

CASE REPORTS

A Rare Case of Early-Onset Periapillary Adenocarcinoma in a Neurofibromatosis Type 1 Patient

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Abstract:

Neurofibromatosis type 1 (NF1) is a common autosomal dominant disorder primarily associated with neurocutaneous manifestations. Gastrointestinal involvement, though less recognized, can include both benign and malignant neoplasms. We describe a rare case of a 26-year-old woman with NF1 presenting with progressive obstructive jaundice. Imaging revealed a periapillary mass, and histopathology confirmed a moderately differentiated adenocarcinoma. Ultimately, the patient underwent surgical intervention.

This case highlights the diagnostic challenges of rare gastrointestinal malignancies in NF1 patients, particularly in resource-limited settings. Clinicians should maintain a high index of suspicion for malignant GI lesions in NF1 patients presenting with unexplained jaundice. Early multidisciplinary evaluation is essential to improve outcomes.

Keywords: Neurofibromatosis type 1, periapillary carcinoma, obstructive jaundice, ERCP.

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Introduction:

Neurofibromatosis type 1 (NF1), also known as von Recklinghausen disease, is one of the most common autosomal dominant genetic disorders, with an estimated incidence of approximately 1 in 3,000 live births globally. It results from mutations in the NF1 gene on chromosome 17q11.2, which encodes neurofibromin—a tumor suppressor protein that negatively regulates the RAS/MAPK signaling pathway. Loss of neurofibromin function leads to increased cell proliferation and tumorigenesis in multiple tissues, including those of neural, cutaneous, and gastrointestinal origin.^{1,2} The

clinical diagnosis of NF1 is established using the National Institutes of Health (NIH) criteria, which include features such as six or more café-au-lait macules, axillary or inguinal freckling, cutaneous or plexiform neurofibromas, Lisch nodules of the iris, distinctive osseous lesions, and/or a first-degree relative with NF1.³ While cutaneous and neurological manifestations are well recognized, visceral involvement—particularly of the gastrointestinal (GI) tract—is underappreciated but clinically significant. Gastrointestinal manifestations occur in approximately 10% to 25% of patients with NF1 and span a wide range of pathologies. These

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include benign tumors such as ganglioneuromas and neurofibromas, as well as malignant entities like gastrointestinal stromal tumors (GISTs), neuroendocrine tumors, and adenocarcinomas.⁴⁻⁶ Among these, periampullary tumors—including those originating from the ampulla of Vater, distal common bile duct, duodenum, or pancreatic head—are particularly rare and pose diagnostic and therapeutic challenges.⁷ GISTs are the most commonly reported GI tumors in NF1 patients. Unlike sporadic GISTs, NF1-associated GISTs typically lack KIT and PDGFRA mutations, suggesting a distinct molecular pathogenesis.^{5,8} In contrast, periampullary adenocarcinomas in NF1 are exceedingly rare but may exhibit aggressive behavior, occur at a younger age, and necessitate complex surgical interventions such as pancreatoduodenectomy.^{9,10} The mechanism underlying periampullary adenocarcinoma in NF1 is poorly understood, but recent evidence suggests that epithelial neoplasms may arise independently of the classic neurofibromin pathway. This raises questions about alternative mechanisms of epithelial tumorigenesis in NF1 beyond its well-established neural crest involvement.¹¹ Moreover, in resource-limited settings, early diagnosis is hampered by restricted access to advanced imaging, histopathology, and molecular diagnostics, often resulting in delayed intervention and worse outcomes. We are presenting a rare case of moderately differentiated periampullary adenocarcinoma in a young woman with NF1, highlighting the importance of heightened clinical vigilance and early multidisciplinary involvement, particularly in resource-constrained health care environments.

Case Presentation:

A 26-year-old woman with a known history of NF1—evidenced by multiple café-au-lait spots, cutaneous neurofibromas, and a positive family history—was admitted to the Department of Hepatology at tertiary Medical College Hospital

in September 2024 with complaints of progressive jaundice for 2 months. This was associated with pale stool, dark urine, intense pruritus. Initial Evaluation revealed Total bilirubin: 17.6 mg/dL (Direct: 14.1 mg/dL) and ALP: 325 U/L. ALT, AST, albumin, PT/INR within normal limits, Viral markers: Negative, CA 19-9: 13, Autoimmune and metabolic profiles: Unremarkable, Imaging: MRCP: Showed narrowing at terminal CBD suggestive of stricture involving the distal CBD with upstream biliary and pancreatic ductal dilatation, distended gallbladder with sludge, and features of multifocal cholangitis. ERCP was performed in December 2024, and a plastic stent was placed. Biopsy was obtained from the periampullary growth; however, the histo-pathology was inconclusive. In the absence of a definitive tissue diagnosis, surgical intervention was deferred, and the patient was advised regular follow-up. Post-ERCP, the patient's symptoms improved significantly with resolution of jaundice. In March 2025, she presented again with recurrent jaundice, dark urine, upper abdominal pain (dull, non-radiating, unrelated to meals), intermittent fever (up to 103°F), and 2 kg weight loss. There were no prodromal symptoms, GI bleeding, or signs of chronic liver disease. On Examination: Deep jaundice and mild anemia, Multiple café-au-lait spots and cutaneous neurofibromas, Abdominal exam reveals tender hepatomegaly (6 cm) with firm and smooth liver edge, and a palpable gallbladder. Repeat Investigations revealed, CBC: Hb 8.3 g/dL, ESR 103 mm/hr, WBC 21,172/mm³ (Neutrophils 88%), Platelets 54,7362/mm³, Liver enzymes: S. bilirubin 11.8 mg/dL, ALP 363 U/L, CA 19-9: <2.06, MRCP: Showed a periampullary growth suspicious for cholangiocarcinoma involving the terminal CBD with CBD dilated to 3 cm, intrahepatic biliary dilatation, and presence of a stent, Histopathology (repeat biopsy): Moderately differentiated adenocarcinoma.



Figure-1: A :cutaneous neurofibroma , B : MRCP showing perampullary growth and dilated CBD and IHBD , C : CT film showing perampullary growth

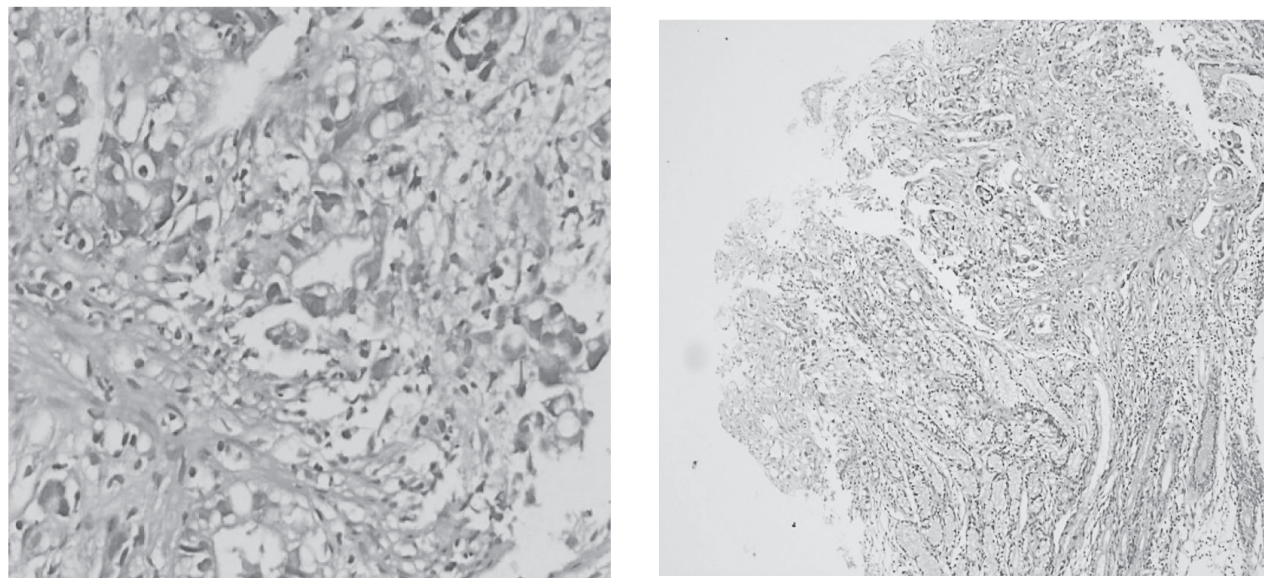


Figure-2: Histopathology showing Moderately differentiated adenocarcinoma case management

Case Management: The biliary stent was removed and patient was transferred for surgical intervention.

Case Discussion:

Periampullary tumors in patients affected by Neurofibromatosis Type 1 (NF-1) are usually carcinoids¹¹ or stromal tumors⁶ and, rarely, adenocarcinomas.⁷ We report a case of an adenocarcinoma of the ampulla of Vater¹³ in a 24-year-old woman with NF-1 admitted to the hospital with jaundice and undergoing pancreato-duodenectomy. The ampullary and periampullary adenocarcinomas in NF-1

patients have peculiar features, suggesting a widespread predisposition to cancer development in periampullary tissues and requiring widely demolitive surgery.¹⁴ Moreover, they occur at a younger age than those occurring in non-NF-1 patients, are often operable and may present long survival.¹⁴ The recurrent obstructive pattern, radiological evidence, and histopathology confirmed periampullary adenocarcinoma in this case. Early diagnosis was challenged by resource limitations, leading to a delay in histological confirmation. This case

underscores the need for high clinical suspicion and timely oncological referral in similar NF1 patients presenting with unexplained cholestatic jaundice.

Conclusion:

This case highlights a rare presentation of periampullary adenocarcinoma in a young woman with Neurofibromatosis Type 1 (NF1), underscoring the importance of considering gastrointestinal malignancies in NF1 patients with unexplained cholestatic symptoms. Although NF1 is classically associated with neural and cutaneous tumors, this case expands the clinical spectrum to include early-onset epithelial cancers such as periampullary adenocarcinoma. Diagnostic delays due to resource limitations and limited access to advanced imaging—further complicated timely intervention. Despite these challenges, endoscopic management, imaging, and multidisciplinary care ultimately led to diagnosis and referral for surgery. Clinicians should maintain a high index of suspicion for GI malignancies in NF1 patients presenting with jaundice or other atypical symptoms. Early recognition and referral are crucial, especially in low-resource settings, to improve outcomes. Further research is needed to understand the mechanisms and optimal management of such rare malignancies in NF1.

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