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Case Report
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Pancreaticoduodenectomy Following Chemotherapy for Locally Advanced Adenocarcinoma of the Pancreatic Head: Case Report

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Abstract

Context: Pancreatic ductal adenocarcinoma is the fourth leading cause of cancer-related mortality. It has an extremely poor prognosis and prolonged survival is achieved only by resection with macroscopic tumor clearance. Locally advanced pancreatic adenocarcinoma is characterized by the abutment or invasion of major vascular structures preventing surgeons from achieving optimal R0 resection.

Aims: We report a case of 52 years old patient with locally advanced, unresectable pancreatic ductal adenocarcinoma. The patient was treated initially with neoadjuvant chemotherapy and subsequent radical surgery. An objective response was obtained and the patient's health improved.

Conclusion: Patients with locally advanced/unresectable tumors should be included in neoadjuvant protocols and subsequently be reevaluated for resection, which is possible in a relevant number of patients.

Keywords: Pancreatic adenocarcinoma; Neoadjuvant chemotherapy; SMV

Abbreviations

PDA: Pancreatic Ductal Adenocarcinoma; CT-scan: Computed Tomography Scan; LAPA: Locally Advanced Pancreatic Adenocarcinoma; SMA: Superior Mesenteric Artery; SMV: Superior Mesenteric Vein; NCCN: National Comprehensive Cancer Network

Introduction

Pancreatic Ductal Adenocarcinoma (PDA) remains as one of the most devastating human cancers, with an overall 5-year survival of <5% [1]. It has an extremely poor prognosis and prolonged survival is achieved only by resection with macroscopic tumor clearance [2].

Pancreatic tumors can be classified as resectable (stage I or II), locally advanced defined as an unresectable tumor with no evidence of distant metastasis (stage III), or metastatic (stage IV). However, with recent advances in pancreatic imaging and surgical techniques, a distinct subset of tumors is emerging that blurs the distinction between resectable and locally advanced disease: tumors of 'borderline resectability [3].

There is a strong rationale for a neoadjuvant approach, since a relevant percentage of pancreatic cancer patients present with non-metastatic but locally advanced disease and microscopic incomplete resections are common [2]. Therefore, in patients with locally advanced pancreatic adenocarcinoma, neoadjuvant treatment has been proposed as a way to decrease tumor burden and downstage tumors [4].

We report our first locally advanced, unresectable PDA case treated initially with neoadjuvant chemotherapy and subsequent radical surgery.

Case Presentation

A 52-year-old man presented to us with a history of epigastric pain and weight loss. This pain was accompanied by a history of dyspepsia and progressively increasing jaundice with clay-colored stools. There was no history of fever or pruritus.

On physical examination, there was evidence for icterus without any palpable neck

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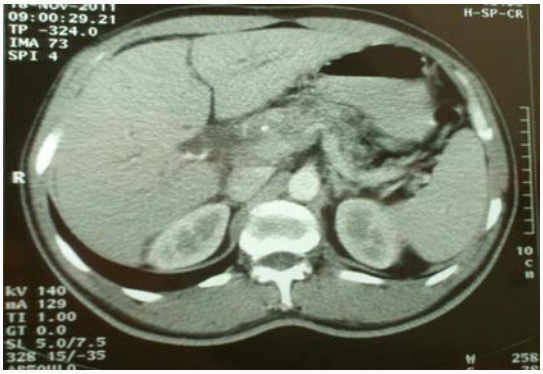

Figure 1: Abdominal CT at the time of diagnosis.

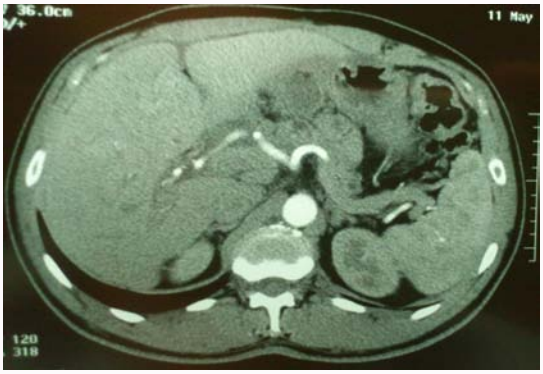

Figure 2: Control CT after neoadjuvant therapy.

lymphadenopathy. The gallbladder was not palpable and no evidence was found for ascites or peripheral edema.

Laboratory results demonstrated a cholestatic pattern; bilirubin 86.1 µmol/L (reference: range: 0 µmol/L to 17 µmol/L), alkaline phosphatase 448 IU/L (reference: range: 40 IU/L to 120 IU/L), and GGT 552 IU/L (reference: range: 0 IU/L to 150 IU/L). CA19-9 was 17.8 UI/ml (reference: range: 0 U/ml to 35 U/ml), ACE was 15.3 ug/L (reference: range: 0 ug/L to 4.5 ug/L).

Abdominal and chest computed tomography scan confirmed the presence of solid tumor at the pancreatic head. The axial diameter of the tumor was 4 cm. Unfortunately, it was not possible to perform a needle biopsy due to technical difficulties. However, images were analyzed by a group of expert radiologists and evaluated with a multidisciplinary team composed of oncologists, gastroenterologists and surgeons, who agreed in the diagnosis of pancreatic cancer.

This tumor was classified as resectable on CT-scan in the absence of contact with the main peripancreatic vessels to a "significant extent" (superior than 180_) and obvious signs for peritoneal carcinomatosis or other distant metastases (Figure 1).

The patient underwent primary explorative laparotomy which revealed a pancreatic node compatible with a pancreatic tumor encasing the porto-splenic confluence (arrow) and attachment to the HA (arrowhead) Therefore, the tumor was not resected. The patient was treated by palliative surgical procedures: a biliodigestive anastomosis with cholecystectomy and relief of jaundice was achieved. Lymph node biopsy of the hepatic artery was made. Pathology revealed a well differentiated pancreatic-type adenocarcinoma. The patient then commenced chemotherapy with gemcitabine (1,000 gm/m^2) in combination with cisplatin (50 mg/m^2) every two weeks. He completed three cycles of chemotherapy. During chemotherapy, cross sectional imaging suggested partial tumor regression with no evidence of metastatic disease (Figure 2). Six months after the initial diagnosis the patient underwent surgery with curative intent in the form of a Whipple procedure. He had an uneventful recovery period.

The whole pancreatic specimen was sent for pathological examination. Macroscopically, there was no evidence of tumor.

Histopathological analysis of the specimen demonstrated moderately differentiated pancreatic adenocarcinoma with extensive signs of regression, with multiple microscopic infiltrative foci. Surgical margins were free of disease.

The general condition of the patient remains stable and he is still alive 19 months after diagnosis. Follow-up CT-scan did not identify local or distant recurrences.

Discussion

Pancreatic ductal adenocarcinoma is the fourth leading cause of cancer-related mortality [5], and is associated with an extremely poor prognosis, reflected by a median survival of 5-8 months and a 5 year survival probability of less than 5% when all stages are combined [5,6].

At the time of diagnosis, tumors are classified according to radiological findings: the improvement of helical dual phase scanning sensitivity and surgeons experience has advanced the classification from resectable and unresectable to resectable, borderline and unresectable [3,7]. Locally Advanced Pancreatic Adenocarcinoma (LAPA), comprising both borderline and unresectable tumors, is characterized by the abutment or invasion of major vascular structures preventing surgeons from achieving optimal R0 resection. The criteria used to define resectability, especially the definitions of BR and UR disease, seem to differ among practitioners [8,9].

Locally advanced, unresectable PDA was defined as the presence of PDA with an encasement (tumor involvement, >180° of the circumference of the vessel) of one or more of the following vessels: Superior Mesenteric Artery (SMA), celiac trunk, aorta, inferior vena cava, portal vein, or Superior Mesenteric Vein (SMV); presence of thrombosis of the portomesenteric venous system was considered as unresectable disease as well.

Borderline resectable tumor was defined as PDA with an abutment (tumor involvement, <180° of the circumference vessel) of the SMV or portal vein and of the SMA or hepatic artery. Short-segment encasement/occlusion of the SMV or portal vein amenable to vascular resection and reconstruction was considered as borderline resectable disease as well [10]. The designation of borderline resectable tumors has emerged to describe a subpopulation of potentially resectable tumors. The National Comprehensive Cancer Network (NCCN) has defined this subgroup as locally advanced, resectable tumors. These patients are at a high risk for margin positive resection with initial surgery [11,12].

In fact, patients with borderline resectable tumors treated with surgical resection alone can be expected to have a higher rate of local and systemic disease recurrence and worse survival compared with patients who presented with initially resectable disease [11].

Treatment of LAPA has been challenging. Operation without

preoperative therapy frequently results in explorative laparotomy alone or pancreatic resection with microscopic or macroscopic residual disease all of which do not seem to provide any survival benefit [13].

Surgical resection with negative margins (R0) continues to be the only opportunity for cure [14]. It is necessary to ensure long-term survival. Thus, patients diagnosed with LAPA are likely to be spared from surgery; rapid disease progression and poor clinical status means patients undergo exclusively medical treatment with poor survival rates [10,15,16].

However, patients diagnosed with non-metastatic LAPA with a good clinical status are likely to undergo chemoradiation [17]. Although it is impossible for patients with arterial adhesion/ invasion to undergo resection, venous involvement proved not to be a contraindication to resection [18,19]. Thus, despite low resection rates, several reports showed interesting results on overall survival after pancreaticoduodenectomy for LAPA [20].

The role of neoadjuvant therapy in LAPA is a highly debated topic [8,9]. This modality of treatment may allow tumor downsizing, reduce the incidence of positive resection margins, delivery of treatment to intact well-vascularized tissues, and higher rates of treatment completion. Also, it facilitates selection for surgery of patients with favorable tumor behavior. Patients who do not develop progressive disease prior to rescue surgery or patients with significant downsize response may have a better prognosis, and moreover, those with poor tumor biology are selected out via disease progression, thereby avoiding the morbidity of futile surgery [21].

A systematic review analyzed the role of neoadjuvant chemoradiotherapy for the treatment of both resectable and initially labeled as unresectable pancreatic cancer. This study demonstrated that patients with unresectable pancreatic cancer who underwent neoadjuvant chemoradiotherapy achieved comparable 1-year survival as those with initially resectable disease; 40% of borderline or unresectable cases were ultimately resected. Also, it was not associated with a statistically significant increase in the rate of pancreatic fistula or overall complications in the chemoradiation group [11,22].

Mura Assifi et al. analyzed a total of 14 phase II clinical trials including 536 patients. Patients were divided into two groups: patients with initially resectable tumors (Group A), and patients with borderline/unresectable tumors (Group B). A total of 14 phase II clinical trials including 536 patients were analyzed. Following treatment, resectability was 65.8% (95% CI 55.4% to 75.6%) compared with 31.6% in Group B (95% CI 14.0% to 52.5%). A significant partial response was observed in patients with borderline/ unresectable tumors; 31.8 (95% CI 24.2% to 39.8%) in Group B, and 9.5% (95% CI 2.9% to 19.4%) in Group A (p=0.003). Progressive disease was seen in 17.0% (95% CI 11.9% to 22.7%) of patients in Group A *vs.* 21.8% (95% CI 10.1% to 36.5%) in Group B (p=0.006). Median survival in resected patients was 23 months for Group A, and 22.3 months for Group B. Nearly one-third of tumors initially deemed marginal for operative intervention were ultimately able to be resected following treatment. Until more effective targeted chemotherapeutics are developed, the only groups of patients with pancreatic cancer that may benefit from neoadjuvant treatment are those with locally advanced disease. From this data we conclude that patients with borderline/unresectable disease have increased partial response rates and a survival time similar to patients with resectable disease after receiving neoadjuvant treatment plus resection [4].

Gillen S et al. reviewed studies concerning the effects of neoadjuvant therapy on tumor response, toxicity, resection, and survival percentages in pancreatic cancer. The most important findings was that in the group of resectable tumor patients, resection and survival rates after neoadjuvant therapy were similar to the ones observed in primarily resected tumor that are treated by adjuvant therapy. Thus, in this group of patients, the current data did not point to an obvious advantage of neoadjuvant therapy. In contrast, in patients initially staged locally advanced/unresectable, approximately one third of the patients could be resected following neoadjuvant therapy with comparable survival rates as patients who were staged as resectable before treatment [2].

As of now, the available data strongly suggest that patients with locally advanced/unresectable tumors should be included in neoadjuvant protocols and subsequently be reevaluated for resection, which is possible in a relevant number of patients [2].

Conclusion

Surgical resection after downstaging of locally advanced and borderline resectable pancreatic cancer should be offered to all surgically fit patients without an increased postoperative mortality/ morbidity. Patients resected after neoadjuvant treatment have at least the same survival rate of patients with resectable disease who undergo primary resection.

Our initial experience in this case with locally advanced, unresectable PDA treated with neoadjuvant chemoradiation is encouraging. In this case, these results are consistent with the published literature, suggesting a clear benefit in terms of curative surgical resection. At this time our center is actively enrolling more patients to be considered for this modality of treatment.

References

1. Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Altekruse SF, et al, (editors): SEER Cancer Statistics Review, 1975–2008. Bethesda, MD: National Cancer Institute; 2011.
2. Gillen S, Schuster T, Meyer zum Bu¨schenfelde C, Friess H, Kleeff J. Preoperative/Neoadjuvant Therapy in Pancreatic Cancer: A Systematic Review and Meta-analysis of Response and Resection Percentages. PLoS Med. 2010;7(4):e1000267.
3. Varadhachary GR, Tamm EP, Abbruzzese JL, Xiong HQ, Crane CH, Wang H, et al. Borderline resectable pancreatic cancer: definitions, management, and role of preoperative therapy. Ann Surg Oncol. 2006;13(8):1035-46.
4. Assifi MM, Lu X, Eibl G, Reber HA, Li G, Hines OJ. Neoadjuvant therapy in pancreatic adenocarcinoma: a meta-analysis of phase II trials. Surgery. 2011;150(3):466-73.
5. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin. 2009;59(4):225-49.
6. Sultana A, Tudur Smith C, Cunningham D, Starling N, Neoptolemos JP, Ghaneh P. Meta-analyses of chemotherapy for locally advanced and metastatic pancreatic cancer: results of secondary end points analyses. Br J Cancer. 2008;99(1):6-13.
7. Talamonti M. Borderline resectable pancreatic cancer: a new classification for an old challenge. Ann Surg Oncol. 2006;13(8):1019-20.
8. Turrini O, Viret F, Moureau-Zabotto L, Guiramand J, Moutardier V, Lelong B, et al. Neoadjuvant chemoradiation and pancreaticoduodenectomy for initially locally advanced head pancreatic adenocarcinoma. Eur J Surg Oncol. 2009;35(12):1306-11.

9. Lee JL, Kim SC, Kim JH, Lee SS, Kim TW, Park DH, et al. Prospective efficacy and safety study of neoadjuvant gemcitabine with capecitabine combination chemotherapy for borderline-resectable or unresectable locally advanced pancreatic adenocarcinoma. Surgery. 2012;152(5):851-62.

10. Barugola G, Partelli S, Crippa S, Capelli P, D'Onofrio M, Pederzoli P, et al. Outcomes after resection of locally advanced or borderline resectable pancreatic cancer after neoadjuvant therapy. Am J Surg. 2012;203(2):132-9.

11. Galindo J, Gabrielli M, Guerra JF, Cassina JC, Garrido M, Jarufe N, et al. Neoadjuvant chemoradiation therapy for borderline pancreatic adenocarcinoma: report of two cases. World J Surg Oncol. 2013;11:37.

12. Crane CH, Varadhachary G, Wolff RA, Pisters PW, Evans DB. Preoperative chemoradiation for localized, radiographically resectable pancreatic cancer. Best Pract Res Clin Gastroenterol. 2006;20(2):365-82.

13. Massucco P, Capussotti L, Magnino A, Sperti E, Gatti M, Muratore A, et al. Pancreatic resections after chemoradiotherapy for locally advanced ductal adenocarcinoma: analysis of perioperative outcome and survival. Ann Surg Oncol. 2006;13(9):1201-8.

14. Heinrich S, Pestalozzi BC, Schafer M, Weber A, Bauerfeind P, Knuth A, et al. Prospective phase II trial of neoadjuvant chemotherapy with gemcitabine and cisplatin for resectable adenocarcinoma of the pancreatic head. J Clin Oncol. 2008;26(15):2526-31.

15. Sultana A, Smith CT, Cunningham D, Starling N, Neoptolemos JP, Ghaneh P. Meta-analyses of chemotherapy for locally advanced and metastatic pancreatic cancer. J Clin Oncol. 2007;25(18):2607-15.

16. Haddock MG, Swaminathan R, Foster NR, Hauge MD, Martenson JA, Camoriano JK, et al. Gemcitabine, cisplatin, and radiotherapy for patients with locally advanced pancreatic adenocarcinoma: Results of the North Central Cancer Treatment Group Phase II Study N9942. J Clin Oncol. 2007;25(18):2567-72.

17. White RR, Reddy S, Tyler DS. The role of chemoradiation therapy in locally advanced pancreatic cancer. HPB (Oxford). 2005;7(2):109-13.

18. Wang C, Wu H, Xiong J, Zhou F, Tao J, Liu T, et al. Pancreaticoduodenectomy with vascular resection for local advanced pancreatic head cancer: A single center retrospective study. J Gastrointest Surg. 2008;12(12):2183-90.

19. Ishikawa O, Ohigashi H, Imaoka S, Furukawa H, Sasaki Y, Fujita M, et al. Preoperative indications for extended pancreatectomy for locally advanced pancreas cancer involving the portal vein. Ann Surg. 1992;215(3):231-6.

20. Katz MH, Pisters PW, Evans DB, Sun CC, Lee JE, Fleming JB, et al. Borderline resectable pancreatic cancer: The importance of this emerging stage of disease. J Am Coll Surg. 2008;206(5):833-46.

21. Van Tienhoven G, Gouma DJ, Richel DJ. Neoadjuvant chemoradiotherapy has a potential role in pancreatic carcinoma. Ther Adv Med Oncol. 2011;3(1):27-33.

22. Laurence JM, Tran PD, Morarji K, Eslick GD, Lam VW, Sandroussi C. A systematic review and meta-analysis of survival and surgical outcomes following neoadjuvant chemoradiotherapy for pancreatic cancer. J Gastrointest Surg. 2011;15(11):2059-69.