

CASE REPORT

Liver Abscesses Mimicking Metastatic Disease in a Patient with Pancreatic Cancer Following Neoadjuvant FOLFIRINOX Therapy

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ABSTRACT

Context Based on the results of the ACCORD11/PRODIGE4 Trial, FOLFIRINOX is nowadays increasingly used in a neoadjuvant setting in borderline resectable or locally advanced pancreatic cancer. **Case report** We report the case of a 59 year old jaundiced patient with a mass in the pancreatic head that was initially judged unresectable by an explorative laparotomy. The patient was referred for FOLFIRINOX chemotherapy. At the time of restaging the patient had developed three liver lesions that were suspicious for liver metastases on both CT and MRI imaging. Ultrasonography guided biopsy revealed no malignancy but positive microbiology suggestive for cholangitis abscesses. This was confirmed by a second explorative laparotomy in which the primary tumor was resected with an uneventful postoperative course. **Conclusion** Liver abscesses are a known complication of FOLFIRINOX treatment and are sometimes difficult to differentiate from metastases. Therefore, newly developed liver lesions under FOLFIRINOX treatment must be thoroughly analyzed prior to making a decision against surgery. In cases of uncertainty an explorative laparotomy/laparoscopy must be considered.

INTRODUCTION

Pancreatic cancer is one of the most aggressive cancers and is the fourth most frequent tumor related cause of death in the western world [1]. The prognosis remains extremely poor and 75-80% of patients present with advanced, unresectable and/or metastatic disease at the time of diagnosis. Overall median survival is only 5-8 months and less than 5% of all patients have a long term survival of more than 5 years. Neoadjuvant treatment regimens are more and more being used in initially locally advanced or borderline-resectable pancreatic tumors. Since FOLFIRINOX has been shown to be superior to Gemcitabine in stage IV cancers, it is now increasingly used in the neoadjuvant setting [2]. The case of the reported patient underlines the effectiveness of neoadjuvant FOLFIRINOX in locally advanced/borderline-resectable pancreatic cancer but more importantly shows that FOLFIRINOX induced liver abscesses may very easily be mistaken for liver metastases. Therefore, explorative (re-)laparotomy should be considered after neoadjuvant FOLFIRINOX even when newly diagnosed liver lesions are present at the time of restaging.

CASE REPORT

A fifty-nine-year-old man presented to a regional hospital with painless jaundice. Contrast-enhanced computed tomography demonstrated a mass in the head of the pancreas without evidence of distant metastasis (Figure A, arrow). Exploratory laparotomy was performed at that hospital and the tumor was judged to be locally unresectable due to invasion of the portal vein. Biopsies were taken which confirmed ductal adenocarcinoma. A palliative hepaticojejunostomy was performed.

Two weeks later, the patient presented at our outpatient clinic for a second opinion. Given the borderline resectable stage of the tumor without distant metastasis, the unfavorable time point for reoperation, and the excellent performance status of the patient, treatment with FOLFIRINOX was initiated with the intention to re-explore the patient if there would be no signs of tumor progress (i.e. in a preoperative/neoadjuvant intention). The patient completed six cycles of chemotherapy and tolerated this reasonably well with no grade three or four toxicities.

Contrast-enhanced CT scan at re-staging demonstrated a stable disease concerning the pancreatic mass with a presumed persisting infiltration of the portal vein and was therefore classified locally as borderline resectable. However, there were three new masses in the liver. MRI (Figure B + D, arrows) and diffusion MRI scan (Figure C, arrows) confirmed the presence of these lesions in liver segments IVa, V and VI highly suspicious of liver metastasis. Ultrasonography-guided biopsy of the lesion in segment V revealed no malignancy but demonstrated a biliary abscess. Taken together, all of

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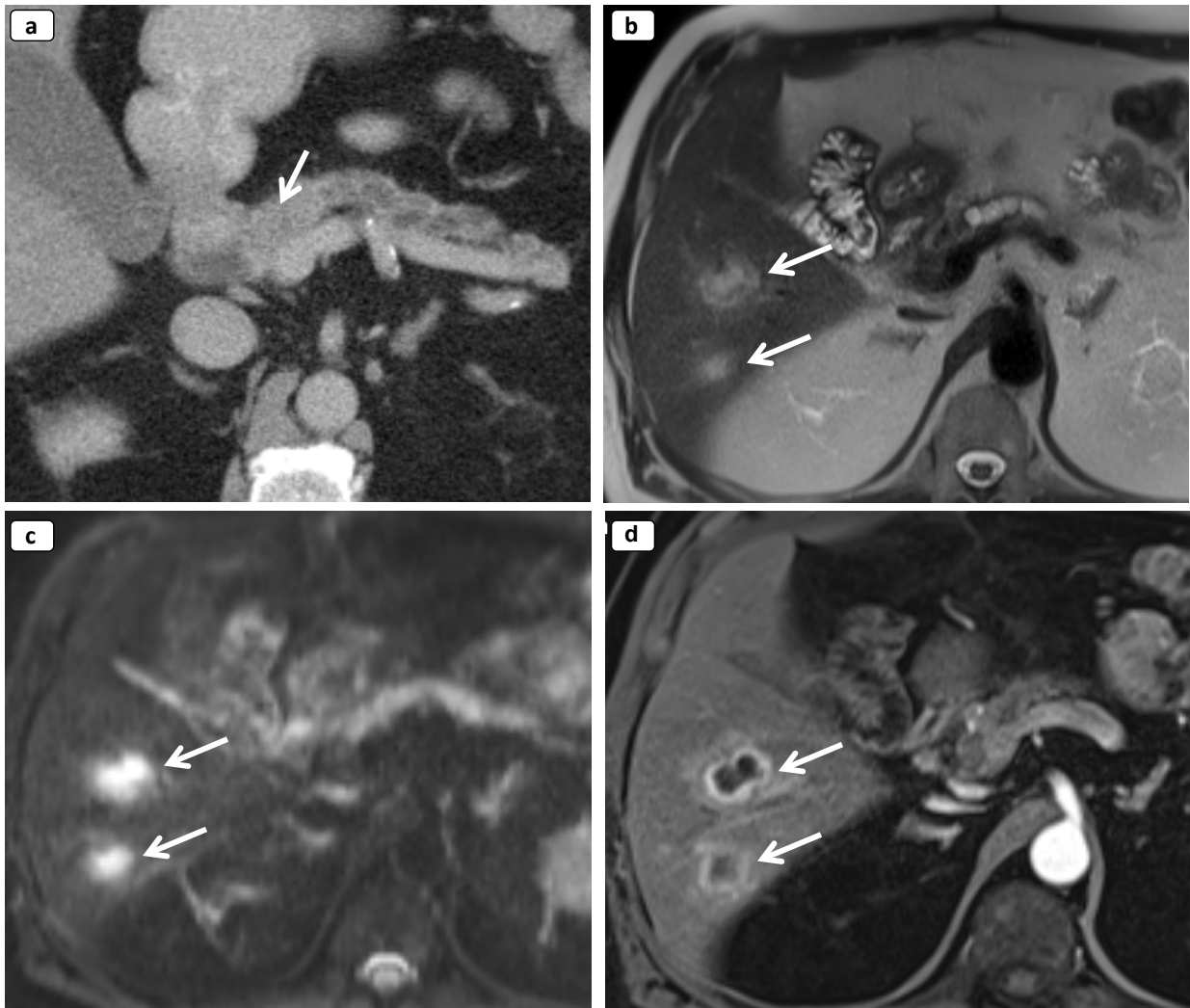


Figure 1. Axial, contrast-enhanced CT scan, portal venous phase, with a locally advanced mass in the pancreatic head (a. arrow) but no evidence for distant metastases at the time of diagnosis. MRI scan (b. + d. arrows; b. axial, T2-weighted TSE (turbo spin-echo) sequence, d. axial, contrast-enhanced, fat-saturated T1-weighted GRE (gradient recalled echo) sequence in the arterial phase) and diffusion MRI scan (c. arrows; axial, diffusion-weighted image (SSEPI sequence; b 600) after neoadjuvant FOLFIRINOX showed presence of newly developed lesions in liver segments IVa, V and VI highly suspicious of liver metastasis.

the three lesions were rather cholangitis-induced abscesses than liver metastases and we therefore decided to perform re-exploratory laparotomy after a preoperative course of definitive intravenous antibiotic therapy which was continued after surgery. At the time of surgery, no disease other than in the pancreas was found and the tumor was deemed locally resectable; thus, a partial pancreaticoduodenectomy with standard reconstruction was done following take down of the hepaticojejunostomy. Final pathology demonstrated a pT3, pN1 (2/17), L1, V0, Pn1, G2, R0 tumor. The postoperative course was uneventful and the liver lesions disappeared upon intravenous antibiotic treatment. The patient was discharged home on post-operative day nine and was referred to oncology for adjuvant gemcitabine chemotherapy [3].

DISCUSSION

Pancreatic cancer is well known to be an aggressive and highly malignant tumor with an extremely poor prognosis. Surgery remains the only option for cure but only 10-20 % of patients are candidates for curative resection at the time of diagnosis. Recent evidence suggests, that

up to one third of initially un-resectable tumors may be resectable after aggressive neoadjuvant therapy; survival of this select subgroup of patients has been reported to be comparable to that of primarily resectable patients [4]. It should be noted that due to the extensive desmoplastic reaction of pancreatic cancer, response evaluation remains difficult after neoadjuvant treatment and that surgical re-exploration of all patients stable following neoadjuvant therapy should be considered [5]. Previous data are derived from various radiochemotherapy protocols that have been used and analyzed in the past. Nowadays, however, with the advance of more effective chemotherapy regimen [4, 6], centers implement more often the FOLFIRINOX regimen for neoadjuvant treatment of locally advanced and borderline-resectable pancreatic cancers. This regimen has initially shown impressive improvements in patients with stage IV pancreatic cancer. Here, response rates, progression-free survival, and overall survival were dramatically improved over single-agent gemcitabine [2]. In our particular case, the patient was initially deemed un-resectable whereas we felt that resection might be possible. This is a common situation

when patients are seen at smaller hospitals initially – rather than at referral centers for pancreatic cancer surgery [7, 8]. Secondly, cholangitis and liver abscesses are a common complication of FOLFIRINOX treatment. Furthermore, the patient in this case had received a hepaticojejunostomy at the time of the first surgical exploration which is known to markedly increase cholangitis rates by itself [9]. Therefore, patients with a hepaticojejunostomy *and* postoperative chemotherapy have a relevant risk to develop cholangitis and biliary liver abscesses. Thus, liver lesions following such a therapy have to be thoroughly analyzed prior to making a decision for or against surgery. Several investigators have evaluated the utility of MR imaging for differentiating hepatic abscesses from metastases. In those reports, the signal intensity of both entities frequently appeared hypointense on T1-weighted images and hyperintense on T2-weighted images, and marked arterial rim enhancement was present, which was also demonstrated in our patient. This overlap makes the differentiation of both entities difficult. High signal intensities in the center of a lesion as seen in diffusion-weighted MR imaging have been reported to be suggestive of hepatic abscesses. However, larger series investigating the role of DWI in the differentiation of abscesses from metastases are still pending. In cases of uncertainty, image guided biopsy is a powerful tool to distinguish malignant from benign lesions [10]. We would even argue for exploratory laparotomy/laparoscopy with extensive intraoperative ultrasound, biopsies and frozen sections in cases of uncertain dignity of suspicious liver lesions. Underutilization of surgery for such patients is a great concern [11] and precludes them from a substantial survival benefit derived from removing the tumor. In summary, the case of this patient is an example for the mimicking of metastases by biliary abscesses after FOLFIRINOX therapy.

Conflict of interest

The authors have no conflict of interest to declare.

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