Case Report

iMedPub Journals
www.imedpub.com

Journal of Neoplasm
ISSN 2576-3903

2019
Vol.4 No.1:5

DOI: 10.21767/2576-3903.100136

Sunitinib as Neoadjuvant Treatment of Neuroendocrine Pancreatic Tumors: Case Report

O Al Jarroudi[1]*, T El harroudi[2], B Serji[2], T Bouhout[2], E Eggyr[2], A Zaimi[1], L Jaouani[1], SA Brahmi[1] and S Afqir[1]

1 Medical Oncologic Department, Hassan 2nd Hospital, Medical School, Mohammed Ist University Oujda, Morocco
2 Surgical Oncologic Department, Hassan 2nd Hospital, Medical School, Mohammed Ist University Oujda, Morocco

***Corresponding author:** O Al Jarroudi

aljarroudi.ouissam@gmail.com

Medical Oncologic Department, Hassan 2nd Hospital, Medical School, Mohammed Ist University Oujda, Morocco

Citation: Jarroudi OA, Harroudi TE, Serji B, Bouhout T, Eggyr E, et al. (2019) Sunitinib as Neoadjuvant Treatment of Neuroendocrine Pancreatic Tumors: Case Report . J Neoplasm Vol.4 No.1:5.

Abstract

Pancreatic Neuroendocrine Tumors (PNETs) are rare tumors. Surgery is the only potential treatment for cure. There is a paucity of data to support an optimal neoadjuvant approach for inoperable tumors. We present a case of 39-year-old women admitted for management of nonfunctioning locally advanced PNET with the invasion of the Superior Mesenteric Vein (SMV) and duodenum. The patient received neoadjuvant treatment by sunitinib (37.5 mg/day). After 8 weeks of treatment, the tumor was successfully resected and the patient has remained recurrent free for 18 months. Sunitinib seems to be a valuable option in the neoadjuvant setting for nonfunctioning locally advanced PNET.

Keywords: Pancreatic neuroendocrine tumors; Sunitinib; Neoadjuvant treatment; Vascular invasion

Received: May 08, 2019; **Accepted:** May 21, 2019; **Published:** May 25, 2019

Introduction

Pancreatic neuroendocrine tumors (PNETs) are uncommon neoplasms that account for approximately 1% of pancreatic cancers by incidence and 10% of pancreatic cancers by prevalence [1]. The tumors are categorized as functional or non-functional based on hormone production, biological effects, and symptoms. Approximately 10%-30% of PNETs are functional [2]. They are also classified by the degree of differentiation, as NET G1 (low grade), NET G2 (intermediate grade) and poorly differentiated neuroendocrine carcinomas considered high grade, for which management may differ [3].

Complete surgical resection is the only potentially curative treatment for localized PNETs [4,5]. Recently, molecular targeting agents such as everolimus and sunitinib were found to be effective for locoregional unresectable or metastatic PNETs [6,7]. But, there is a paucity of data to support an optimal neoadjuvant approach with the expectation of down-staging to allow for curative resection [8].

Here, we describe, in this case, report, our experience with sunitinib as an effective treatment in the neoadjuvant setting for locally advanced PNETs.

Case Report

A 39-year-old woman without medical history consulted for abdominal pain and postprandial vomiting. Physical examination revealed an epigastric mass. Abdominal ultrasound showed a pancreatic mass concerning for malignancy. Thoraco-abdominopelvic contrast-enhanced Computed Tomography (CT) revealed a tumor of the duodenopancreatic region with a maximum diameter of 111 mm with superior mesenteric vein (SMV) invasion and repression of the duodenum. No metastases were found in other organs **Figure 1**. The oesogastroduodenal fibroscopy showed extrinsic compression of the bulb. The pathological analysis identified the tumor as a PNET. Immunohistochemical analysis revealed that the tumor was positive for chromogranin A, synaptophysin and Ki 67 labeling index was <1% indicating the tumor was a grade 1 PNET in 2010 world health organization classification.

We concluded that the tumor was unresectable. Accordingly, treatment options were discussed by the interdisciplinary tumor board. The patient began a course of sunitinib therapy (37.5 mg/day) which she tolerated well. The toxicity was limited to Hypothyroidism corrected by supplementation.

She was monitored after 2 months of treatment by sunitinib radio

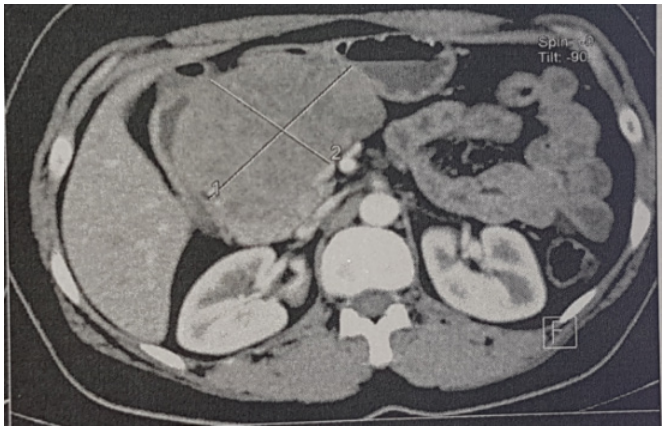

Figure 1 CT findings of pancreatic mass: Prior to neoadjuvant treatment by sunitinib.

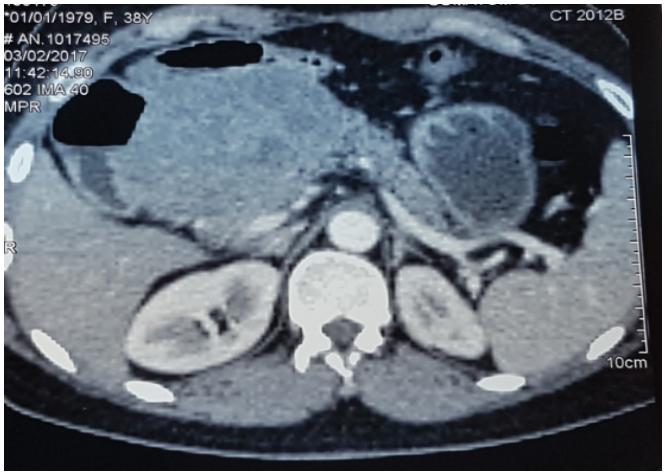

Figure 2 After 2 cycles of neoadjuvant treatment.

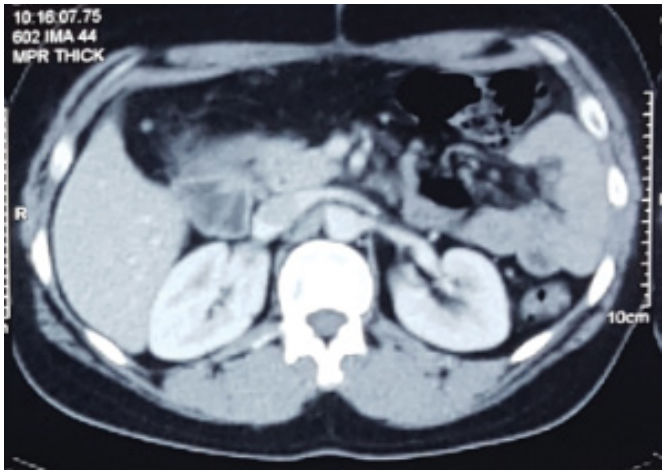

Figure 3 After 18 months from surgical resection.

logically. The response was a tumor's stability with the formation of a central zone of necrosis which is classed by RECIST criteria as stable disease **Figure 2**.

Three weeks after withdrawing sunitinib, the patient underwent laparotomy and the tumor was successfully resected without SMV resection or reconstruction and final pathology revealed a 10 cm mass confined to the pancreas with negative margins. The patient's postoperative course was marked by the development of a pancreatic fistula which improved with parenteral nutrition and treatment by octreotide. The patient was discharged on postoperative day 27. Eighteen months after surgery she remains free of disease recurrence by CT imaging **Figure 3**.

Discussion

Neuroendocrine tumors are relatively rare tumors, with most of the available evidence deriving from case reports or small case series treating heterogeneous tumors [9]. Surgical resection is the only curative treatment for patients with PNETs and remains the cornerstone therapy, even in patients with advanced disease. The goals for surgical resection are a cure, relief from functioning tumors, or relief from non-functioning tumors causing symptoms related to mass effect (biliary obstruction, gastric outlet obstruction, abdominal pain, gastrointestinal hemorrhage) [10].

Regarding inoperable PNETs: for selected patients with the unresectable disease who are asymptomatic and have low tumor burden and stable disease, observation can be considered. For symptomatic patients with unresectable disease, those who initially present with clinically significant tumor burden or those with clinically significant disease progression, first-line therapy is considered. Treatment options include biological agents (sunitinib, everolimus), chemotherapy, arterial embolization, chemoembolization, ablative therapy, cytoreductive surgery, supportive medical care and somatostatin analogs [11].

Randomized controlled studies on the best sequential order of treatments for locally advanced PNETs are lacking. Based on previous encouraging experience with pancreatic adenocarcinomas, neoadjuvant therapy followed by surgical treatment in responders has been tried as a therapeutic option in locally advanced PNET patients. Several therapeutic options have been described mainly in case reports or small case series to downsize locally advanced tumors and make them resectable seem perfectly reasonable. Treatment recommendation for PNETs may not strictly follow the current guidelines and must include individualization and optimization of management to define the optimal treatment algorithm [12]. In our case, we described the efficacy of preoperative sunitinib therapy for locally advanced non-functional PNET with low grade even if this therapy did not appear to reduce the size of the tumor, but it decreased the vascular invasion, thus allowing surgical resection.

To our knowledge, different therapeutic regimes have been tested only in a limited number of studies, of which the vast majority are case reports. In a Dutch series of 29 patients with non-functioning PNETs, Van Vliet et al. [13] concluded that neoadjuvant treatment with Lu-octreotide is a valuable option for patients with non-functioning PNETs. Devata et al. [8] reported the effectiveness in the neoadjuvant setting of capecitabine and temozolomide regimen for locally advanced PNET.

Everolimus, a Mammalian Target of Rapamycin (MTOR) inhibitor,

was analyzed as a neoadjuvant option for locally advanced PNET. The arterial invasion was improved by using everolimus alone or the combination of everolimus and somatization analogy preoperatively [14,15].

Sunitinib malate is an oral, multi-targeted Tyrosine Kinase Inhibitor (TKI) of VEGF receptors-1, 2 and 3, PDGFRs a and b, stem-cell factor (KIT) receptor, FMS-like tyrosine kinase 3, colony-stimulating factor 1 receptor and glial cell line-derived neurotrophic factor receptor and it is approved for the treatment of unresectable or metastatic, well-differentiated PNET [16,17]. In our present case, we successfully resected a locally advanced PNET with vascular invasion after neoadjuvant treatment by sunitinib.

Further studies are needed to compare these different regimens in order to determine the best option in the neoadjuvant setting.

Conclusion

Neoadjuvant treatment with sunitinib appears to be useful for nonfunctioning locally advanced PNET and warrants consideration for clinical trial exploration.

Conflict of Interest

The authors declare that they have no conflict of interest.

Consent of Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

References

1 Yao JC, Eisner MP, Leary C, Dagohoy C, Phan A, et al. (2007) Population-based study of islet cell carcinoma. Ann Surg Oncol 14: 3492-3500.

2 Liakakos T, Roukos D (2011) Everolimus and sunitinib: From mouse models to treatment of pancreatic neuroendocrine tumors. Future Oncol 7: 1025-1029.

3 Vinik AI, Raymond E (2013) Pancreatic neuroendocrine tumors: An approach to treatment with a focus on sunitinib. Ther Adv Gastroenterol 5: 396-411.

4 Falconi M, Bartsch DK, Eriksson B, Klöppel G, Lopes JM, et al. (2012) ENETS consensus guidelines for the management of patients with digestive neuroendocrine neoplasms of the digestive system: Well-differentiated pancreatic non-functioning tumors. Neuroendocrinology 95: 120-134.

5 Öberg K, Knigge U, Kwekkeboom D, Perren A (2012) ESMO Guidelines working group neuroendocrine gastro-entero-pancreatic tumors: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 23: 124-130.

6 Yao JC, Shah MH, Ito T, Bohas CL, Wolin EM, et al. (2011) Everolimus for advanced pancreatic neuroendocrine tumors. N Engl J Med 364: 514-523.

7 Raymond E, Dahan L, Raoul JL, Bang YJ, Borbath I, et al. (2011) Sunitinib malate for the treatment of pancreatic neuroendocrine tumors. N Engl J Med 364: 501-513.

8 Devata S, Kim EJ (2012) Neoadjuvant chemotherapy with capecitabine and temozolomide for unresectable pancreatic neuroendocrine tumor. Case Rep Oncol 5: 622-626.

9 Ong SL, Garcea G, Pollard CA, Furness PN, Steward WP, et al. (2009) A fuller understanding of pancreatic neuroendocrine tumors combined with aggressive management improves outcome. Pancreatology 9: 583-600.

10 Halfdanarson TR, Rabe KG, Rubin J, Petersen GM (2008) Pancreatic neuroendocrine tumors (PNETs): Incidence, prognosis and recent trend toward improved survival. Ann Oncol 19: 1727-1733.

11 Castellano D, Grande E, Valle J, Capdevila J, Reidy-Lagunes D, et al. (2014) Expert consensus for the management of advanced or metastatic pancreatic neuroendocrine and carcinoid tumors. Cancer Chemother Pharmacol 75: 1099-1114.

12 Perysinakis I, Aggeli C, Kaltsas G, Zografos GN (2016) Neoadjuvant therapy for advanced pancreatic neuroendocrine tumors: An emerging treatment modality? Hormones 15: 15-22.

13 Van Vliet EI, Van Eijk CH, Krigger RR, Van Dijkum EJ, Teunissen JJ, et al. (2015) Neoadjuvant treatment of nonfunctioning pancreatic neuroendocrine tumors with [177Lu-DOTA0,Tyr3] octreotate. J Nucl Med 56: 1647-1653.

14 Sato A, Masui T, Sankoda N, Nakano K, Uchida Y, et al. (2017) A case of successful conversion from everolimus to surgical resection of a giant pancreatic neuroendocrine tumor. Surg Case Rep 3: 82.

15 Takano M, Yamagata S, Shida H, Azuma H, Negishi M, et al. (2015) A case of the pancreatic neuroendocrine tumor with tumor embolus in the portal vein resected surgically after neoadjuvant chemotherapy. J Jpn Surg Assoc 76: 885-889.

16 Mendel D, Laird A, Xin X, Louie S, Christensen J, et al. (2003) In vivo antitumor activity of SU11248, a novel tyrosine kinase inhibitor targeting vascular endothelial growth factor and platelet-derived growth factor receptors: determination of a pharmacokinetic/pharmacodynamic relationship. Clin Cancer Res 9: 327-337.

17 Zhou C, Zhang J, Zheng Y, Zhu Z (2012) Pancreatic neuroendocrine tumors: a comprehensive review. Int J Cancer 131: 1013-1022.