

# Local Recurrence of Primary Non-Ampullary Adenocarcinoma of Duodenum after Surgical Treatment – A Case Report and a Literature Review

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## ABSTRACT

*Worldwide there is no general attitude on optimal surgical procedure in treatment of primary non-ampullary adenocarcinoma of duodenum, especially for early stage of duodenal cancer. Some authors prefer local excision and segmental resection while others rather perform duodenopancreatic resection, even in the case of early stage of duodenal cancer with aim to avoid tumor recurrence. In this paper we present a rare clinical course of a 60-year-old male patient with an endoscopically and pathohistologically proven early stage duodenal cancer that was treated by wide local excision. Three years after operation, control endoscopy showed »flat« polyp in the duodenum and radical duodenopancreatic resection was performed. Pathohistological examination of resected specimen showed cancer that had spread throughout the duodenal wall with metastases in the regional lymph nodes. According to our findings and literature review we gave some direction concerning the optimal diagnostic and surgical procedure for this rare tumor.*

**Key words:** duodenum, non-ampullary duodenal cancer, duodenopancreatic resection

## Introduction

Although the small intestine accounts for 75% of the length and 90% of the surface area of the gastrointestinal (GI) tract, small-bowel cancers are rare and account for only 1.4% of gastrointestinal neoplasms. The incidence of small-bowel cancer was reported in 1994 as 1.6 per 100,000 of the population<sup>1,2</sup>.

Compared to other GI tumors, our knowledge of natural history and the prognosis of patients with small bowel tumors is limited because of the fact that these neoplasms are relatively rare and there are several different tumor types.

It has been estimated that 40% of small bowel tumors are adenocarcinomas, 40% are carcinoids, 15% are sarcomas (GI stromal tumors) and less than 5% are lymphomas<sup>3</sup>. Small bowel adenocarcinomas account for 2% of gastrointestinal tumors and 1% of gastrointestinal deaths<sup>4</sup>.

The duodenum consists only 8% of the small bowel length<sup>5</sup> although it is the site of one-half to two thirds of all small bowel adenocarcinomas. It is possible that the duodenum is at highest risk because it is the first site to

be exposed to a variety of potentially injurious agents, both those consumed and those produced within the GI tract; bile, pancreatic secretions, stomach acid.

Primary adenocarcinoma of the duodenum, excluding that of the ampulla of Vater, is an uncommon condition. It represents about 0.35% of all malignant neoplasms of the gastrointestinal tract and 33%–45% of malignant neoplasms of the small intestine<sup>6–8</sup>.

In the studies that were published before 1990 because of high morbidity and mortality after Whipple procedure, local excision was preferred but it has resulted in low survival rate: 0–50%<sup>9–11</sup>. On the other hand when duodenopancreatic resection (DP, Whipple procedure) was performed survival rate of 40–60% had been reported<sup>12,13</sup>. This increase in survival rate can be explained by radical lymphadenectomy in radical surgical procedure.

Some authors favorite DP for all patients with adenocarcinoma of the duodenum including those tumors located in the third and fourth portion of the duodenum, to ensure adequate en block resection and wide lymphadenectomy<sup>6,14</sup> while other groups advocate the use of DP

for proximal duodenal carcinomas – first and second segment, but segmental resection for cancers of the third and fourth portion which secures negative resection margins and local lymphadenectomy. Their theory is based on the fact that lymphatic pathways of the distal two duodenal portions flow into the small bowel mesentery, not into the pancreaticoduodenal lymphatic region that is removed by DP procedure<sup>9,15,16</sup>.

### Case Report

Sixty years old male patient has been hospitalized in Surgery Clinic »Sestre milosrdnice« because of recurrent tumor of the second duodenal part. First symptoms appeared three years ago and were presented with obscure pain in upper abdomen – epigastrium, right upper quadrant pain, and progressive weight loss (17 kg in 3 months), without nausea or vomiting. Patient's past history did not include risk factors for duodenal cancer. He was a healthy man, a non-smoker and wasn't consuming alcohol. Thus, radiography by using the barium swallow enema was performed and fill up defect in the descending portion of duodenum was seen (Figure 1). Endoscopic and pathohistologic examination revealed an adenoma on the anterior wall of the descending duodenal segment that measured 2 cm in diameter. Therefore, operation in general endotracheal anesthesia was performed. At sur-

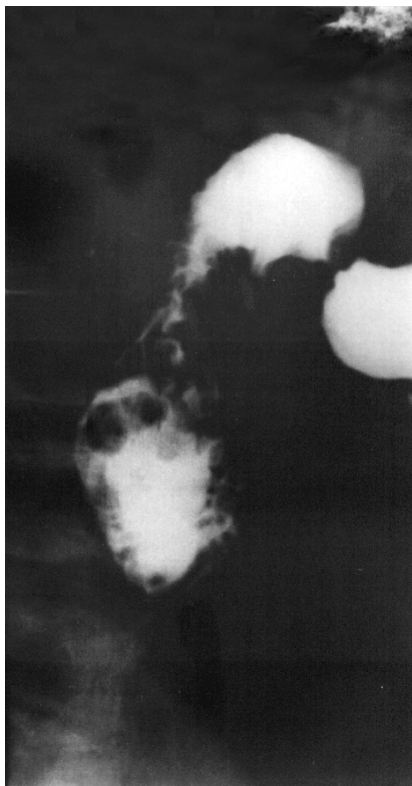


Fig. 1. Barium swallow enema radiography shows the fill up defect in the descending portion of duodenum measuring the 2 to 2.5 cm in the diameter.

gical exploration, an intraluminal duodenal palpable mass was found, with no signs of disseminated disease. Duodenotomy and polypectomy with partial excision of anterior duodenal wall was performed. In the same act, Heller's operation due to achalasia was performed. Operation and postoperative period passed without any complications and the patient was discharged from hospital at eleventh postoperative day.

Macroscopically, a broad base polypoid tumor in the resected duodenum that measured 4x2.5x1 cm was found. Histological section of the tumor showed invasive adenocarcinoma of the duodenum that was made of atypical glandular formations covered with atypical cylindrical epithelial cells. Tumor tissue infiltrated submucosa, but did not infiltrate the muscularis propria layer. Resection lines were free of tumor. Tumor was classified as the T1NxMx according to American Joint Committee on Cancer (AJCC) grading classification for malignant neoplasm of the small intestine that is based on the extent of local spread of the tumor, lymph node status and visceral metastasis<sup>17</sup> (Figure 2).

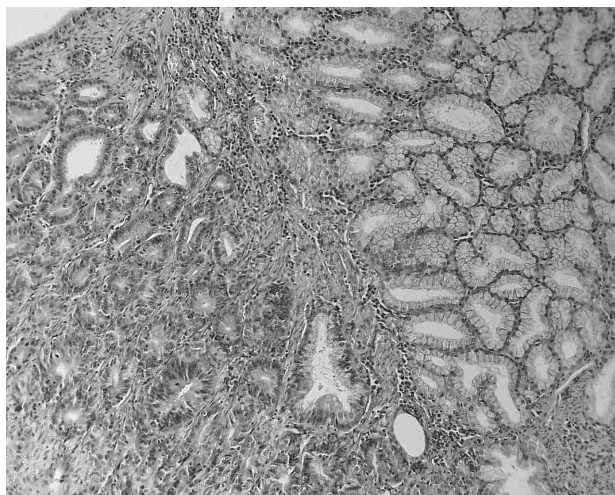


Fig. 2. Invasive adenocarcinoma of the duodenum that was made of atypical glandular formations covered with atypical cylindrical epithelial cells. Tumour tissue infiltrated submucosa, but did not infiltrate the muscularis propria layer.

With regard to the pathohistological findings, frequent control endoscopy examinations of gastrointestinal tract were performed with the aim to detect possible early tumor recurrence. Frequency of following up was every three months at first two years and after that every six months. Thus, on routine control duodenoscopy, three years after the first operation, duodenal »flat« polypus was found. Pathohistological examination of ten biopsy specimens that measured from 0.1 to 0.2 cm in diameter, showed atypical glandular tumor formation covered with clusters of necrotic and atypical, polymorphic cells, with inflammatory reaction in surrounding stromal tissue.

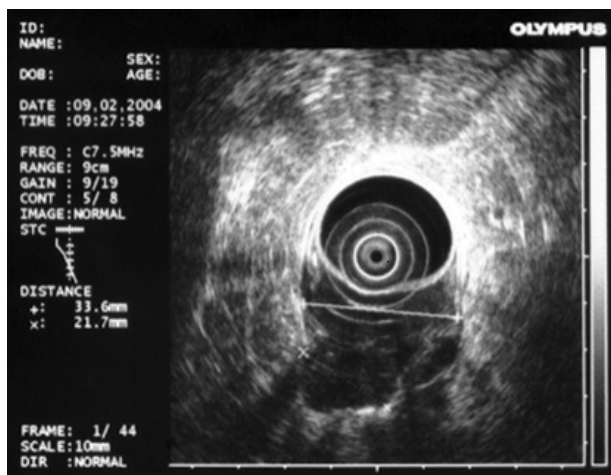


Fig. 3. Endoscopic ultrasonography shows a tumor measuring 3x4 cm in the descending duodenal portion that spreads throughout the duodenal wall and enlarged regional lymph nodes.

Endoscopic ultrasonography showed tumor in the descending duodenal portion measuring 3x4 cm that had spread throughout the duodenal wall with enlargement of local lymph nodes (Figure 3). All laboratory findings were normal including the serum tumor markers: CA19-9: 8.7 U/mL (normal range < 37 U/mL), AFP: 13.4 U/mL (normal range 0.8–8.8 U/mL), CEA: 0.6 ng/mL (normal range 0–5 ng/mL).

Therefore, cephalic pancreatoduodenectomy with dissection of the respective regional lymph nodes (D2) was performed, followed by pancreaticogastrostomy. Surgical examination of abdominal cavity did not reveal any signs of visible malignant dissemination.

Macroscopic examination of the resected specimen made of stomach that measured 6x6x2 cm, duodenum with part of small intestine sized 28 cm and part of pancreas that measured 6x5x3 cm showed fungoid formation

that protruded into the duodenal cavity. The formation was ulcerated, white colored, soft in consistency and measured 5 cm in diameter. Microscopically, tumor was formed of glandular formations with atypical epithelial cells that produced large amount of mucus. Tumor extended through all duodenal layers but it didn't infiltrate pancreas or papilla of Vater. In the surrounding fat tissue of the pancreas, four lymphatic nodes were found (less than 1 cm in diameter). One of them was infiltrated with the tumor that broke its capsule. No tumor was found in any of four perigastric lymph nodes. Thus tumor was classified as T2N1M0, G2.

Postoperative period passed without complications and the patient was discharged from hospital in good condition. In June 2004 patient received the last out of six cycles of chemotherapy by the following regimen: Leukovorin 40 mg + 5-FU 850 mg intravenously during 5 days. Between each cycle there was a pause of three weeks.

Control endoscopy, computed tomography and serum tumor markers level didn't reveal any signs of tumor recurrence.

## Discussion

The duodenum is the shortest, widest, and the most fixed part of the small intestine. It is divided into four parts; a superior or first part, a descending or second part, a horizontal or third part and an ascending or fourth part of duodenum<sup>18</sup>. Duodenal carcinoma usually develops in the descending segment while carcinoma of the horizontal and ascending segment are extremely rare<sup>7</sup>. Causative factors of duodenal cancer have not been clearly identified yet, but there are several well known potential factors: familial polyposis (2–4.5% of all cases of duodenal adenocarcinoma would be expected to have arisen in FAP patients)<sup>4</sup>, Gardner syndrome, duodenal polyps without a predisposing family history, duodenal

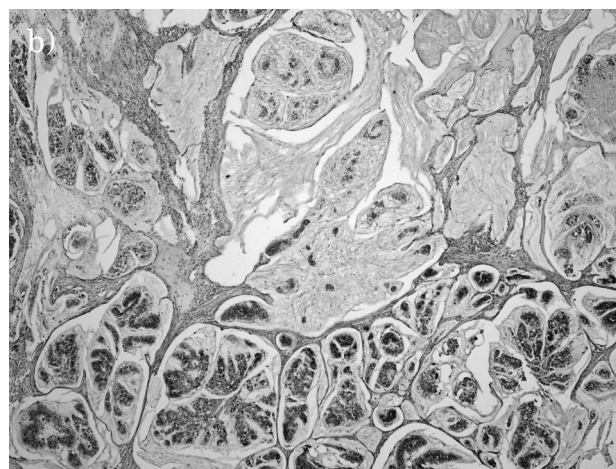


Fig. 4. Macroscopic (a) and microscopic (b) specimen showed that recurrent tumor was formed of glandular formations with atypical epithelial cells that produced large amounts of mucus. Tumor extended through all duodenal layers but it didn't infiltrate pancreas or papilla of Vater.

adenomas<sup>19–21</sup>, and villous tumors (up to 50% of cases may harbor carcinoma at the time of diagnosis)<sup>22,23</sup>. Patients with duodenal adenocarcinoma tend to have non-specific signs and symptoms like abdominal pain, weight loss, nausea, vomiting, obstruction and chronic GI bleeding. In patients with upper abdominal complaints, ultrasonography is widely used as the first imaging procedure, together with the endoscopy examinations of the stomach and duodenum. The ultrasonographic appearance of duodenal carcinoma has been described in a few studies<sup>24,25</sup>. Careful observations during routine abdominal ultrasonography may be helpful in the proper localization and diagnosis of a duodenal tumor, although duodenal endoscopy with biopsy is essential to confirm the diagnosis. Endoscopic ultrasound is a relatively new and very useful method for making the diagnosis and the staging of these tumors. Other methods are upper gastrointestinal tract radiography or barium swallow test and CT with aim to assess extent of disease. Dudiak et al<sup>26</sup> in his study evaluated the CT findings in patients with duodenal cancers and showed that duodenal adenocarcinomas (n=15) frequently appear as solitary proximal small bowel masses rarely greater than 8 cm in diameter. Ulceration was seen in one third of all adenocarcinomas and lymphadenopathy was seen in one half of tumors<sup>26</sup>. In summary, diagnosis of duodenal tumor is the most reliable using endoscopy and biopsy, whereas endoscopic ultrasonography and CT are best for assessing the tumor extension.

Gastrointestinal flat adenoma is a rare disorder, first described by Muto et al. in 1985<sup>27</sup> as adenomas that are characteristically elevated and plaque-like, with a reddish surface and sometimes a central depression. Therefore, these lesions are difficult to detect using standard endoscopy techniques, and special techniques using dyes to identify flat gastrointestinal adenomas are required<sup>28,29</sup>. Flat adenomas are associated with higher frequency of aneuploidy compared to the polypoid adenomas<sup>30</sup>. Also, flat adenomas were 10 times more likely to contain high-grade dysplasia than polypoid adenomas and there is some evidence to suggest that flat lesions have a higher malignant potential than the polypoid type<sup>31,32,33</sup>.

Surgical methods that are widely used in treatment of duodenal carcinoma are: endoscopic excision, local excision, segmental resection, pancreaticoduodenectomy (Whipple procedure – PD) and pylorus-preserving pancreaticoduodenectomy. The most important prognostic factors in patients with duodenal carcinoma are resectability, tumor diameter, histological grading, transmural invasion and presence of distant metastasis<sup>34,35</sup>. Lymph node metastases are significantly related to the occurrence of distant metastases<sup>36–38</sup>. 5-year survival rate was 43% after performing PD with lymphadenectomy in the patients

with a positive node status<sup>37,39</sup>. One of the main prognostic factors is advanced tumor stage. Thus, in the cases of pancreatic invasion, preoperative chemoradiotherapy plus extended lymphadenectomy is strongly recommended as the most promising approach<sup>40,41</sup>.

There are many controversies according to the optimal surgical procedure in the cases of early duodenal cancers and multiple studies have failed to demonstrate a survival difference between local duodenal resection and PD<sup>15,42–44</sup>. Alwmark et al<sup>11</sup> performed a segmental duodenectomy more preferentially (62%) and showed that regional recurrence was a common cause of cancer death. It can be explained by residual cancer cells in the regional lymph nodes or pancreatic parenchyma when the segmental duodenectomy is used. Delcore et al.<sup>12</sup> in his study showed that 5-year survival rate after PD for this cancer was 52% whereas there was no 2-year survivor after segmental duodenectomy. However, recent studies show that PD should not longer be considered the appropriate therapy for primary adenocarcinoma of the third and fourth portions of the duodenum, because duodenal segmentectomy is associated with negligible rates of morbidity and mortality, while allowing for satisfactory margin clearance and adequate lymphadenectomy<sup>15,29,46,47</sup>. On the other hand, overall hospital mortality after PD is 3–12.5%<sup>45</sup> while the 5-year survival rate is 100% for patients with stage I, 52% for stage II and 45% for stage III tumors<sup>15,35</sup>.

In conclusion, this case report shows that transduodenal resection is an inadequate operation even for early stage of duodenal carcinoma because this procedure carries a significant risk for recurrence. This is supported by studies in which transduodenal local excision of villous adenomas leads to 30% local failure<sup>29,48</sup>. It is also worth noting that standard endoscopy examination failed to detect disease recurrence in early tumor stage due to the flat nature of recurred adenoma in our patients. Therefore, we believe that PD is the best surgical procedure for all stages of duodenal cancers in first and second part of duodenum especially in patients that are in good general medical condition. In old and chronically ill patients (ASA score III or IV), in whom the diagnosis of early duodenal cancer (T1) is established and confirmed by endoscopic ultrasonography and CT, but at high operative risk for Whipple procedure, local excisional procedure can be performed. For these patients we proposed follow-up every three months and each time endoscopic ultrasonography or die endoscopy examination has to be performed with the aim to identify possible tumor recurrence. Standard endoscopy and blood tumor markers measurement (CEA and CA19-9) are not helpful methods for early tumor recurrence detection.

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### LOKALNI RECIDIV PRIMARNOG NEAMPULARNOG ADENOKARCINOMA DUODENUMA NAKON KIRURŠKOG ZAHVATA – PRIKAZ SLUČAJA I PREGLED LITERATURE

#### SAŽETAK

U svijetu ne postoji općeprihvaćeno mišljenje glede optimalnog kirurškog zahvata u liječenju primarnog neampularnog adenokarcinoma duodenuma, osobito u slučajevima ranog stadija. Neki autori preferiraju lokalnu eksciziju i segmentalnu resekciju duodenuma, dok drugi radije pribjegavaju duodenopankreatičnoj resekciji, čak i u slučajevima ranog stadija duodenalnog karcinoma s ciljem da spriječe nastanak recidiva tumora. U ovom radu iznosimo klinički tijek bolesti kod 60 godina starog bolesnika, kod kojega je endoskopski i patohistološki dokazan početni karcinom duodenuma te je primarno kirurški liječen širokom lokalnom ekscizijom tumora. Tri godine nakon operacije, na kontrolnoj endoskopiji nađen je ravni, »flat« polip duodenuma radi čega je učinjen radikalni kirurški zahvat; resekcija duodenuma i gušterače. Patohistološka analiza reseciranog tkiva pokazala je da se radi o adenokarcinomu koji se proširio kroz sve slojeve duodenuma te metastazirao u regionalne limfne čvorove. Na temelju našeg slučaja te pregledom svjetske literature, u ovom radu donosimo smjernice koje se odnose na dijagnostiku i optimalno kirurško liječenje ove rijetke bolesti.