

Long term survival of a metastatic patient with pancreatic adenocarcinoma: a rare case report and review of the literature

Uzun süreli sağkalım gösteren metastatik pankreas adenokanserli olgu:
Nadir bir olgu ve literatürün taranması

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Despite recent advances in therapeutics, the prognosis of patients with advanced pancreatic cancer has remained poor. Median survival of patient is 3-6 months and five year survival rate is less than 5%. We report a case of fifty-five-year-old male with complaints of abdominal pain and weight loss. Patient was diagnosed as pancreas adenocarcinoma with multiple hepatic metastases. Then, the patient received gemcitabine 1250 mg/m² at day 1 and 8; cisplatin 80 mg/m² at day 1 and a cycle of therapy was defined as 21 days. After six cycles, partial response was achieved, but associated with grade 3 neutropenia. So, cisplatin was stopped and patient was treated with gemcitabine monotherapy. After 18 cycles, complete response in hepatic metastases was observed with magnetic resonance imaging. Due to hematologic and renal toxicity, only gemcitabine monotherapy was continued in our patient, but still indicating complete remission in his fifth year.

Key words: Metastasis; long-term survival; pancreatic cancer.

Tedavi alanındaki önemli gelişmelere rağmen ileri evre pankreas kanseri olan hastaların prognozu oldukça kötüdür. Hastaların ortalama yaşam süresi üç-altı aydır ve beş yıl süreli yaşam oranı ise %5'ten azdır. Bu yazıda, karın ağrısı ve kilo kaybı şikayetleri ile başvuran 55 yaşında bir erkek hasta sunuldu. Hastanın çoklu karaciğer metastazı olan pankreas kanseri olduğu saptandı. Takiben hastaya, 21 günde bir gemcitabin 1250 mg/m² birinci ve sekizinci gün; cisplatin 80 mg/m² birinci gün olan kemoterapi protokolü uygulandı. Altıncı kür sonunda parsiyel yanıt alındığı, fakat buna üçüncü derece nötropeninin eşlik ettiği saptandı. Bu yüzden cisplatin kesildi ve tedaviye tek başına gemcitabin ile devam edildi. 18 siklus sonunda manyetik rezonans görüntüleme ile karaciğer metastazlarının tamamen kaybolduğu görüldü. Hematolojik ve böbrek toksisitesi nedeniyle tedaviye gemcitabin ile devam edilebildi ve beşinci yılın sonunda tam yanıt halen sürmekteydi. Literatürü taradığımızda tam yanıt alınıp uzun süreli sağkalımı olan çok az sayıda olguya rastlanmaktadır.

Anahtar sözcükler: Metastaz; uzun süreli sağkalım; pankreas kanseri.

Pancreatic adenocarcinoma is one of the most aggressive cancers and most patients are diagnosed with advanced or metastatic disease at first presentation. In most cases they developed metastatic

disease even if curable resection is applied. For the last 10 years, gemcitabine, an antimetabolite agent, is widely used for the first-line treatment of metastatic pancreatic cancer. To improve the clini-

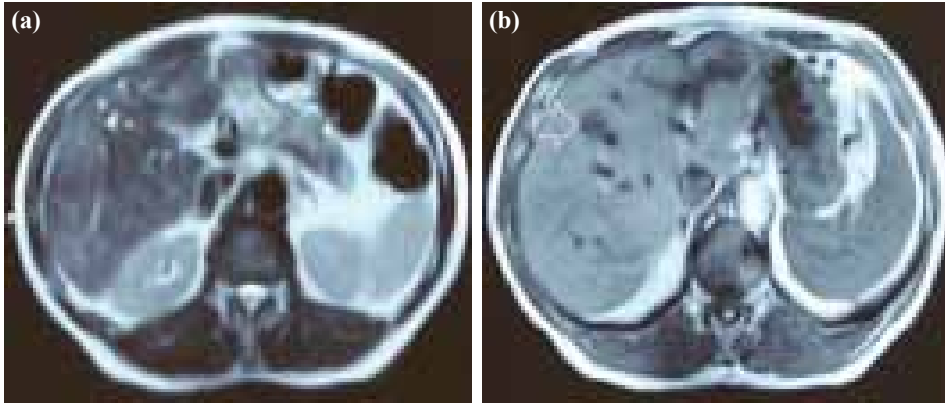


Fig. 1. Abdominal MRI before chemotherapy, hepatic metastases with 3 cm in greatest diameter were observed.

cal efficacy of gemcitabine, it is frequently used in combinations with platinum analogs, fluorouracil and targeting agents. Cisplatin shows its effect by creating DNA-DNA cross-links and DNA protein cross-links, and it is assumed that resistance developed against gemcitabine is surpassed with cisplatin combination. Here, we report our experience of treating a metastatic pancreatic cancer patient with gemcitabine plus cisplatin. Though rare, long-term survival is sometimes possible even when pancreas cancer has spread.

CASE REPORT

In May 2008, 55 years old male patient was admitted with complaints of severe abdominal pain, weight loss and loss of appetite. There was no additional disease. In physical examination, blood pressure was 100/60 mmHg, heart rate was 80 beat/minute and severe epigastric tenderness was present. In laboratory examinations, liver function tests were moderately high (aspartate aminotransferase: 63 IU/L, alanine aminotransferase: 137 IU/L). No pathologic finding was observed in gastroscopy and colonoscopy. Abdominal magnetic resonance imaging (MRI) scan revealed; lesions consistent with metastasis in all lobes and segments of the liver parenchyma and in large quantities with the largest size of 3 cm, a 2 cm mass located at the junction of the pancreatic corpus and tail and additionally, regional lymphadenopathies observed in peripancreatic region (Figure 1). Adenocarcinoma of the pancreas was diagnosed by fine needle aspiration biopsy specimen sampled from both pan-

creas and hepatic metastasis (Figure 2).

On June 5, 2008, the first chemotherapy was initiated with gemcitabine 1250 mg/m²/d 1, 8 and cisplatin 80 mg/m²/d 1 and a cycle of therapy was defined as 21 days. After 2 cycles, patient's symptoms were improved and liver function tests were returned to normal range. Following the third cure, partial response was detected in radiologic examination. Combination chemotherapy was associated with hematologic toxicity (grade 3 neutropenia) after 5 cycles and from 6th cycle; patient was treated with single-agent gemcitabine. Response to monotherapy was assessed by radiologic evaluation with 3 months intervals and complete response was ob-

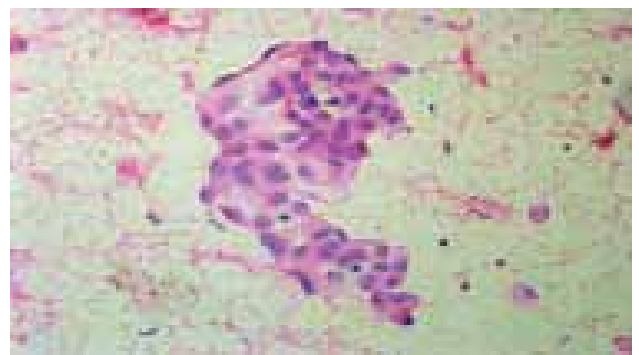


Fig. 2. H&E staining. Pancreatic Adenocarcinoma: USG guided transabdominal FNAB revealed epithelial three dimensional clusters with tubular configurations on a dirty background. Tumor cells have round nuclei with prominent nucleoli, some cytoplasm are vacuolated. Nucleocytoplasmic ratio is moderately high. Cytologic diagnosis is "adenocarcinoma G II".

Color figure can be viewed in the online issue, which is available at (www.onkder.org)

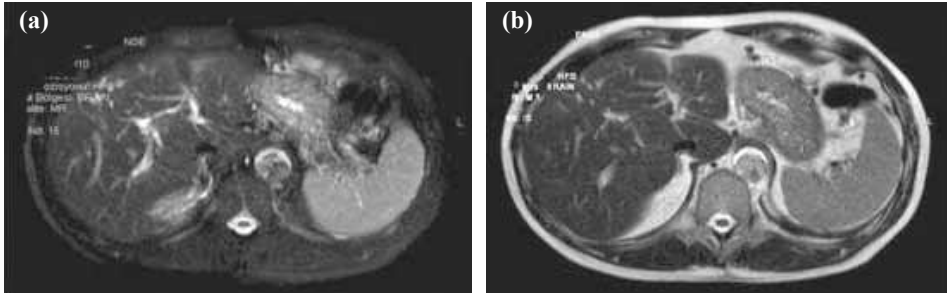


Fig. 3. Abdominal MRI after 18 cycles of chemotherapy, complete disappearance of hepatic metastases.

served in abdominal MRI subsequent to 18th cycle on June 18, 2009. Afterwards, chemotherapy was continued with a 25% reduction in gemcitabine dose due to grade 2 thrombocytopenia and weight-loss. The last 67th cycle, a dose of 800mg/day gemcitabine was given to the patient on November 21, 2012. Thereafter, chemotherapy was terminated because of gemcitabine related toxicities such as hypertension and renal toxicity. Patient was still observed as relapse-free. Radiological examinations taken in the last abdominal MRI and PET/CT showed no evidence of metastases and local recurrence (Figure 3). From the time of diagnosis for metastatic pancreatic cancer, patient had received chemotherapy for nearly 5 years and still without evidence of local and metastatic disease.

DISCUSSION

Metastatic pancreatic cancer patients mostly die from the disease because of its propensity for late presentation with advance stage and resistance to chemotherapy. Less than 25% of the metastatic patients are associated with significant clinical response.^[1] More than 5 years of survival is observed in only a few cases.^[2] Perineural invasion, lymphatic and venous infiltration, poor differentiation, peritoneal metastases and tumor size ≥ 2 cm in diameter are poor prognostic factors.^[3] Although poor prognostic factors are well established, limited information is available about the good prognostic factors. Furthermore, we did not know the potential predictor markers that may have a role to identify patients who benefit most from the chemotherapeutic agents.

Systemic chemotherapy with single-agent gemcitabine or gemcitabine-based regimens became

standard for patients with advanced pancreatic cancer and proved to be superior to 5-Fluorourasil (5-FU)-based chemotherapy in terms of both clinical response and survival.^[4] Combination of gemcitabine and cisplatin are synergistic, and there are many phase III trials comparing this combination with gemcitabine monotherapy. Overall survival and progression-free survival were more favorable in the combination arm, although the difference did not reach to statistical significance.^[5,6]

In the CONKO-001 study, which established gemcitabine after resection as adjuvant therapy, 54 among 354 patients (15%) with an overall survival ≥ 5 years were identified. It was possible to obtain tumor specimens of 39 patients (72%) with adenocarcinoma in 38 patients.^[7] In a Swedish cancer register analysis, less than 3% of patients with a histopathologically confirmed diagnosis of pancreatic adenocarcinoma including both early and advanced stage, survived five years or longer.^[8] In the literature, there was also a similar pancreatic cancer patient with hepatic metastasis and after pancreaticoduodenectomy successfully treated by S-1 and gemcitabine combination chemotherapy and achieved long-term survival.^[9] In another case report with inoperable multiple hepatic metastases, long-term survival for more than 10 years was accomplished with multiple lines of treatment.^[10]

When we analyzed the aforementioned randomized studies and searched the related articles in literature, we found very few cases that have been reported to have long term survival. Our case indicated long term survival greater than five years although he had multiple hepatic metastatic lesions and poor prognostic features at the time of diag-

nosis. To date from the time of diagnosis, patient has been symptom and relapse-free for 65 months and complete response is observed for a long period of time. So, our metastatic patient is one of the rare cases in literature and represents a subgroup of pancreatic cancer patients with favorable outcome that may be more responsive to chemotherapy.

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