Crimson Publishers
Wings to the Research

Case Report

Unusual Survival Beyond 24 Months in an Untreated Case of Periampullary Carcinoma with Neuroendocrine Differentiation

Aiman Majid[1]*, Maheen Zahid[2], Taimur Arain[3] and Naila Zahid[4]

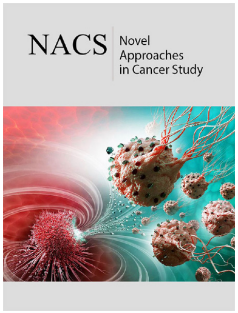
[1]Medical oncologist, Liaquat national Hospital, Pakistan

[2]Agha Khan University Hospital, Pakistan

[3]M.B.B.S, Ziauddin University Hospital, Pakistan

[4]Head of Department oncology, Liaquat National Hospital, Pakistan

ISSN: 2637-773X



***Corresponding author:** Aiman Majid, Medical oncologist, Liaquat National Hospital, Pakistan

Submission: April 09, 2025
Published: April 29, 2025

Volume 8 - Issue 2

How to cite this article: Aiman Majid*, Maheen Zahid, Taimur Arain and Naila Zahid. Case Report on Survival of Patient with Glioblastoma Multiforme After Incomplete Resection and Role of Bevacizumab. Nov Appro in Can Study. 8(2). NACS. 000683. 2025.
DOI: 10.31031/NACS.2025.08.000683

Abstract

Periampullary tumors are neoplasms that arise near the ampulla of Vater and may originate from the pancreas, duodenum, distal common bile duct (CBD), or ampullary complex. Timely diagnosis and appropriate surgical intervention often depend on the initial evaluating physician. We present the case of a 60-year-old man who presented to a tertiary care hospital in June 2023 with obstructive jaundice. He underwent CBD stenting, and imaging studies including ERCP and CT scan suggested periampullary carcinoma. A subsequent biopsy confirmed the diagnosis of malignancy. However, due to severe financial constraints and symptomatic relief, the patient was lost to follow-up. Remarkably, he remained clinically stable and active for two years without receiving any oncological treatment. He later re-presented with epigastric pain and nausea. Repeat imaging showed localized disease, and he subsequently underwent a Whipple procedure. Histopathology confirmed stage IIB (pT3b N0) periampullary carcinoma of the intestinal type. The patient received adjuvant chemotherapy with FOLFOX for six months. This case highlights the need for further research into prognostic factors and molecular profiling to better predict survival outcomes in periampullary carcinoma.

Introduction

Cancer that arises in the vicinity of the ampulla of Vater-such as in the pancreas, duodenum, distal common bile duct, or structures of the ampullary complex is classified as periampullary carcinoma. In contrast, ampullary cancer specifically originates within the ampullary complex, distal to the confluence of the common bile duct and pancreatic duct.

Most intestinal mucosal neoplastic transformations occur near the ampulla of Vater more frequently than at any other site in the small intestine. The incidence of ampullary carcinoma is approximately 4 to 10 cases per million population, underscoring its rarity [1]. It accounts for only 6% of lesions arising in the periampullary region [2], yet it is a significant cause of obstructive jaundice responsible for approximately 20% of such cases [3]. Preoperatively, it can be challenging to distinguish primary ampullary carcinoma from other periampullary tumors. However, true ampullary cancers generally have a better prognosis than periampullary malignancies originating from the pancreas or bile duct. Resectability rates are higher, and the five-year survival rate is approximately 30% to 50% in patients with limited lymph node involvement. In contrast, fewer than 10% of patients with completely resected, node-positive pancreatic cancer survives beyond two years. Therefore, an aggressive approach to the diagnosis and treatment of periampullary tumors is essential to ensure that patients with these comparatively favorable malignancies receive optimal care.

Furthermore, ampullary and periampullary adenocarcinomas can be classified into distinct subsets based on histologic subtype and immunohistochemical staining patterns, which have important prognostic implications [2,4-6]. In a retrospective study of 208 patients treated for ampullary adenocarcinoma in Sydney, Australia, those with a histomolecular pancreaticobiliary phenotype characterized by positive staining for MUC1 and negative for CDX2 and MUC2 (regardless of CK20 status) had significantly worse outcomes compared to those with an intestinal phenotype. The intestinal subtype typically demonstrates an immunophenotypic profile similar to that of colonic-type adenocarcinomas, such as positivity for CK20, CDX2, or MUC2 with negative MUC1, or positivity for CK20, CDX2, and MUC2 irrespective of MUC1 staining. Median survival in patients with the pancreaticobiliary phenotype was 16 months, compared to 116 months in those with the intestinal phenotype [3].

Identification of prognostically relevant subgroups has also been achieved through gene expression profiling, combined with immunohistochemical staining for cytokeratins 7 and 20 [7]. However, molecular techniques such as these are not yet ready for routine clinical application.

For periampullary cancer, surgery remains the primary modality of treatment in cases of resectable disease. Currently, there are no clear guidelines recommending the use of histological typing to guide the selection of adjuvant therapy. Instead, adjuvant treatment decisions are primarily based on the tumor's histological subtype [8].

Case Presentation

A 60-year-old man, a known case of diabetes, initially presented to a tertiary care hospital with complaints of yellow discoloration of the eyes. Workup revealed obstructive jaundice, and he subsequently underwent ERCP on June 19, 2021. The procedure revealed a periampullary mass characterized by a bulky, large ampulla with an ulcerated ampullary orifice and a distal CBD stricture. An adequate papillotomy was performed, followed by the placement of a plastic stent.

A CT scan showed significant dilation of the CBD and pancreatic duct, with abrupt cut-offs at their distal ends and mild soft tissue thickening in the periampullary region. The CBD measured 1.4cm in caliber, while the pancreatic duct measured 0.8cm. Heterogeneous signal intensities were noted within the CBD, along with a meniscus sign at its distal end suggestive of sludge with possible small calculi. Subtle abnormal heterogeneous signals were also noted in the pancreatic duct, possibly due to sludge or tiny calculi. Mild to moderate intrahepatic biliary dilation was also observed. A biopsy of the periampullary mass was later performed, which came back negative for malignancy.

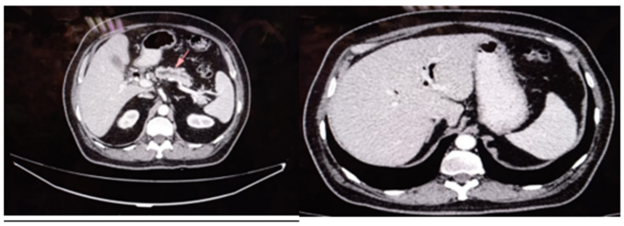
In October 2021, the patient presented again with melena and a low haemoglobin level. He underwent an esophagogastroduodenoscopy, which revealed LA grade B esophagitis, pan-gastric erythema and a periampullary mass.

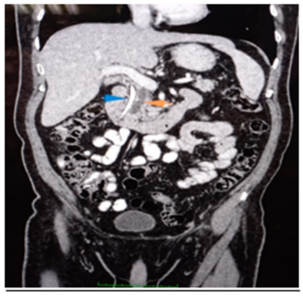
ERCP revealed abnormal periampullary mucosa. A biopsy was taken, which showed dysplasia with invasion into the muscularis mucosa. The previously placed blocked stent was removed. A cholangiogram demonstrated a distal CBD stricture and a dilated CBD; a 10Fr, 9cm plastic stent was placed. This time, the biopsy came back positive for malignancy. However, due to financial constraints, the patient was lost to follow-up until June 2023, when he re-presented with complaints of epigastric pain and nausea.

ESOPHAGASTRODUDENOSCOPY

Esophagogastroduodenoscopy was repeated on May 24, 2022. The first part of the duodenum revealed a previously deployed plastic CBD stent, which was blocked and removed using a snare. A large, friable growth was observed surrounding the ampullary opening. Deep cannulation was achieved easily, and contrast dye was injected. The cholangiogram showed a moderately dilated common bile duct (CBD) with a long distal narrowing. A small stone and sludge were noted at the distal CBD. An extractor balloon was used to remove the stone and sludge, and an occlusion cholangiogram confirmed ductal clearance. A plastic stent measuring 11.5 Fr and 10cm in length was deployed in the CBD beyond the stricture, with free flow of dye and bile observed through the stent. Biopsy results confirmed a moderately differentiated infiltrating adenocarcinoma.

Ct scan of the Whole Abdomen





There is no pleural or pericardial effusion seen. Pulmonary parenchymal appears clear, there is biliary stent noted with pneumobilia. There is air fluid noted within the gall bladder lumen. No evidence of calcific gall stones. No evidence of focal mass lesion seen within the liver. Pancreatic duct is grossly dilated measuring approximately a diameter of 13mm at the level of the ampulla. At the level of the ampulla there is a hypodensity medial to the biliary stent measuring 14 x 15 x 26mm (ap x ts x cc) in dimensions. Remaining pancreatic parenchyma is mildly atrophied.

Operative Findings

The patient underwent a Whipple procedure on June 20, 2023. Intraoperative exploration revealed no evidence of diaphragmatic,

hepatic, omental, peritoneal, mesenteric, or serosal metastases. A tumor measuring approximately 2 × 3cm was identified in the periampullary region. There was no local invasion into the portal vein or surrounding structures. An en bloc tumor resection was performed. Pancreatic reconstruction was carried out with a pancreatojejunostomy, and biliary and enteric continuity was restored via loop hepaticojejunostomy and gastrojejunostomy, respectively.

Histopathology

Frozen Section (Pancreatic Tissue): Benign

A) Specimen: Pancreaticoduodenectomy (Whipple's procedure)

a) Tumor Characteristics:

a. Moderately differentiated infiltrating adenocarcinoma with neuroendocrine differentiation

b. Tumor size: 3.1 × 3 cm

c. Tumor site: Periampullary / ampullary duodenal region

d. Tumor invasion: Through duodenal wall into pancreatic and peripancreatic soft tissue

b) Surgical Margins:

a. Common bile duct margin: Tumor-free (3cm from tumor)

b. Pancreatic neck margin: Tumor-free (2.5cm from tumor)

c. Retroperitoneal (uncinate) margin: Tumor-free (2.5cm from tumor)

d. Proximal margin: Tumor-free (5cm from tumor)

e. Distal margin: Tumor-free (24cm from tumor)

c) Lymph Nodes:

a. 13 lymph nodes examined

b. 0 positive for malignancy (0/13)

c. Final TNM Staging: pT3b N0

B) Gastroduodenal lymph nodes: Five benign lymph nodes are seen (0/5) (Figure 1 & 2).

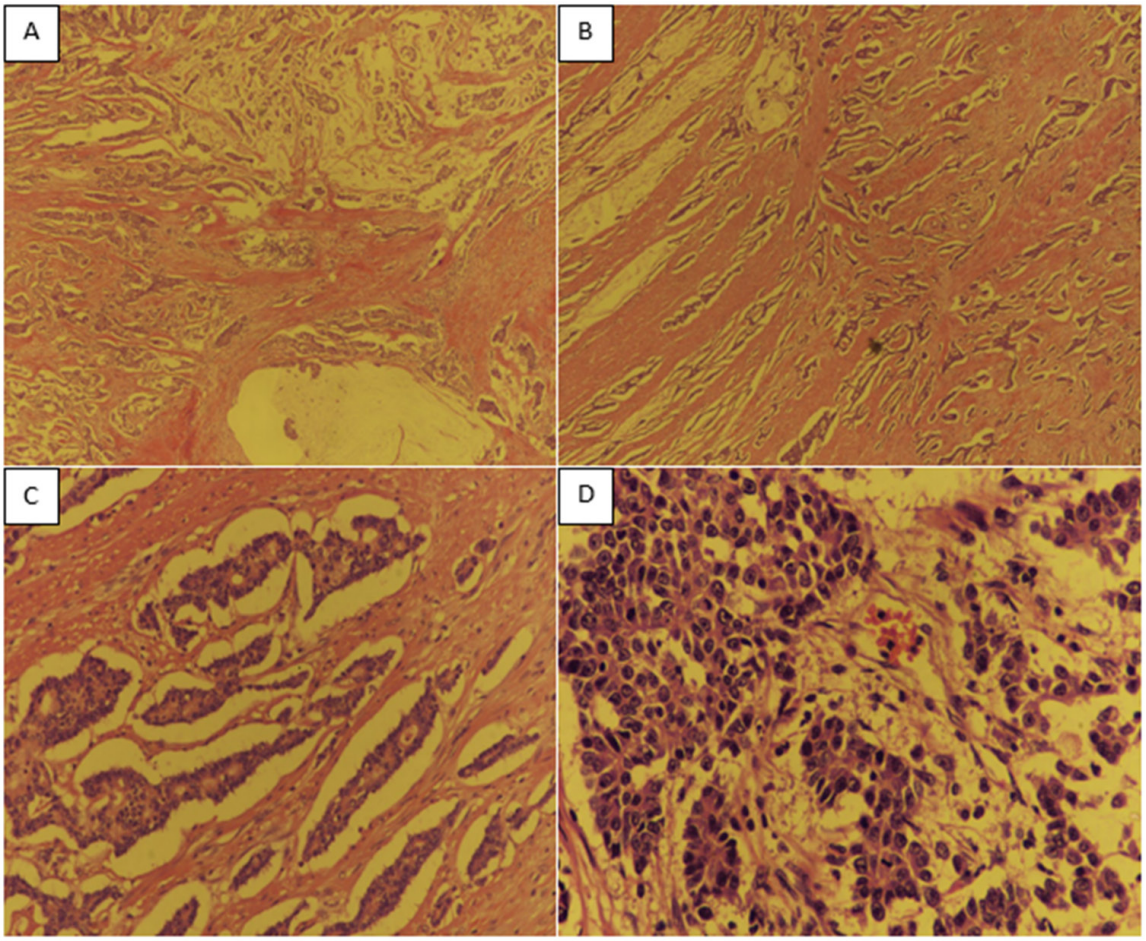


Figure 1: A & B) Hematoxylin and eosin (H & E)-stained section at 100X magnification showing tumor arranged in cords, trabeculae, and clusters with extracellular mucin. C) H & E-stained section at 200X showing tumor cells showing glandular configuration. D) H & E-stained section at 400X magnification revealing tumor with nuclear stratification.

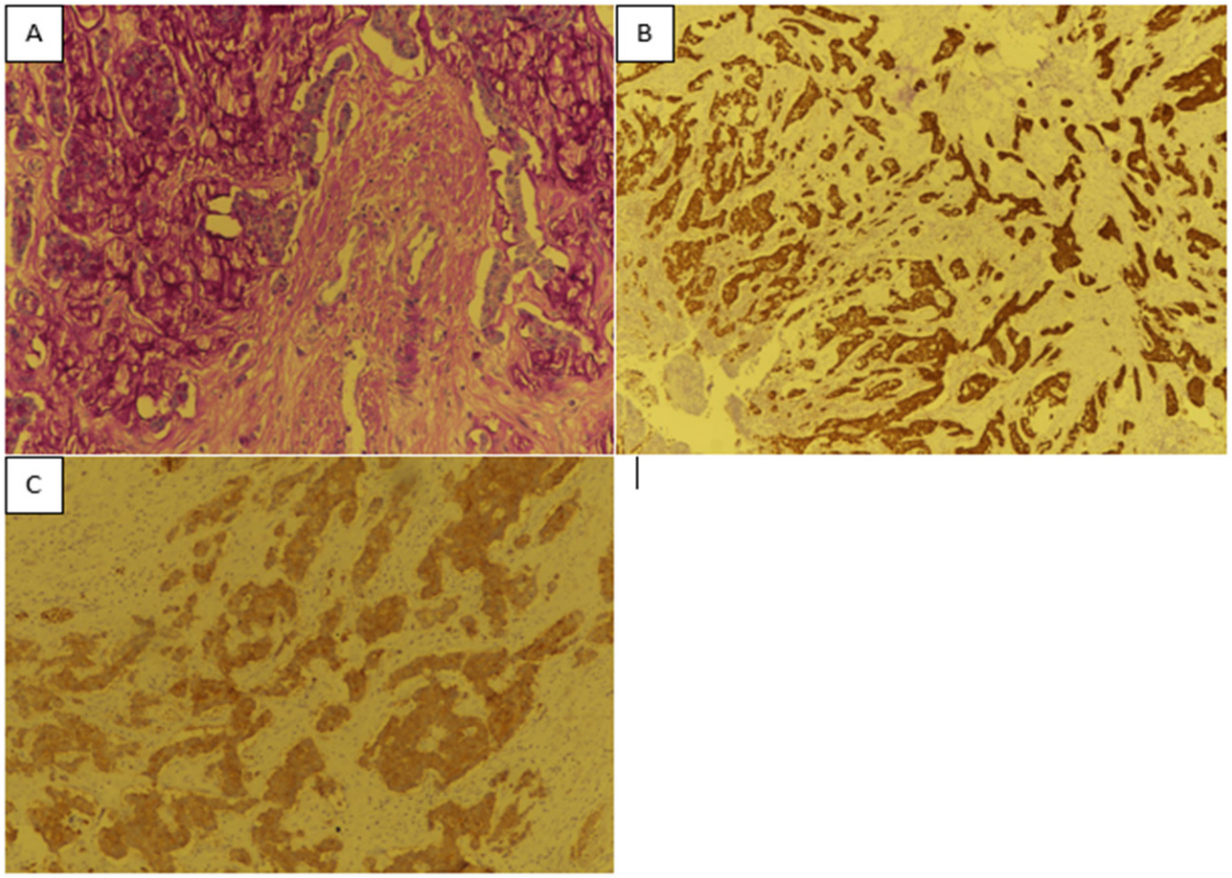


Figure 2: A) Periodic acid schiff with diastase (PASD) stain highlighting intracellular and extracellular mucin. B) CDX2 immunostain showing diffuse nuclear positivity in tumor cells. C) Synaptophysin immunostain showing diffuse positivity in tumor cells.

Patient has received adjuvant chemotherapy with FOLFOX for 6 months as management of periampullary carcinoma intestinal type, stage IIb, and is currently disease-free on follow-up scans.

Discussion

The management of peri-ampullary carcinoma depends on the resectability of the disease in non-metastatic cases. After surgical resection, the histomolecular phenotype, combined with lymph node status, predicts the chances of recurrence and the need for adjuvant treatment. Three subsets of ampullary adenocarcinomas have emerged, each associated with significantly different survival outcomes. Patients with a node-negative, non-pancreaticobiliary histomolecular phenotype have a good prognosis, with an expected 5-year survival rate of 88%. In contrast, patients with a node-positive, pancreaticobiliary phenotype have a poor prognosis, with only a 20% survival rate at 5 years. The remaining patients, which include those with a node-positive, non-pancreaticobiliary phenotype and a node-negative, pancreaticobiliary phenotype, have an intermediate prognosis, with a 47% 5-year survival rate. Histopathological significance has also been noted in other studies, with results comparable to those found in two additional independent cohorts: 90 patients from Glasgow, Scotland, and 46 from Verona, Italy. However, other studies have shown no significant overall survival difference between the intestinal and pancreaticobiliary subtypes of ampullary cancer [6]. Due to these inconsistent findings, the most recent 2017 Tumor, Node, Metastasis (TNM) staging classification of the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) did not include histomolecular phenotype as a component of its prognostic stage groups, as is the case for other tumor sites.

Further studies are needed to identify the importance of prognostically relevant subgroups using gene expression profiling in conjunction with immunohistochemical staining for cytokeratins 7 and 20 [7]. The role of adjuvant chemotherapy according to histomolecular subtype and how this evidence could be used to individualize treatment decisions remains unclear. The impact of adjuvant therapy on outcomes according to histomolecular phenotype could not be addressed in the study, as only a minority of patients (64 of 208) in all three cohorts received adjuvant chemotherapy, and it was not randomly assigned [1].

A recent analysis of a cooperative group study, which initially aimed to examine the effectiveness of adjuvant therapy in peri-ampullary cancers, found no notable improvement in the pancreaticobiliary type compared to the intestinal type of ampullary cancers when comparing the use of adjuvant therapy to no adjuvant

therapy. This conclusion was drawn from a retrospective evaluation of the original prospective, randomized study [9]. However, a prospective study of treatment selection based on histomolecular phenotype is needed before conclusions can be drawn regarding the clinical significance of histomolecular phenotype.

At present, adjuvant therapy recommendations for patients with ampullary cancer follow guidelines established for pancreatic cancer rather than intestinal cancer. Hence, surgical resection remains the primary therapeutic option to improve long-term survival through local resection (ampullectomy), pancreaticoduodenectomy, and pylorus-preserving pancreaticoduodenectomy. Pancreaticoduodenectomy is the widely accepted treatment for peri-ampullary carcinomas, with resection rates ranging from 20% to 50%. However, survival outcomes after resection vary significantly due to the different histological sources and similar anatomical positions of these cancers. After surgical resection, the 5-year survival rates differ: 33% to 68% for ampullary carcinoma, 23% to 30% for distal common bile duct carcinoma, 25% to 59% for duodenal adenocarcinoma and 5% to 20% for pancreatic carcinoma. Metastatic or advanced peri-ampullary carcinomas are characterized by a worse prognosis, with 2-year survival rates ranging from 5% to 10% [8].

In this case, we focus on the patient's exceptional survival without any treatment. This case explores potential factors contributing to this prolonged survival, such as favorable tumor biology, immune response, or spontaneous regression of the tumor. The significance of this case challenges the conventional understanding of the disease.

Conclusion

The curative treatment option for peri-ampullary carcinoma is surgery for resectable cases. In this patient, fortunately, surgery remained a curative option despite a delay in treatment of 2 years. This highlights the remarkable survival outcome of the patient with peri-ampullary carcinoma without any treatment and underscores the need for further investigation into the factors influencing favorable outcomes in this subset of patients. Additionally, it reflects the potential implications for future treatment strategies and the importance of individualized patient management.

References

1. Van Dyke AL, Shiels MS, Jones GS, Pfeiffer RM, Petrick JL, et al. (2019) Biliary tract cancer incidence and trends in the United States by demographic group, 1999-2013. Cancer 125(9): 1489-1498.
2. Zimmermann C, Wolk S, Aust DE, Meier F, Saeger HD, et al. (2019) The pathohistological subtype strongly predicts survival in patients with ampullary carcinoma. Sci Rep 9(1): 12676.
3. Palazzo L (1998) Staging of ampullary carcinoma by endoscopic ultrasonography. Endoscopy 30 Suppl 1: A128-A131.
4. Chang DK, Jamieson NB, Johns AL, Scarlett CJ, Pajic M, et al. (2013) Histomolecular phenotypes and outcome in adenocarcinoma of the ampulla of vater. J Clin Oncol 31(10):1348-1356.
5. Schueneman A, Goggins M, Ensor J, Saka B, Neishaboori N, et al. (2015) Validation of histomolecular classification utilizing histological subtype, MUC1, and CDX2 for prognostication of resected ampullary adenocarcinoma. Br J Cancer 113(1):64-68.
6. Perkins G, Svrcek M, Bouchet-Doumenq C, Voron T, Colussi O, et al. (2019) Can we classify ampullary tumours better? Clinical, pathological and molecular features. Results of an AGEO study. Br J Cancer 120(7): 697-702.
7. Shaib WL, Sharma R, Brutcher E, Kim S, Maithel SK, et al. (2014) Treatment utilization and surgical outcome of ampullary and duodenal adenocarcinoma. J Surg Oncol 109(6): 556-560.
8. Duan Z, Zhang Y, Tang Y, Gao R, Bao J, et al. (2022) Adjuvant therapy for periampullary carcinoma and the significance of histopathological typing: A systematic review. Transl Oncol 20: 101414.
9. Overman MJ, Zhang J, Kopetz S, Davies M, Jiang ZQ, et al. (2013) Gene expression profiling of ampullary carcinomas classifies ampullary carcinomas into biliary-like and intestinal-like subtypes that are prognostic of outcome. PLoS One 8(6): e65144.