunohistochemical markers. Generated illustration. 2026.