

Exocrine Pancreatic carcinoma in Tunisia: A retrospective study about 158 cases.

Adénocarcinome du pancréas en Tunisie : Etude rétrospective à propos de 158 cas.

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R É S U M É

Prérequis : L'adénocarcinome du pancréas (ADP) est généralement découvert à un stade avancé du fait d'une expression clinique tardive de la maladie limitant les options thérapeutiques avec un pronostic redoutable. Les recherches actuelles ouvrent la voie vers l'identification des voies de l'oncogénèse et la recherche des thérapies ciblant ces gènes permettant ainsi une cartographie génique et une personnalisation du traitement offrant un espoir pour les patients.

Objectif : Etudier les caractéristiques épidémiologiques, cliniques, anatomopathologiques, les modalités des traitements et la survie chez des patients Tunisiens atteints d'un adénocarcinome du pancréas (ADP) traités dans le service d'oncologie médicale Abderrahmane Mami Ariana.

Méthodes : Analyse rétrospective de 158 patients traités pour un ADP de 2009 à 2012.

Résultats : On a étudié 158 patients (113 hommes/45 femmes, SR 2.5) avec une médiane d'âge de 64 ans (20-93). La médiane du délai de diagnostic était de 2 mois (1-12). La douleur abdominale, l'ictère et l'amaigrissement étaient les symptômes les plus rapportés, respectivement dans 88,6%, 43% et 55,1% des cas. Le Performance status (PS) était < 2 dans 56,9% (90 pts). Le taux des CA19-9 sérique était élevé dans 86,6% des cas. La tumeur était à un stade III chez 24,7% des patients et stade IV dans 58,2%. La chirurgie a été pratiquée dans 24,7% des cas (39 pts). Elle était curative chez 21 patients. La chimiothérapie néoadjuvante (CTNA) a été administrée à 10,8% des patients, adjuvante chez 13,9% (22 pts) et palliative chez 58,8% des patients. Nous avons utilisé la Gemcitabine hebdomadaire, Gemcitabine-CDDP, Gemcitabine-Oxaliplatine et LV5-FU2-CDDP dans les stades palliatifs dans respectivement 20%, 31,1%, 2,2% et 36,7% des cas. La médiane de survie était de 6 mois (2-60) et la survie à un an à 38,8%.

Conclusion: Le pronostic de l'ADP reste sombre dans notre pays. Dans cette série rétrospective nous avons noté une prédominance des formes localement avancées et métastatiques avec un long délai de diagnostic. Les campagnes de dépistage et de diagnostic précoce doivent être encouragées afin d'améliorer le pronostic.

Mots-clés

Pancréas, cancer, performance status, symptômes, chimiothérapie, chirurgie, palliative, survie.

S U M M A R Y

Background: Exocrine pancreatic carcinoma (EPC) occurs in the majority of cases with early locoregional spread and distant metastasis at diagnosis, leading to dismal prognosis and limited treatment options. Traditional cytotoxic chemotherapy provide only modest benefit to patients with EPC. Identification of different molecular pathways, overexpressed in pancreatic cancer cells, has provided the opportunity to develop targeted therapies with a crucial therapeutic role in this cancer setting.

Objective: Our aim is to study the epidemiological, clinico-pathological characteristics, treatment modality and clinical outcome of pancreatic adenocarcinoma in Tunisian patients treated in the department of medical oncology Abderrahmane Mami Ariana.

Methods: This retrospective study concerned patients with exocrine pancreatic carcinoma treated between 2009 and 2012. We analysed the following data: Anamnesis, age, sex, delay to diagnosis(DD), symptoms, clinical exam, performance status, stage, therapeutic protocol and results.

Results: We collected 158 patients (113 males/45 females, SR 2.5) with a median age of 64 years (20-93). The median DD was 2 months (1-12). Abdominal pain, jaundice and weight loss were the most frequent symptoms, 88.6%, 43% and 55.1% of cases respectively. Performance status was < 2 in 56.9% (90 pts). Seric CA19-9 was increased in 86.6% of cases. Tumor was at stage III in 24.7% and stage IV in 58.2%. Surgery was done in 24.7% of cases (39pts), curative in 21 patients. Neoadjuvant chemotherapy(NACT) was administrated to 10.8% of patients, adjuvant to 13.9% (22 pts) and palliative chemotherapy(PCT) concerned 58.8% of patients. We used weekly Gemcitabine, Gemcitabine-CDDP, Gemcitabine-Oxaliplatine and LV5-FU2-CDDP in palliative setting respectively in 20%, 31.1%, 2.2 and 36.7% of cases. Median survival was 6 months (2-60) and the 1year overall survival at 38.8%.

Conclusion: EPC remains a rare cancer in Tunisia. The prognosis is still grim worldwide and so does in our country. In this retrospective serie, we noted the predominance of locally advanced and metastatic cases with a long delay to diagnosis. Awareness campaigns have to be programmed to improve early diagnosis in EPC and improve outcomes.

Key - words

Pancreas, cancer, performance status, symptoms, chemotherapy, surgery, palliative, survival

Pancreatic adenocarcinoma ranks as the most challenging of human malignancies with poor outcomes. Surgical resection when is possible offers the only curative therapy if the disease is limited and palliation is indicated in most of cases (1-3). Main chemotherapy used for pancreatic adenocarcinoma remains gemcitabine (1). We report the results of a retrospective study of pancreatic adenocarcinoma conducted in a department of medical oncology.

METHODS

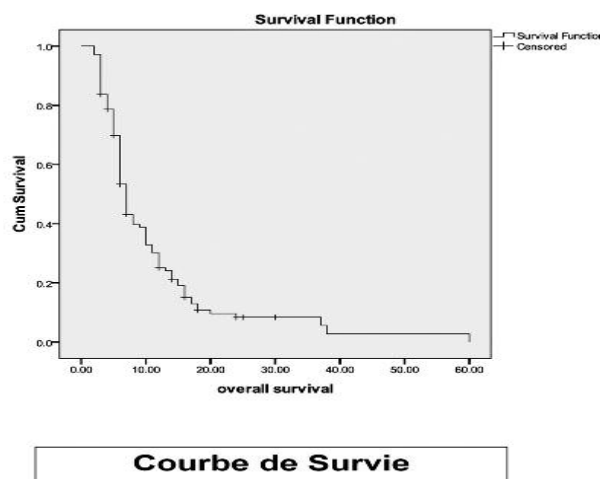
This retrospective study was conducted at the medical oncology department of Abderrahman Mami Hospital of Ariana Tunisia from January 2009 to December 2012. We included patients treated for an histologically confirmed exocrine pancreatic carcinoma (EPC). Initial work-up included: Anamnesis, clinical exam, WHO performance status, symptoms, delay to consultation/diagnosis, seric Ca 19-9, CEA, stage (local or MTS), therapeutic protocol and results. We calculated median survival and overall survival was evaluated by SPSS 18.0 software program. We analysed the following data: Anamnesis, age, sex, delay to diagnosis (DD), symptoms, clinical exam, performance status, stage, therapeutic protocol and results.

RESULTS

We collected 158 patients (113 males/45 females, SR 2.5) with a median age of 64 years (20-93). Six point three percent of patients presented familial history of cancer (1 colon cancer, 3 leukaemia, pancreatic cancer and CHC in 1 case each, gastric cancer in 2 cases, breast and lung cancer in one case each), 4.4% of cases presented a metachronous cancer (1 case endometrial adenocarcinoma and breast cancer in 3 patients). The mean DD was 2 months (1-12). Main symptoms were abdominal pain, jaundice and weight loss representing respectively 88.6%, 43% and 55.1% of cases. PS was =1 in 56.9% (90 pts), PS = 2 in 26.6% (42 pts), PS=3 in 7% (11 pts). Seric CA19-9 and CEA were increased in 86.6% and 51.4% (24 pts) respectively. Twenty four point seven percent of patients had stage III and 58.2% stage IV disease with extension to liver in 49.4%, lung in 3.2% and peritoneum in 12%. Nodal involvement was seen in 40.5% (64 pts). Vascular encasement was seen in 6.3% of cases (10pts). Surgery was done in 24.7% of cases (39pts), curative in 21 patients while palliative biliary bypass was needed in 13.9% associated to a gastro-intestinal bypass in 6.3% of patients. Neoadjuvant chemotherapy (NACT) was administrated to 10.8% of patients (Gemcitabine-Oxaliplatin to 15pts, weekly Gemcitabine to 2 pts), 66% had progressed and 34% had stable disease. Adjuvant chemotherapy was administrated to 22 pts (13.9%). With a median follow-up of 7.5 months (3-60), 16.7% relapsed. Palliative chemotherapy (PCT) concerned 58.8% of pts (90 pts). We used weekly Gemcitabine, Gemcitabine-CDDP, Gemcitabine-Oxaliplatin and LV5-FU2-CDDP in palliative setting respectively in 20%, 31.1%, 2.2 and 36.7% of cases. In second line we used Folfox 4 for 3 pts and capecitabine in 4 cases. We observed under chemotherapy 26.8% of PR (19pts), 28.2% stable disease (20pts) and 45.1% of progression (32pts). Chemotherapy has been well tolerated in 39% of cases. In the other cases, digestive and hematologic toxicities have been described, respectively grade III WHO stomatis in 20.6%, grade II vomitis in 42.9%, grade II

thrombopenia in 7.43%, grade II anemia in 23.96% and grade III in 3%. Grade III neutropenia had been described in 18.8%. Best supportive care was proposed to 34.8% of patients. Median survival was 6 months (2-60) and the 1year overall survival at 38.8%. The event free-survival (EFS) was 52.9% at six months (fig 1).

Figure 1 : Overall survival in exocrine pancreatic carcinoma



DISCUSSION

This study concerned a retrospective serie of 158 patients with EPC treated in a medical oncology unit. EPC incidence is not yet clearly defined in Tunisia and available data arise from cancer registries. In western countries, it is estimated at approximately 9 new cases per 100,000 people (4). Ductal adenocarcinoma is the most common histological type accounting for approximately 90% of all pancreatic malignancies (5). We noted a predominance of male with a SR=2.5 and 6.3% of our patients had familial history of cancer. Four point four percent of them being treated for metachronous neoplasia. As for many other cancers in Tunisia, we noted that patients consult lately, a mean DD of 2.2 months in this serie, and consequently have locally advanced and /or metastatic disease, as observed in 24.7% and 58.2% respectively in our serie. This evidence opens the discussion to implant awareness campaigns for early consultation/ early diagnosis of EPC and others. Due to the predominance of unresectable cases (82.9%), few in our serie benefited from a curative surgery. In that rare cases gemcitabine alone is recognized as the standard treatment (6,7). Neoadjuvant chemotherapy has been proposed by Hosein PJ and al owing to reduce tumor volume and to increase resectability rate (8,9). We used this approach in 10.8% of cases with modest response and rare second surgery. Palliative approach combining chemotherapy and best supportive care was the most used for our patients with the aim to improve quality of life more than improving survival (10). Prognosis of EPC is still grim in Europe and the United states with a 5-year survival rate of 6% (11), and so does in our country. In this retrospective serie the median survival rate was at six month with predominance of locally advanced and metastatic cases. Awareness campaigns have to be programmed to improve early diagnosis in EPC and improve outcomes.

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