

Long-lasting response to third-line chemotherapy in metastatic pancreatic cancer

Alda Tavares, MD*, Alexandra Mesquita, MD

Abstract

At diagnosis, approximately 50% of cases of adenocarcinoma of the pancreas are metastasized and 5-year survival is only 2.9%. We reported a case of a 63-year-old woman with pancreatic adenocarcinoma with multiple hepatic and intra-abdominal metastases that progressed on 2 lines of chemotherapy. She has been under treatment with third-line chemotherapy for 19 months with stable disease and excellent performance status. She has an overall survival of 29 months. There are just a few cases of metastatic disease with long survival described in the literature. The functional status and the good tolerance to treatment may be determinants of prognosis.

Keywords: chemotherapy, long term, metastasis, pancreatic neoplasms

To the Editor

We reported a real case of a patient with stage IV pancreatic adenocarcinoma, with high tumoral burden, with a stable disease under third line of chemotherapy and with overall survival of 29 months. There are just a few cases of metastatic disease with long survival described in the literature. In the discussion of this letter, we make a brief review of what are the prognosis factors of this pathology, considering the evolution of this case report.

Introduction

Pancreatic cancer is the fourth leading cause of cancer death in European countries.¹ At diagnosis, approximately 50% of cases of pancreatic adenocarcinoma are metastasized and 5-year survival is only 2.9%.² The majority of patients have a single organ site of metastases and the liver is the most common site of metastasis.³

Leucovorin, 5-fluorouracil, irinotecan and oxaliplatin (FOLFIRINOX), and nab-paclitaxel plus gemcitabine combination represent the most recent advancements for the first-line treatment, with a median overall survival of 11.1 and 8.7 months, respectively.^{4,5} Although the response to currently available chemotherapy (ChT) remains low, the proportion of

patients candidates to receive second- and third-line regimens increased due to better results with these 2 ChT combinations.⁶

Reports of long-term survival are rare, especially cases of a high tumoral burden at diagnosis and more than 2 lines of treatment.

Case report

A 63-year-old woman with diabetes under insulin therapy uses the emergency department in April 2017 complaining of weight loss (about 12 kg in 3 months) and severe low back pain without irradiation or associated neurological deficits. No gastrointestinal symptoms were reported. She had mild hepatic cholestasis without hyperbilirubinemia. Computed abdominal tomography showed a mass in the cervix of the pancreas, as well as 2 hepatic lesions of 10 and 2.5 cm of greater axis, pathologic adenopathies, a mass in the right adrenal gland, a pelvic mass, and implants suggesting peritoneal carcinomatosis (Fig. 1). Hepatic lesion biopsy was performed, revealing pancreatic adenocarcinoma. Carbohydrate antigen 19.9 (Ca19.9) and carcinoembryonic antigen within the reference values. After discussion of the case in a multidisciplinary oncologic team, it was decided to proceed to palliative ChT.

The patient presented an Eastern Cooperative Oncology Group (ECOG) performance status of 1 and 38 kg of weight. She started ChT with gemcitabine (1000 mg/m²) and nab-paclitaxel (260 mg/m²), on day 1, 8, and 15 of each cycle (every 28 days) with resolution of pain after the first cycle.

After 3 months, there was a dimensional progression of adenopathies and pelvic metastasis reported on computed abdominal tomography scan and Ca19.9 elevation. The patient started a second-line ChT with FOLFOX: oxaliplatin 85 mg/m² and leucovorin 400 mg/m² on day 1, and 5-fluorouracil 2400 mg/m² over 46 to 48 hours (every 14 days), in November 2017. After 3 months of ChT, the disease continued to progress. She initiated a third-line ChT with FOLFIRI: irinotecan 180 mg/m², leucovorin 400 mg/m², and 5-fluorouracil 400 mg/m² bolus on day 1, and 5-fluorouracil 2400 mg/m² over 46 to 48 hours (every 14 days), in February 2018. A dose reduction of 20% starting at the second cycle was done, due to grade 2 neutropenia. Imagiological evaluation reported sustained partial response. Given imaging and clinical benefit, it was decided to maintain ChT with FOLFIRI.

Funding: None declared.

ORCID: <https://orcid.org/0000-0002-3390-3295>

Department of Medical Oncology, Hospital Pedro Hispano, Matosinhos Local Health Unit of Matosinhos, Matosinhos, Portugal.

* Corresponding author. Serviço de Oncologia Médica, Hospital Pedro Hispano, Rua Dr. Eduardo Torres, 4464-513 Senhora da Hora, Matosinhos, Portugal. E-mail address: alda.tavares@ulsm.min-saude.pt (Alda Tavares).

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Porto Biomed. J. (2020) 5:3(e65)

Received: 29 October 2019 / Accepted: 29 March 2020

<https://dx.doi.org/10.1097/j.pbj.0000000000000065>

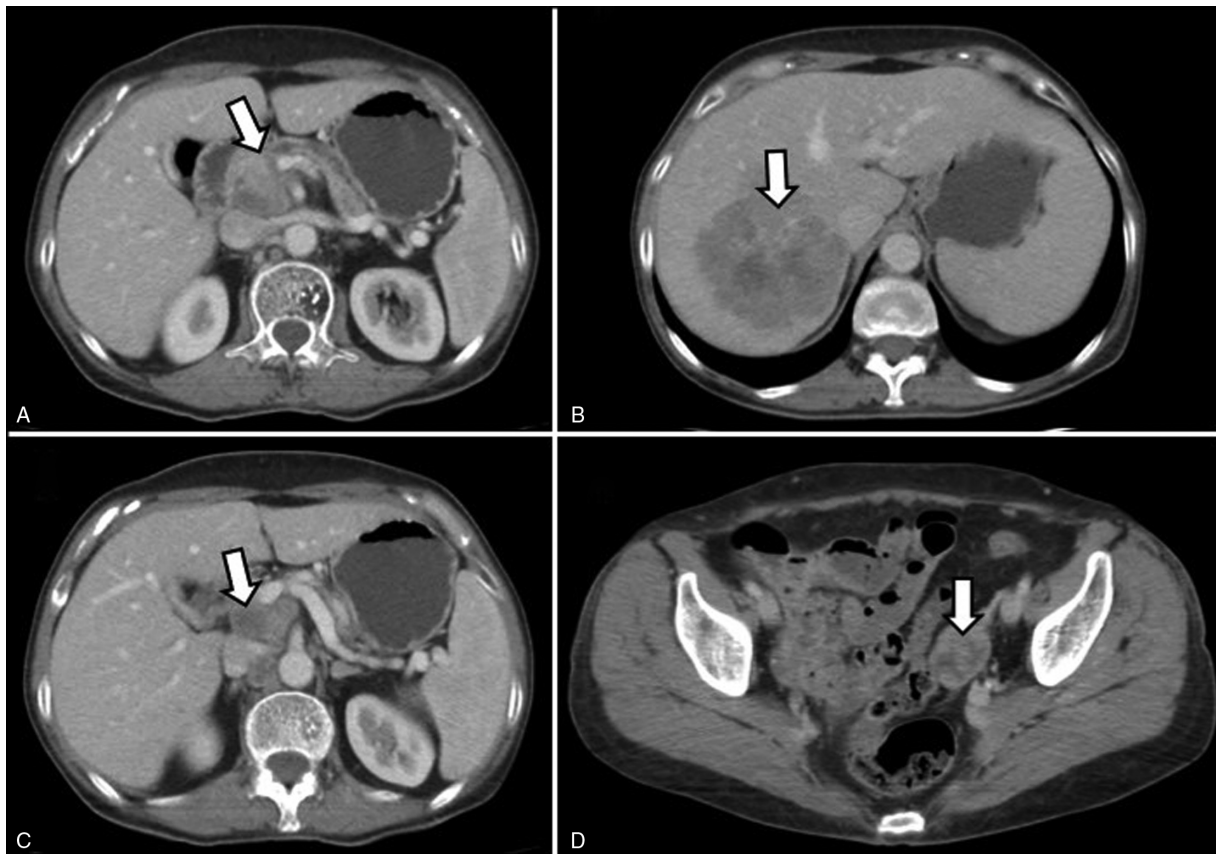


Figure 1. Thoracoabdominopelvic computed tomography showed: (A) mass in the cervix of the pancreas (arrow) associated with an irregular pancreatic duct dilatation; (B) the biggest hepatic lesion in the VII segment; (C) portacaval adenopathy with 2.8 cm of greater axis; (D) left pelvic peritoneal implant with 3.5 cm of greater axis.

Currently, the patient remains asymptomatic and with ECOG performance status of 0. She has fulfilled up to 39 cycles of FOLFIRI, with stable disease and excellent quality of life, with no need for pain medication.

Discussion

The clinical course of pancreatic cancer is generally aggressive with potential for substantial deterioration in the quality of life. In this case report, despite the lack of response to the 2 previous lines, the patient showed clinical improvement after the first cycle of ChT continuing through the third line of ChT.

This case far exceeds the median survival reported in the literature. There are very little case reports of patients with metastatic pancreatic cancer at diagnosis surviving at least 2 years. The paucity of such reports is related to the fact that metastatic long-term survivors are rare and the literature on long-term survival is focused on patients with local or locally advanced resectable disease. In a retrospective study, non-resected ≥ 5 -year survivors represented only 2% (11/544) of all nonresected patients undergoing treatment for pancreatic adenocarcinoma, and then 2 patients had metastatic disease at diagnosis.⁷

Treatment decisions and prognostic differ according to patient- and disease-related factors. Variables associated with better outcomes are: <65 years old,³ excellent performance status, tumors in the head of the pancreas,⁶ low level of serum

Ca19.9.⁸ Surgery to the primary tumor and surgery of the metastatic disease are also associated with better overall survival.³ Site-specific metastases have also a prognostic value. For example, patients with isolated liver metastases have worse outcomes compared to patients with isolated lung or distant nodal metastases.³ There is, however, no difference in terms of survival between single-site versus multiple sites of metastasis.³ So, in this case, the age, ECOG performance status 0 and normal level of Ca19.9 are factors associated with good prognosis. On the contrary, this patient had multiple liver lesions associated with large pelvic masses and retroperitoneal carcinomatosis, normally associated with poor prognosis.

Retrospective studies showed extended overall survival with a second line in patients previously treated with gemcitabine-based therapies with a median overall survival of 12 to 15 months.⁶ But the good response to second line was apparently influenced by longer first-line progression-free survival in these reports.⁹

Given refractoriness to the first 2 lines of treatment, it was not expected that this patient could have stable disease for so many months under the third line of treatment. In France, a retrospective series of 70 patients with metastatic pancreatic adenocarcinoma showed that FOLFIRI regimen had a good outcome after the failure of gemcitabine- and platinum-base regimens.¹⁰ Like this case, most patients received 2 lines of ChT and progression-free survival with the previous line was less than

3 months. Even in this study, 2-year survival was, however, relatively low (32% from the initial diagnosis).

Conclusion

The authors describe a real case of a patient with stage IV pancreatic adenocarcinoma, with high tumoral burden, with a stable disease under the third ChT line, despite no response to previous 2 other ChT regimens. A total survival of 29 months has already been achieved with excellent quality of life. There are few cases of metastatic disease with long survival described in the literature. The functional status and the good tolerance to treatment may be determinants of prognosis.

Acknowledgments

None

Author contributions

All authors contributed to this article. The first draft of the manuscript was written by Alda C.P. Tavares and Alexandra S.A. Mesquita commented on previous versions of the manuscript. Alexandra S.A. Mesquita was responsible for patient analysis and treatment.

Conflicts of interest

The authors declare no conflict of interest.

References

- [1] Ferlay J, Colombet M, Soerjomataram I, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. *Eur J Cancer*. 2018;103:356–387.
- [2] Surveillance E and End Results Program. Cancer Stat Facts: Pancreatic Cancer. National Cancer Institute, Surveillance, Epidemiology, and End Results Program, 2019. Available at: <https://seer.cancer.gov/statfacts/html/pancreas.html>. Accessed August 19, 2019.
- [3] Oweira H, Petrausch U, Helbling D, et al. Prognostic value of site-specific metastases in pancreatic adenocarcinoma: a surveillance epidemiology and end results database analysis. *World J Gastroenterol*. 2017;23:1872–1880.
- [4] Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med*. 2011;364:1817–1825.
- [5] Goldstein D, El-Maraghi RH, Hammel P, et al. Nab-Paclitaxel plus gemcitabine for metastatic pancreatic cancer: long-term survival from a phase III trial. *J Natl Cancer Inst*. 2015;107:pii: dju413.
- [6] Martín AM, Hidalgo M, Alvarez R, et al. From first line to sequential treatment in the management of metastatic pancreatic cancer. *J Cancer*. 2018;9:1978–1988.
- [7] Oh SY, Edwards A, Mandelson MT, et al. Rare long-term survivors of pancreatic adenocarcinoma without curative resection. *World J Gastroenterol*. 2015;21:13574–13581.
- [8] Ploquin A, Truant S, Piessen G, et al. Easily available factors of predictive prolonged survival under gemcitabine. *In Vivo*. 2017;31:731–735.
- [9] Chiorean EG, Von Hoff DD, Tabernero J, et al. Second-line therapy after nab-paclitaxel plus gemcitabine or after gemcitabine for patients with metastatic pancreatic cancer. *Br J Cancer*. 2016;115:e13.
- [10] Neuzillet C, Hentic O, Rousseau B, et al. FOLFIRI regimen as second-/third-line chemotherapy in patients with advanced pancreatic adenocarcinoma refractory to gemcitabine and platinum salts: a retrospective series of 70 patients. *J Clin Oncol*. 2011;29:272–272.