

Biology Over Imaging: Duodenal Adenocarcinoma Recurrence Presenting as a Pancreatic Head Mass in Lynch Syndrome

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Abstract

Duodenal adenocarcinoma (DA) is a rare gastrointestinal malignancy with an increased incidence in patients with Lynch syndrome (LS). Although recurrence following resection is recognised, patterns of relapse are typically predictable, most commonly involving the liver, lymph nodes, or peritoneum. Presentation as a pancreatic mass is exceedingly uncommon and poses a significant diagnostic and treatment challenge. We report the case of a 47-year-old man with PMS2-associated LS who underwent curative resection for DA in 2021. Four years later, he presented with a pancreatic head mass that demonstrated radiological features consistent with a locally advanced (LA) primary pancreatic ductal adenocarcinoma (PDAC). Initial clinical and imaging findings strongly supported this diagnosis. The patient underwent six months of neoadjuvant chemotherapy with significant tumour regression, leading to pancreaticoduodenectomy. Unexpectedly, the final histopathological evaluation revealed the lesion to be a recurrence of the original DA rather than a new PDAC.

This report highlights a rare and misleading pattern of recurrence in LS, where tumour biology overrides conventional anatomical assumptions. It underscores the importance of maintaining diagnostic vigilance in patients with hereditary cancer syndromes and supports an aggressive, multidisciplinary approach, including neoadjuvant therapy, even in cases initially presumed to represent locally advanced PDAC. Recognition of such atypical presentations is essential not only for optimising management but also for reinforcing the central role of tumour biology in guiding diagnosis, therapeutic decision-making, and future research in hereditary malignancies.

Categories: General Surgery, Radiology, Oncology

Keywords: diagnostic dilemma, duodenal adenocarcinoma, hereditary cancer, lynch syndrome, neoadjuvant chemotherapy, pancreatic ductal adenocarcinoma mimic, pancreatic head mass, pancreaticoduodenectomy, recurrence, tumour biology

Introduction

Lynch syndrome (LS) is an autosomal dominant hereditary cancer predisposition syndrome caused by germline mutations in DNA mismatch repair (MMR) genes, most commonly in MLH1, MSH2, MSH6, and PMS2, and is associated with an increased risk of colorectal and several extracolonic malignancies, including small bowel adenocarcinoma [1]. Duodenal adenocarcinoma (DA), although rare in the general population, occurs with increased frequency in patients with LS, with a reported lifetime risk of approximately 4%, significantly higher than in the general population [2]. DA accounts for less than 1% of all gastrointestinal malignancies, and its rarity contributes to the limited evidence guiding management and surveillance strategies [3,4].

Recurrence following resection of DA is well recognised, with reported rates ranging between 40 and 60%, most commonly involving the liver, regional lymph nodes, and peritoneum [5,6]. Patterns of recurrence are generally predictable, with distant metastases predominating [6]. Overall survival following curative resection varies widely, with reported five-year survival rates ranging from 25% to 60%, depending on stage and nodal involvement [6]. Disease-free survival is similarly variable, reflecting both tumour biology and the lack of standardised adjuvant treatment strategies [6,7].

Pancreatic ductal adenocarcinoma (PDAC) remains one of the most aggressive malignancies, with a significant proportion of patients presenting with locally advanced (LA) disease at diagnosis [8]. Neoadjuvant chemotherapy has become an established strategy in locally advanced PDAC, with a subset of patients demonstrating tumour regression sufficient to allow subsequent curative resection [9]. However, radiological differentiation between primary pancreatic malignancy and other peri-pancreatic pathologies remains challenging, particularly in patients with a history of malignancy [10].

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We report this case to highlight the rare isolated pancreatic presentation of recurrent DA in the setting of LS and the significant radiological overlap with pancreatic malignancy. The case underscores the limitations of relying solely on anatomical and imaging-based assumptions in hereditary cancer syndromes and emphasises the importance of tumour biology, multidisciplinary evaluation, and individualised treatment strategies in guiding complex oncological management [10].

Case Presentation

A 47-year-old man presented in May 2021 with a three-month history of unintentional weight loss, fatigue, altered bowel habits, and intermittent melaena. He had no significant past medical history and was not taking any regular medications. His family history was notable for multiple malignancies, including colorectal cancer in his paternal uncles, mesothelioma in a paternal uncle, pancreatic cancer in a paternal aunt, and skin cancer in his grandfather. Contrast-enhanced CT demonstrated features of upper gastrointestinal obstruction secondary to a semi-annular lesion centred at the duodenojejunal flexure. Fluorodeoxyglucose positron emission tomography-CT (FDG PET-CT) demonstrated increased tracer uptake corresponding to the primary lesion, with no evidence of distant metastatic disease (Figure 1).

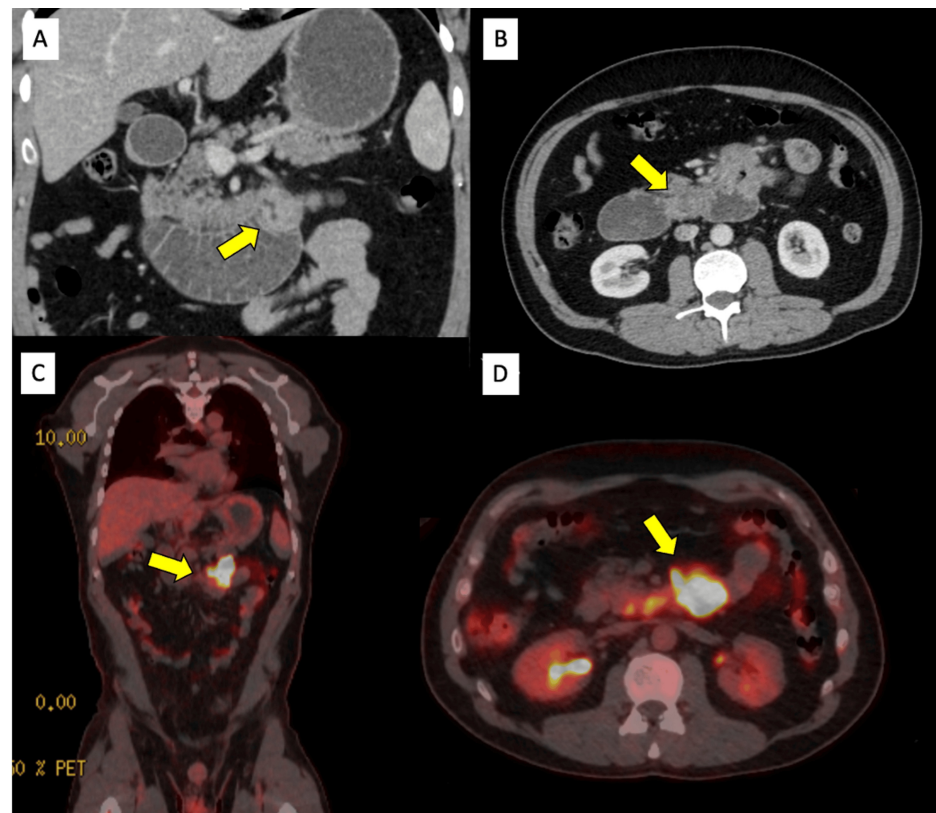


FIGURE 1: Contrast-enhanced CT and FDG PET-CT demonstrating primary DA at presentation (2021)

(A) Coronal contrast-enhanced CT showing a semi-annular mass at the duodenojejunal flexure causing luminal narrowing (yellow arrow). (B) Axial contrast-enhanced CT demonstrating the same lesion (yellow arrow) associated with proximal duodenal dilatation consistent with obstruction. (C) Coronal FDG PET-CT demonstrating intense FDG uptake at the site of the primary tumour (yellow arrow), consistent with metabolically active malignancy. (D) Axial FDG PET-CT confirming focal FDG avidity corresponding to the lesion (yellow arrow), with no evidence of distant metastatic disease

CT: computed tomography; FDG PET-CT: fluorodeoxyglucose positron emission tomography-computed tomography; DA: duodenal adenocarcinoma

Upper gastrointestinal endoscopy confirmed a tight stricture at this level, and histopathological analysis of biopsy specimens revealed a moderately differentiated adenocarcinoma. Following multidisciplinary team (MDT) discussion, the tumour was staged as T3N1M0. Two months later, the patient underwent distal duodenectomy with cholecystectomy. Histopathological examination demonstrated a 43 mm moderately differentiated adenocarcinoma with serosal involvement and metastases in multiple regional lymph nodes, with clear resection margins. Final pathological staging was pT4N2 (6/16) LV1PN1R0. He subsequently completed a six-month course of adjuvant chemotherapy with oxaliplatin and 5-fluorouracil, over the following six months, which was well tolerated.

Surveillance imaging over the subsequent two years demonstrated no evidence of disease recurrence. During follow-up, germline genetic testing identified a pathogenic PMS2 variant (c.736_741del; p.Pro246fs), confirming a diagnosis of LS. The patient was subsequently enrolled in a hereditary cancer surveillance programme and received counselling regarding colonoscopic surveillance and aspirin-based chemoprevention.

Approximately four years after initial resection, he re-presented with a three-week history of right upper quadrant pain, pale stools, and mild jaundice. Contrast-enhanced CT demonstrated a 30 × 28 mm hypoaattenuating mass in the pancreatic head, associated with biliary and pancreatic ductal dilatation. The lesion was radiologically assessed as locally advanced pancreatic head malignancy, with approximately 90° encasement of the portal vein and in contact with the superior mesenteric artery (SMA). FDG PET-CT confirmed a solitary FDG-avid lesion confined to the pancreatic head, with no evidence of distant metastatic disease (Figure 2).

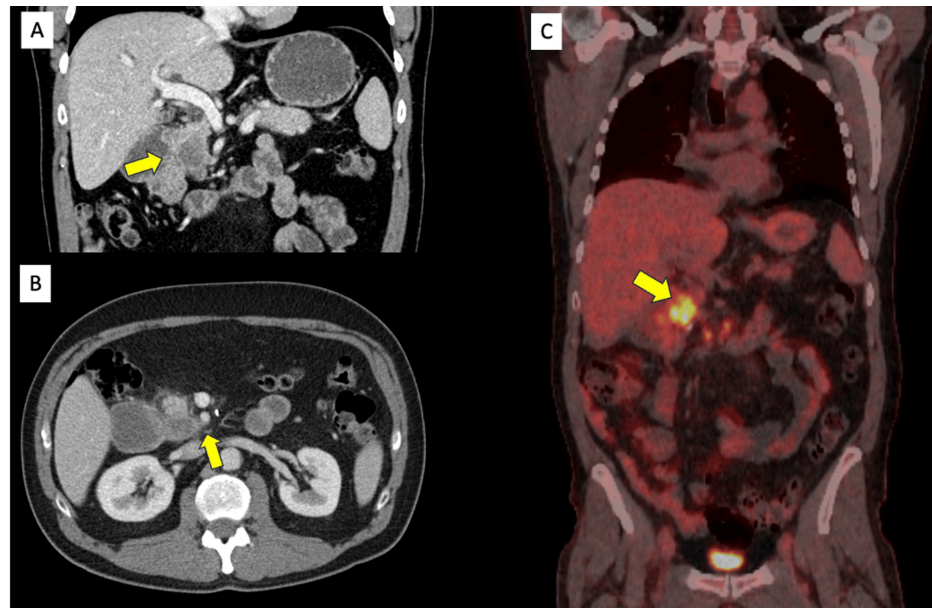


FIGURE 2: Contrast-enhanced CT and FDG PET-CT demonstrating pancreatic head mass at re-presentation (January 2025)

(A) Coronal contrast-enhanced CT showing a mass in the head of the pancreas (yellow arrow). (B) Axial contrast-enhanced CT demonstrating tumour abutment and contact with the SMA (yellow arrow). (C) Coronal FDG PET-CT demonstrating intense FDG uptake within the pancreatic head mass (yellow arrow), consistent with metabolically active disease

CT: computed tomography; FDG PET-CT: fluorodeoxyglucose positron emission tomography-computed tomography; SMA: superior mesenteric artery

Endoscopic ultrasound (EUS)-guided biopsy demonstrated a moderately differentiated adenocarcinoma with intestinal-type features. Immunohistochemistry showed a CK7-/CK20+/CDX2+ profile, which is atypical for primary PDAC and raised suspicion for recurrence of the previously resected duodenal primary. These findings confirmed the lesion as a recurrence of the original duodenal primary, despite its pancreatic location. The case was discussed at the MDT meeting, and systemic therapy with neoadjuvant intent was recommended. In the context of underlying LS, a de novo pancreatic primary was considered plausible.

Systemic chemotherapy with FOLFIRINOX was commenced. Interim contrast-enhanced CT assessment after six cycles demonstrated a reduction in tumour size, although persistent contact with the SMA was noted, and the disease remained locally advanced. Further cycles of chemotherapy were administered, and repeat imaging following completion of chemotherapy with 11 cycles, demonstrated significant tumour regression, with reduction in size to 11 × 8 mm, indicating treatment response (Figure 3). The lesion was now considered resectable, and the patient was offered pancreaticoduodenectomy.

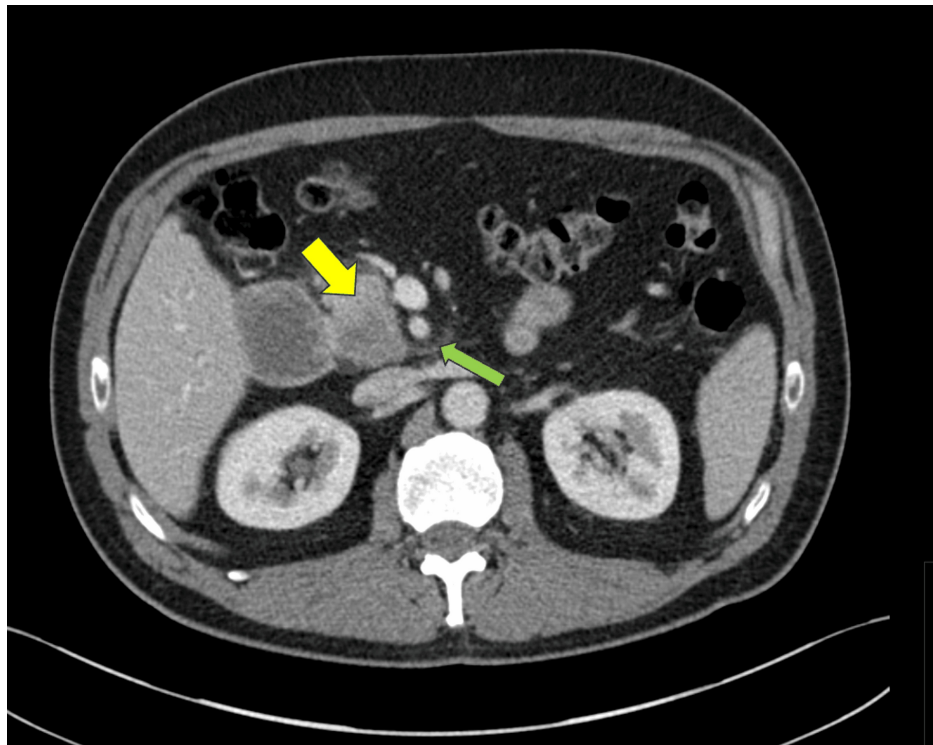


FIGURE 3: Contrast-enhanced CT demonstrating tumour downstaging following neoadjuvant chemotherapy (August 2025)

Axial contrast-enhanced CT showing a residual pancreatic head lesion (yellow arrow) with restoration of a clear fat plane separating the tumour from the SMA (green arrow), consistent with interval tumour regression and improved resectability

CT: computed tomography; SMA: superior mesenteric artery

The procedure was uneventful, and the postoperative course was uncomplicated. The patient was discharged in good clinical condition. Histopathological examination of the resected specimen demonstrated a 30 mm moderately differentiated intestinal-type adenocarcinoma involving the duodenum, ampulla of Vater, and pancreatic parenchyma, with lymph node metastases identified in 11 of 22 nodes examined. Resection margins were free of tumour.

Immunohistochemistry showed tumour cells positive for CK20 and CDX2 and negative for CK7, supporting an intestinal phenotype. The overall morphological and immunophenotypic features were consistent with recurrence of the previously resected DA rather than a primary PDAC (Figure 4).

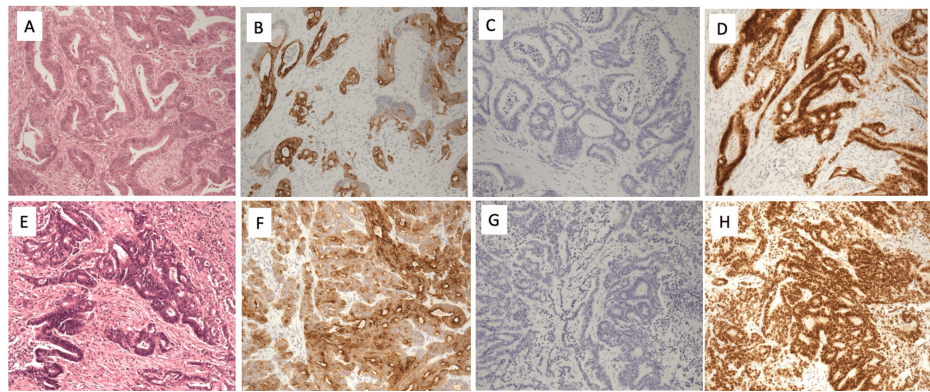


FIGURE 4: Histopathological and immunohistochemical comparison between the primary DA and recurrent pancreatic lesion

(A-D) Primary DA resected in 2021 demonstrating moderately differentiated intestinal-type adenocarcinoma on haematoxylin and eosin staining (A), positive CK20 staining (B), absent CK7 expression (C), and retained nuclear CDX2 expression (D). (E-H) Recurrent pancreatic head tumour resected following pancreaticoduodenectomy in 2025, demonstrating morphologically similar moderately differentiated intestinal-type adenocarcinoma on haematoxylin and eosin staining (E), positive CK20 staining (F), absent CK7 expression (G), and retained nuclear CDX2 expression (H), supporting recurrence of the original duodenal primary rather than primary pancreatic ductal adenocarcinoma

DA: duodenal adenocarcinoma; CK7: cytokeratin 7; CK20: cytokeratin 20; CDX2: caudal type homeobox 2

The patient developed early disease recurrence four months postoperatively, with FDG PET-CT demonstrating extensive FDG-avid lymphadenopathy within the abdomen extending into the mediastinum, without evidence of solid organ metastases (Figure 5). Given the underlying PMS2-associated LS and progressive recurrent disease, systemic immunotherapy with pembrolizumab was initiated following multidisciplinary discussion. He has received six cycles to date and remains under active oncological follow-up, with response assessment imaging planned.

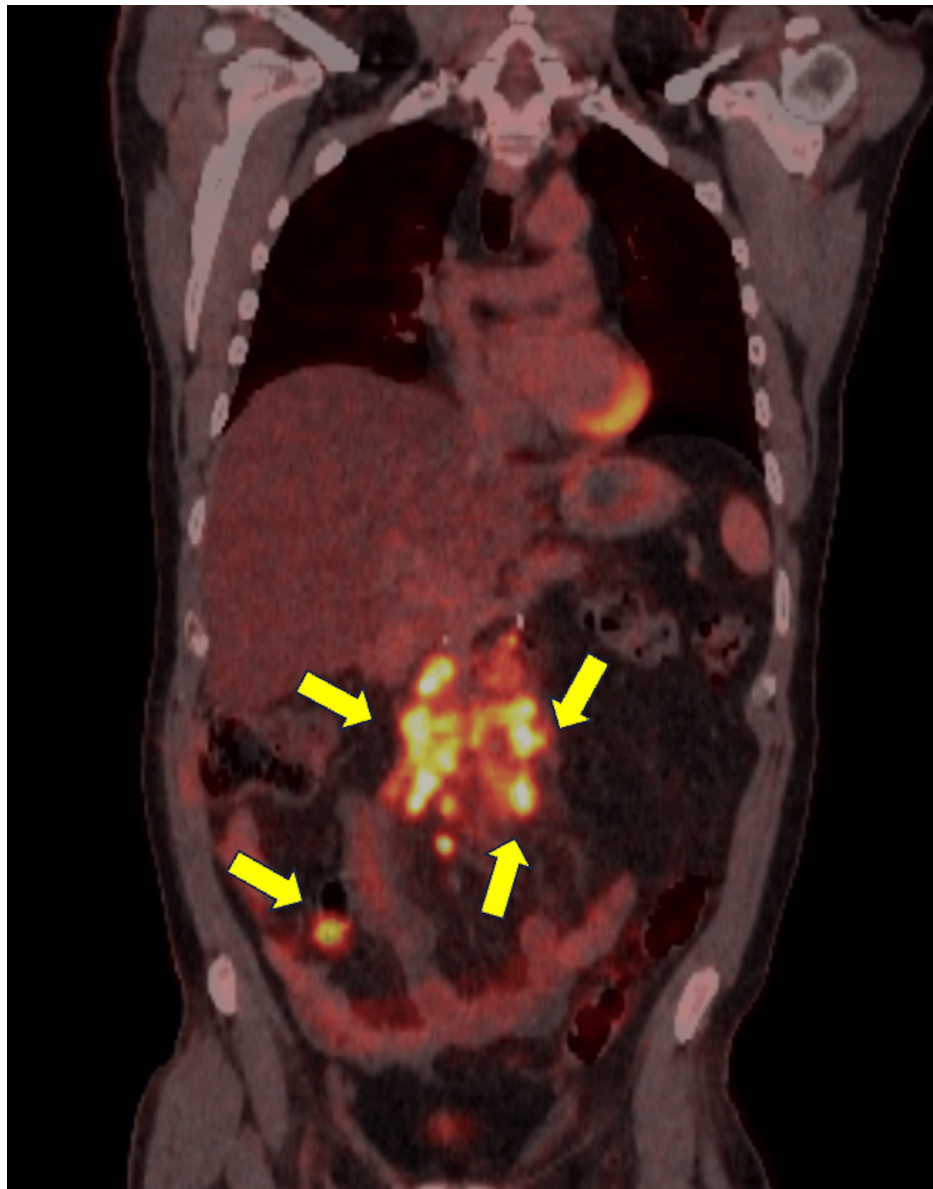


FIGURE 5: FDG PET-CT demonstrating early postoperative recurrence with extensive lymph node involvement (January 2026)

Coronal FDG PET-CT showing extensive FDG-avid lymphadenopathy within the abdomen (yellow arrows), consistent with widespread nodal metastatic disease, without evidence of solid organ metastases

FDG PET-CT: fluorodeoxyglucose positron emission tomography-computed tomography

A clinical timeline summarising the patient's disease course, treatments, recurrence, and ongoing management is presented in Figure 6.

Clinical Timeline of Recurrent Duodenal Adenocarcinoma in Lynch Syndrome

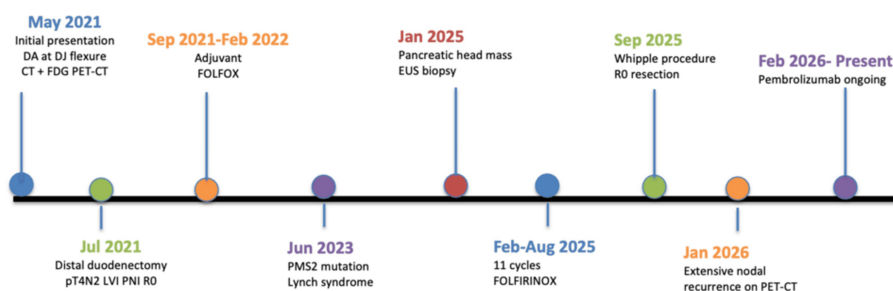


FIGURE 6: Clinical timeline summarising the presentation, treatment course, recurrence, and ongoing management of recurrent DA associated with LS

The timeline illustrates the initial presentation with DA in 2021, surgical and systemic treatments, subsequent pancreatic head recurrence in 2025, neoadjuvant chemotherapy response enabling pancreaticoduodenectomy, postoperative nodal recurrence, and initiation of pembrolizumab immunotherapy in 2026

DA: duodenal adenocarcinoma; DJ: duodenojejunal; FDG PET-CT: fluorodeoxyglucose positron emission tomography-computed tomography; EUS: endoscopic ultrasound; LS: Lynch syndrome

Image credit: authors

Discussion

DA is a rare malignancy, accounting for less than 1% of gastrointestinal cancers, with an increased incidence observed in patients with LS due to underlying MMR deficiency [1,2]. Despite this association, the natural history and optimal management of DA remain poorly defined, largely owing to its rarity and the absence of prospective data [3]. Surgical resection remains the cornerstone of treatment for localised disease, often combined with adjuvant chemotherapy extrapolated from colorectal cancer protocols [3,6]. However, outcomes remain variable, reflecting both tumour biology and the heterogeneity of disease presentation [6,7].

Recurrence following resection of DA is well recognised, most commonly involving the liver, regional lymph nodes, and peritoneum, reflecting haematogenous and lymphatic dissemination patterns [6]. Recurrence occurs in approximately 50% of patients and typically within the first one to two years after surgery, with early distant metastases reported in a substantial proportion of high-risk patients, reflecting aggressive tumour biology and limited disease-free survival [6,11,12]. Reported median disease-free survival ranges between 20 and 64 months, with five-year disease-free survival rates of approximately 40-45% following curative resection [11,13].

While systemic therapy may achieve meaningful tumour regression and prolong overall survival, durable disease-free survival remains uncommon, and most patients ultimately experience disease recurrence or progression [3,6]. Notably, late recurrence beyond three years is infrequently reported, suggesting that such presentations may reflect distinct tumour biology. In this context, recurrence at four years, as observed in the present case, represents a relatively late event and further supports the role of tumour biology in disease behaviour.

Systemic therapy plays a critical role in recurrent and advanced DA, with emerging evidence demonstrating meaningful survival benefit despite historically poor outcomes. Retrospective data suggest that chemotherapy improves prognosis compared to best supportive care, with progression-free survival extended by approximately eight months and median overall survival reaching 20.4 months with oxaliplatin-based regimens, alongside objective response rates of up to 50% [14]. Combination and targeted chemotherapy regimens have demonstrated encouraging survival outcomes, with selected cases achieving durable disease control, including complete remission and prolonged recurrence-free intervals [14].

This case illustrates a highly unusual pattern of recurrence, in which DA re-presented as a solitary pancreatic head mass closely mimicking a primary pancreatic malignancy. The atypical site and pattern of recurrence are notable, particularly in the absence of disseminated solid organ disease. Furthermore, the marked response to neoadjuvant chemotherapy, enabling subsequent curative-intent pancreaticoduodenectomy, highlights the potential for selected patients to benefit from an aggressive, multidisciplinary approach. This favourable treatment response further underscores the importance of tumour biology as a key determinant

of disease behaviour and prognosis.

The subsequent early postoperative recurrence, manifesting as extensive lymph node disease without solid organ involvement, adds further complexity and highlights a heterogeneous disease course. The initiation of immunotherapy in this context reflects evolving, biology-driven treatment strategies in LS-associated malignancies, where conventional paradigms may not fully apply. This case, therefore, emphasises the importance of integrating tumour biology, clinical context, and multidisciplinary decision-making in guiding management.

Conclusions

This report highlights a rare pattern of recurrence in LS-associated DA, presenting as a pancreatic head mass mimicking a primary pancreatic malignancy. It underscores the limitations of relying solely on anatomical and radiological assessment and supports an aggressive, multidisciplinary approach, as demonstrated by the favourable response to neoadjuvant chemotherapy enabling curative-intent resection. The subsequent early lymph node-only recurrence and use of immunotherapy reflect a heterogeneous, biology-driven disease course. The report emphasises the importance of vigilant surveillance, flexible management strategies, and the growing role of tumour biology in guiding treatment decisions in hereditary malignancies.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Acquisition, analysis, or interpretation of data: Evangelia Florou, Memoona Mukhtar, Muhammad Sarmad Mukhtar, Rohit Sasidharan

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Critical review of the manuscript for important intellectual content: Evangelia Florou, Parthi Srinivasan, Rohit Sasidharan

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Disclosures

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