TAURUNUM
MEDICAL JOURNAL
VOL 39 No 2 2025
DOI: 10.63696/TMJ202502183

SYNCHRONOUS GASTROINTESTINAL STROMAL TUMOR AND PANCREATIC DUCTAL ADENOCARCINOMA: A RARE CASE REPORT WITH CLINICAL IMPLICATIONS AND MOLECULAR OVERLAPS

Nebojša Mitrović[1,2], Nemanja Trifunović[1], Jovana Trifunović[3], Milica Lakićević[4]

1. Department of General Surgery, Clinical Hospital Center Zemun
2. Faculty of Medicine, University of Belgrade
3. Oncology Hospital, Clinical Hospital Center Zemun
4. Department of Radiology, Clinical Hospital Center Zemun

Correspondence to: Nebojša Mitrović, Vukova 9, Belgrade, Serbia
Tel: +381637754029, Email: mitrovicdrnebojsa@yahoo.com

SINHRONI GASTROINTESTINALNI STROMALNI TUMOR I DUKTALNI ADENOKARCINOM PANKREASA: REDAK PRIKAZ SLUČAJA SA KLINIČKIM IMPLIKACIJAMA I MOLEKULARNIM PREKLAPANJIMA

Nebojša Mitrović[1],[2], Nemanja Trifunović[1], Jovana Trifunović[3], Milica Lakićević[4],

1. Odeljenje opšte hirurgije, Kliničko-bolnički centar Zemun
2. Medicinski fakultet, Univerzitet u Beogradu
3. Bolnica za onkologiju, Kliničko-bolnički centar Zemun
4. Služba radiologije, Kliničko-bolnički centar Zemun

Autor za korespondenciju: Nebojša Mitrović, Vukova 9, Beograd, Srbija
Tel: +381637754029, Email: mitrovicdrnebojsa@yahoo.com

ABSTRACT

The synchronous occurrence of a gastrointestinal stromal tumor (GIST) and pancreatic ductal adenocarcinoma (PDAC) is exceptionally rare and poses significant diagnostic and therapeutic challenges. We report a 67-year-old female presenting with biliary obstruction, right upper quadrant pain, and dyspeptic symptoms. CT imaging revealed a pancreatic head mass, while a submucosal gastric lesion was identified only intraoperatively. Laparotomy enabled excision of a pedunculated gastric GIST, whereas the unresectable pancreatic tumor involved critical vascular structures, necessitating a palliative double bypass comprising cholecystectomy, hepaticojejunostomy, gastrojejunostomy, and enteroenterostomy. Histopathology confirmed a low-risk GIST and a moderately differentiated PDAC with distinct immunohistochemical profiles, supporting the presence of two independent primary tumors.

This case underscores the critical importance of meticulous intraoperative exploration, particularly in the presence of atypical or incidentally discovered lesions, and demonstrates the durable palliation afforded by surgical bypass in unresectable PDAC. Beyond the clinical context, potential molecular overlaps—activation of MAPK/ERK and PI3K/AKT/

mTOR pathways, VEGF-mediated angiogenesis, and defects in DNA repair—provide a plausible biological basis for the synchronous occurrence of these otherwise unrelated neoplasms, informing potential strategies for personalized therapy.

Keywords: Gastrointestinal stromal tumor, Pancreatic ductal adenocarcinoma, Synchronous tumors, Molecular overlaps, Surgical management

SAŽETAK

Sinhrona pojava gastrointestinalnog stromalnog tumora (GIST) i pankreasnog duktalnog adenokarcinoma (PDAC) izuzetno je retka i predstavlja značajan dijagnostički i terapijski izazov. Prikazujemo slučaj 67-godišnje pacijentkinje sa opstrukcijom žučnih puteva, bolom u desnom gornjem kvadrantu i dispeptičkim simptomima. CT je otkrio masu u glavi pankreasa, dok je submukozni tumor želuca identifikovan tek intraoperativno. Laparotomijom je ekscidiran pedunkulirani želudačni GIST, dok je neoperabilni pankreasni tumor obuhvatao ključne vaskularne strukture, zahtevajući palijativni dvostruki bypass, uključujući holecistektomiju, hepatojejunostomiju, gastrojejunostomiju i enteroenterostomiju. Histopatološka analiza potvrdila je niskorizični GIST i umereno diferentovani PDAC sa jasno različitim imunohistohemijskim profilima, što potvrđuje postojanje dve nezavisne primarne lezije.

Ovaj slučaj naglašava ključnu ulogu temeljne intraoperativne inspekcije, naročito u prisustvu nesvakidašnjih ili slučajno otkrivenih tumora, i pokazuje relevantnost hirurškog bypass-a kao trajne palijativne opcije kod neoperabilnog PDAC-a. Pored kliničkih implikacija, ističe se potencijalno molekularno preklapanje, uključujući aktivaciju MAPK/ERK i PI3K/AKT/mTOR puteva, VEGF-posredovanu angiogenezu i defekte u reparaciji DNK, što pruža biološko objašnjenje za sinhronu pojavu ovih različitih neoplazmi i može informisati buduće strategije personalizovane terapije.

Ključne reči: Gastrointestinalni stromalni tumor, Pankreasni duktalni adenokarcinom, Sinhroni tumori, Molekularna poklapanja, Hirurško lečenje

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract, most frequently arising in the stomach (60–70%) and small intestine (20–30%) [1]. They originate from interstitial cells of Cajal and are typically driven by activating mutations in KIT or PDGFRA, which trigger downstream signaling through the MAPK/ERK and PI3K/AKT/mTOR pathways [2]. GISTs exhibit a broad spectrum of biological behavior, ranging from indolent lesions to highly aggressive tumors.

Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive malignancy characterized by early local invasion, lymph node involvement, and systemic metastasis, with a 5-year survival rate below 10% despite advances in surgery and systemic therapy [3]. KRAS mutations are present in over 90% of PDAC cases, often accompanied by alterations in TP53, CDKN2A, and SMAD4 [4]. The MAPK/ERK and PI3K/AKT/mTOR pathways, central to GIST oncogenesis, are also engaged downstream of KRAS in PDAC, suggesting that, despite

different cellular lineages, these tumors share convergent signaling mechanisms that promote proliferation and resistance to apoptosis [2,4,5,6].

The synchronous presentation of GIST and PDAC is extraordinarily rare. While some occurrences may be coincidental, overlapping molecular signaling cascades provide a plausible explanation for simultaneous tumorigenesis. Reports suggest that up to 20% of patients with GIST harbor additional primary malignancies, most commonly gastrointestinal or genitourinary carcinomas [7]. However, synchronous detection of PDAC remains exceptionally uncommon, with only isolated case reports in the literature [7–9].

Management of patients with synchronous GIST and PDAC is particularly challenging, especially when PDAC is unresectable due to vascular involvement. Although endoscopic stenting is considered first-line therapy for malignant biliary obstruction, surgical bypass (hepaticojejunostomy and gastrojejunostomy) remains relevant, particularly when laparotomy is already indicated for concurrent lesions [10–13].

Here, we report a rare case of synchronous gastric GIST and unresectable PDAC, describing clinical presentation, intraoperative findings, histopathological confirmation, surgical decision-making, and potential molecular overlaps that may underlie this unusual coexistence.

CASE REPORT
CLINICAL PRESENTATION

A 67-year-old female was admitted for evaluation of a pancreatic lesion detected on CT scan. She reported several weeks of intermittent right upper quadrant pain accompanied by dyspeptic symptoms, nausea, and occasional vomiting, without significant weight loss. Her medical history included hypertension and type 2 diabetes mellitus, and prior surgeries consisted of appendectomy and tonsillectomy.

Laboratory analysis revealed conjugated hyperbilirubinemia, elevated alkaline phosphatase (ALP) and gamma-glutamyl transferase (gGT), mild elevation of AST and ALT, and markedly raised tumor markers: CA19-9 1100 U/mL, CEA 21 ng/mL, and CA72-4 21.4 U/mL.

Contrast-enhanced CT showed a hypodense mass measuring 3 × 3 cm in the pancreatic head/uncinate process, with significant intra- and extrahepatic bile duct dilation (common bile duct ~20 mm). The main pancreatic duct was not separately visualized. Incidentally, a 2 cm submucosal lesion was observed on the anterior wall of the gastric antrum.

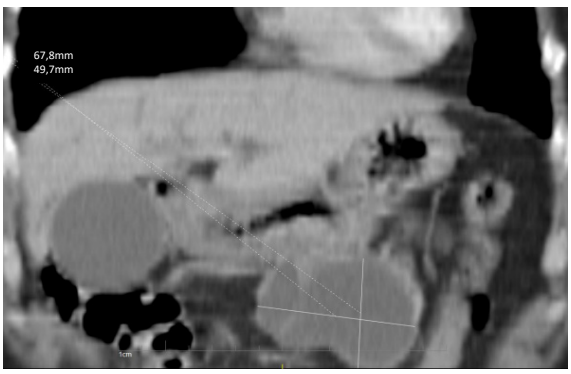

Figure 1. CT imaging confirmed the presence of a gastric gastrointestinal stromal tumor (GIST)

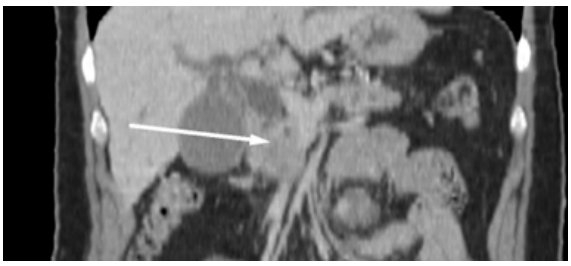

Figure 2. CT imaging demonstrates a pancreatic carcinoma

SURGICAL PROCEDURE

Following preoperative preparation, the patient underwent exploratory laparotomy. Intraoperatively, a pedunculated, lobulated, partially cystic tumor of approximately 5 cm was identified on the anterior wall of the gastric antrum, showing torsion and venous congestion, consistent with GIST. The tumor was completely excised with extramucosal resection of its pedicle.

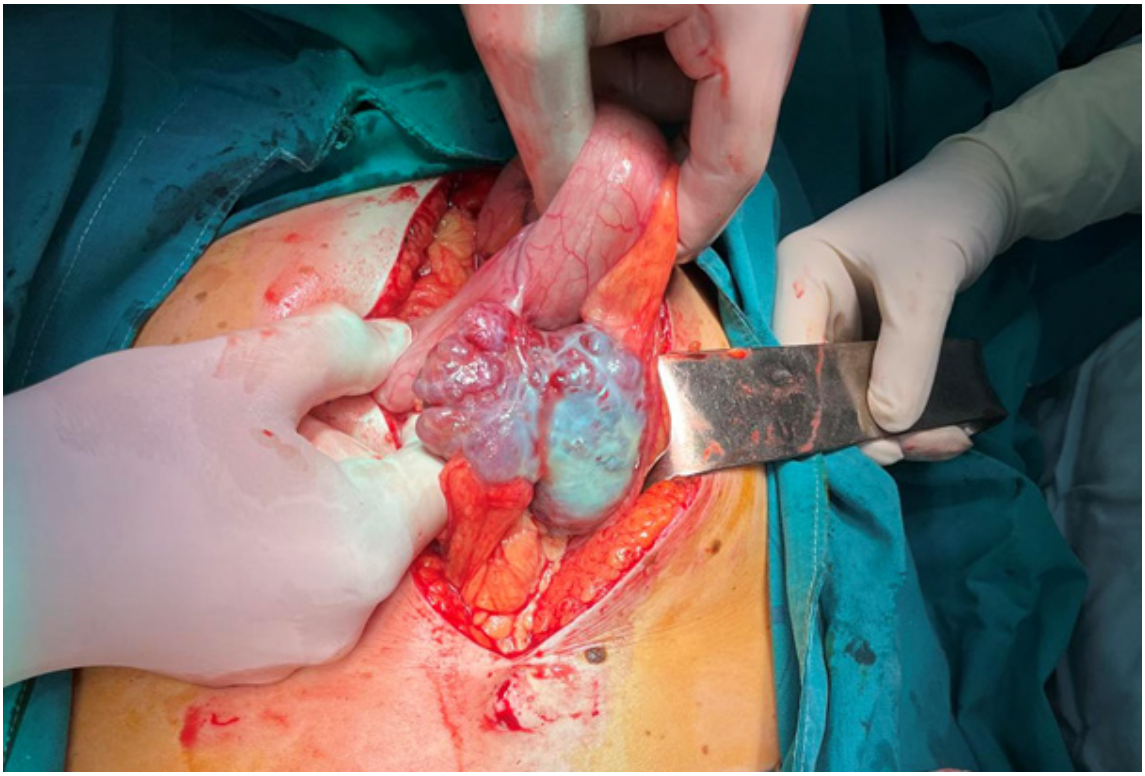

Figure 3. Intraoperative finding of a lobulated, well-demarcated gastric GIST with venous congestion.

The gallbladder appeared distended and elongated; cholecystectomy was performed after decompression and careful dissection of Calot's triangle. The extrahepatic bile ducts were markedly dilated, measuring around 2 cm. Further exploration revealed a firm, 3 × 4 cm mass in the pancreatic head and uncinate process, encasing nearly three-quarters of the superior mesenteric vein and extending toward the portal vein confluence, accompanied by bulky locoregional lymphadenopathy. Frozen section of a peripancreatic lymph node showed nonspecific sinus histiocytosis. Due to extensive vascular involvement, the pancreatic lesion was deemed unresectable.

A palliative double bypass was performed, consisting of hepaticojejunostomy with Roux-en-Y enteroenterostomy, antecolic gastrojejunostomy, and drainage of the operative field. The patient was initially managed in the intensive care unit and subsequently transferred to the surgical ward. She remained hemodynamically stable and afebrile, gradually resuming oral intake. The surgical wound healed by primary intention without complications.

HISTOPATHOLOGY

The gastric lesion was a spindle-cell tumor arranged in fascicles with low mitotic activity (2/50 HPF). Immunohistochemistry demonstrated positivity for CD117, DOG1, and CD34, and negativity for SMA and S100, with a Ki-67 proliferative index below 5%, consistent with low-risk GIST.

Histopathological examination of the biopsy specimen from the pancreatic mass revealed a moderately differentiated ductal adenocarcinoma infiltrating peripancreatic fat, showing perineural and lymphovascular invasion. Immunohistochemistry demonstrated strong CK7 and CK19 positivity with focal CA19-9 expression, confirming the diagnosis of pancreatic ductal adenocarcinoma.

DISCUSSION

The synchronous occurrence of GIST and PDAC is exceptionally rare and represents a significant diagnostic and therapeutic challenge. Most GISTs are discovered incidentally during imaging or surgery, whereas PDAC often presents at an advanced stage with biliary obstruction [6–9]. In our patient, preoperative CT demonstrated a pancreatic head/uncinate mass with biliary dilation, but the gastric lesion was identified only intraoperatively. This underscores the importance of meticulous intraoperative exploration, particularly when atypical findings are present or incidental lesions are suspected.

Histopathological analysis confirmed two independent primary tumors. The gastric lesion was a low-risk spindle-cell GIST with low mitotic activity (2/50 HPF), diffuse CD117 and DOG1 positivity, and Ki-67 <5%. The pancreatic lesion was a moderately differentiated ductal adenocarcinoma, immunohistochemically positive for CK7, CK19, and focally for CA19-9. The distinct immunohistochemical profiles support synchronous primary tumors [1,7].

MOLECULAR CONSIDERATIONS

Despite arising from different cellular lineages—interstitial cells of Cajal and pancreatic ductal epithelium—GIST and PDAC share activation of key oncogenic pathways. In GIST, constitutive activation of KIT or PDGFRA drives MAPK/ERK and PI3K/AKT/mTOR signaling, whereas in PDAC, KRAS mutations activate similar downstream pathways [2,4,5]. These convergent pathways promote proliferation, survival, and resistance to apoptosis in both tumor types.

The mTOR pathway, crucial for GIST cell survival, particularly in imatinib-resistant disease, is also implicated in PDAC progression, although clinical outcomes with mTOR inhibitors have been modest [2,5]. VEGF-mediated angiogenesis represents another shared feature, though the tumor microenvironment differs: GISTs are typically hypervascular, whereas PDAC exhibits a hypovascular, desmoplastic stroma with active VEGF and HIF signaling [2,5]. Rare germline mutations, such as BRCA2, may predispose patients to both tumors through impaired DNA damage repair. TP53 inactivation, highly prevalent in PDAC (~70%), has been documented in high-risk GISTs, suggesting overlapping mechanisms of tumorigenesis [2,4,5].

CLINICAL MANAGEMENT

The pancreatic lesion in our patient was unresectable due to circumferential involvement of the superior mesenteric vein and extension to the portal vein confluence. In such cases, palliation of biliary and gastric outlet obstruction is essential to improve quality of life. Endoscopic stenting offers minimally invasive relief with lower initial morbidity, but carries higher rates of recurrent obstruction and need for re-intervention [10,11]. Surgical bypass provides durable palliation, particularly in patients undergoing laparotomy for other indications, as in this case [12].

Given the intraoperative detection of a gastric GIST requiring resection, a double bypass procedure was performed, consisting of hepaticojejunostomy with Roux-en-Y enteroenterostomy and antecolic gastrojejunostomy. This approach allowed simultaneous management of both lesions, ensuring biliary and gastric decompression. Literature supports combined resection and bypass as a reasonable approach in fit patients with unresectable PDAC [10–13].

This case emphasizes several key points: the rarity of synchronous GIST and PDAC, the diagnostic challenge posed by incidental lesions, the importance of thorough intraoperative exploration, and the continued role of surgical bypass in unresectable pancreatic malignancy. Additionally, it highlights the potential molecular overlap between these two distinct tumors, suggesting that molecular characterization may inform understanding of synchronous tumorigenesis and guide personalized therapeutic strategies.

CONCLUSION

This case demonstrates the exceptionally rare coexistence of gastric gastrointestinal stromal tumor and pancreatic ductal adenocarcinoma. It highlights the critical importance of thorough intraoperative exploration, the role of surgical bypass as a durable palliative option in patients with unresectable pancreatic cancer, and the value of histopathological and immunohistochemical analysis in confirming the presence of two distinct primary tumors. Additionally, the case underscores potential shared molecular mechanisms, including activation of MAPK/ERK and PI3K/AKT/mTOR pathways, VEGF-mediated angiogenesis, and defects in DNA repair, which may provide a biological rationale for the synchronous occurrence of these otherwise unrelated neoplasms.

CONFLICT OF INTEREST AND FUNDING

The authors declare no conflict of interest.

This research received no external funding. The study and manuscript preparation were conducted solely within the regular professional activities of the authors.

REFERENCES

1. Liszka Ł, Zielińska-Pajak E, Pajak J, Gołka D, Huszno J. Coexistence of gastrointestinal stromal tumors with other neoplasms. J Gastroenterol. 2007 Aug;42(8):641-9. doi: 10.1007/s00535-007-2082-4. Epub 2007 Aug 24. PMID: 17701127.
2. Corless CL, Barnett CM, Heinrich MC. Gastrointestinal stromal tumours: origin and molecular oncology. Nat Rev Cancer. 2011 Nov 17;11(12):865-78. doi: 10.1038/nrc3143. PMID: 22089421.
3. Boulay BR, Parepally M. Managing malignant biliary obstruction in pancreas cancer: choosing the appropriate strategy. World J Gastroenterol. 2014 Jul 28;20(28):9345-53. doi: 10.3748/wjg.v20.i28.9345. PMID: 25071329; PMCID: PMC4110566.
4. Ohshima K, Fujiya K, Nagashima T, Ohnami S, Hatakeyama K, Urakami K, et al. Driver gene alterations and activated signaling pathways toward malignant progression of gastrointestinal stromal tumors. Cancer Sci. 2019 Dec;110(12):3821–33. doi: 10.1111/cas.14202. PMID: 31553483; PMCID: PMC6890443.
5. Rawat M, Kadian K, Gupta Y, Kumar A, Chain PSG, Kovbasnjuk O, Kumar S, Parasher G. MicroRNA in Pancreatic Cancer: From Biology to Therapeutic Potential. Genes (Basel). 2019 Sep 25;10(10):752. doi: 10.3390/genes10100752. PMID: 31557962; PMCID: PMC6827136.
6. Yasuda A, Sawai H, Takahashi H, Ochi N, Matsuo Y, Funahashi H, Sato M, Okada Y, Takeyama H, Manabe T. The stem cell factor/c-kit receptor pathway enhances proliferation and invasion of pancreatic cancer cells. Mol Cancer. 2006 Oct 18;5:46. doi: 10.1186/1476-4598-5-46. PMID: 17044945; PMCID: PMC1634869.
7. Bailey P, Chang DK, Nones K, Johns AL, Patch AM, Gingras MC, et al. Genomic analyses identify molecular subtypes of pancreatic cancer. Nature. 2016 Mar 3;531(7592):47–52. doi: 10.1038/nature16965. PMID: 26909576.
8. A/L Chandrasekaran T, Sahid NA, Maiyauen TK. Synchronous Gastrointestinal Stromal Tumor (GIST) with pancreatic adenocarcinoma: A case report. Ann Med Surg (Lond). 2022 Apr 11;77:103588. doi: 10.1016/j.amsu.2022.103588. PMID: 35638052; PMCID: PMC9142392.
9. Fiore M, de Stefano G, Coppola N, Giorgio A. Synchronous and metachronous gastric GIST with pancreatic adenocarcinoma: report of 2 cases and a review of literature. Gastroenterol Hepatol Bed Bench. 2015;8(4):298–301.
10. Chen X, Tan Y, Gong A. Coexistence of small gastrointestinal stromal tumor and pancreatic cancer: A case report and literature review. Oncol Lett. 2023 Oct 11;26(6):509. doi: 10.3892/ol.2023.14096. PMID: 37920429; PMCID: PMC10618927.
11. Mahfoudhi D, Sebai A, Ouedi Y, Atri S, Fteriche F, Kacem JM. Pancreatic extra gastrointestinal stromal tumor: a case report. Open Archive. 2024;26(Suppl 1):S342–S343.
12. Glazer ES, Hornbrook MC, Krouse RS. A meta-analysis of randomized trials: immediate stent placement vs. surgical bypass in the palliative management of malignant biliary obstruction. J Pain Symptom Manage. 2014 Feb;47(2):307-14. doi: 10.1016/j.jpainsymman.2013.03.013. Epub 2013 Jul 3. PMID: 23830531; PMCID: PMC4111934.
13. Taylor MC, McLeod RS, Langer B. Biliary stenting versus bypass surgery for the palliation of malignant distal bile duct obstruction: a meta-analysis. Liver Transpl. 2000 May;6(3):302–308. doi: 10.1053/lv.2000.5196.