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Case Report

Advanced Gastric Cancer after Two Liver and One Renal Transplantation. Case Report

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Abstract

Introduction: An estimated 20% increase of malignancy incidence has been found on liver and renal transplanted populations, probably associated with long-term use of immunosuppressant agents. Therapeutic approach for these patients was often treacherous and risky. Late detection of tumors and graft related complications was a common scenario. Nowadays the transplant recipients are able to receive multiple oncologic treatments.

Case Report: A 69-year-old male was submitted to multiple organ transplantation surgeries being those, two liver and one renal transplantations on a 16 year period. The liver transplantations were in 1994 and 1999 due to HCV infection. He remained stable until 2005 when chronic uses of immunosuppressive drugs lead him to chronic renal failure and he received a deceased donor kidney graft in 2007. Two years later, after dyspeptic symptoms, initial investigation and workup was done with EGD and abdominal CT and a gastroesophageal junction adenocarcinoma was diagnosed. Surgical treatment was then performed with a limited lymphadenectomy due to adhesions. Pathology results were an IIIB stage stomach carcinoma.

Discussion: Although the most common malignancies found among liver and renal transplanted populations are lymphoproliferative and skin tumors, there´s an increased incidence of gastric malignancies when compared to non-transplanted patients. The impact of overall medical costs related to malignancy in transplanted patients is high and close surveillance and early detection of such malignancies is important.

Conclusion: Transplanted populations are at higher risk of developing neoplasm in different locations. An aggressive screening with early detection and treatment it´s crucial to avoid lethal outcomes.

Keywords: *Transplant, Gastric Cancer, Immunotherapy*

Introduction

The overall increase of survival in patients receiving transplantations of different organs is a constant fact around the globe. On the other hand, the raising in survival rates is also promoting higher incidence of many other diseases such as malignant neoplasm and tumors probably related to chronic use of immunosuppressive agents [1-3,17].

There is an estimate 20% higher incidence of malignant tumors among renal and hepatic transplantation recipients than general populations [8,9]. For renal transplantation recipients alone this incidence varies from 7% to 12% [4-7].

Oncological treatment options in the past were limited and there was an enormous risk of compromising or even losing the graft after the surgical procedure, a situation hardly accepted by the patients. Nowadays, the scenario has changed, enhanced clinic control and surveillance of transplanted patients has increased our options of treatment for malignancies, being able to offer surgery, combined or exclusive chemo radiation and other novel technologies according to each case, improving even more overall survival.

New types of immunosuppressant medications and a better control of the immune system of this patients has allowed them to receive new organ transplantations increasing the chance of malignancy onset.

The authors present a case of a patient submitted to three organ transplantations, (two liver and one renal transplantations) in different times and an advanced gastric cancer (AGC) after the transplant surgeries.

Case Report

A 69-year-old male, with a previous trauma surgery and spleen tear due to an automobile accident at age 32, was submitted to urgent surgery and received blood transfusion (1974). Several years after, he was diagnosed with hepatitis C virus (HCV), which induced chronic infection evolving to severe liver fibrosis and cirrhosis. He was listed for liver transplantation (LT) and in 1994 was submitted to a living donor liver transplantation (LDLV) with an uneventful outcome for two years. He presented cerebral vascular accident (CVA) due to a brain aneurysm and was operated with success. In 1999 he presented hepatic injury attributed to progression of HCV induced fibrosis and also to tuberculosis medications toxicity. He was then submitted to a deceased donor liver transplantation that same year.

Since the first LT, the patient became diabetic from the immunosuppressive regimen, leading to chronic renal failure and hemodialysis in 2005. Two years later (2007) he received a deceased donor kidney transplantation at our institution (FOR/HRIM/UNIFESP). In 2009, after dyspeptic complaints, he performed an esophagogastroduodenoscopy (EGD) being at the time diagnosed with adenocarcinoma of the esophagogastric junction. Staging CT scan showed focal enhancement thickening of the upper third gastric wall, with perigastric infiltration and enlarged lymph nodes without signs of distant metastasis. He was then submitted to a total gastrectomy with D1 lymphadenectomy on November 2009. We found major technical difficulties intraoperatively due to the previous LT surgeries. Local adhesions around the vascular and biliary anastomoses allowed us to perform only perigastric lymph node dissection (D1). Peritoneal washing cytology was negative. The postoperative period was uneventful, and the patient was well on discharge ten days following the surgical procedure. Pathology report confirmed a poor differentiated signet ring cell adenocarcinoma with serosal invasion and 4 metastatic lymph nodes with also positive *H. pylori* infection. Final stage: pT4apN2cM0 - IIIB (AJCC/UICC 7th Ed. 2010).

Discussion

There are two major aspects to be discussed. First, refer to the transplants this patient was submitted. Overall survival of transplanted patients has increased significantly in the last decades allowing this population to receive further treatments and even other organ transplantations. This progress is attributed to better patient selection programs, enhanced surgical transplantation and organ procurement techniques, better anesthesia and postoperatively support and a better control of acute and long-term rejection with new immunosuppressive agents.

The second aspect it is the relation between the transplanted population and the onset of malignant disease, with a 7 to 20% incidence [4-9,15]; much higher than the incidence shown in the non-transplanted population [17,26]. Hematologic malignancies also known as PTLD (post-transplant lymph proliferative disorder) are the most common with an incidence of over 43% [13-15]. PTLD has been reported in many sites such as skin, small intestine, colon, rectum, stomach, liver, lung, CNS and in the kidney allograft; although site-specific incidence varies from different country reports [13,14,18,19,23-25].

The probable causes for higher incidence of malignancy among transplanted patients are: immunosuppressive drugs, antimetabolic agents and co-existing viral infections [10-12]. *Helicobacter pylori* stands actually as a class 1 carcinogen for gastric cancer [15,16] and

estimates are that *H. pylori* infection roughly doubled the risk of a gastric neoplasm among the transplanted population compared to other immune deficient populations such as HIV/AIDS patients [1].

In this case, added to the long term immunosuppressive regimen he was submitted because of the three transplantations, there´s also an increased chance for this patient to develop esophagogastric junction tumors according to data shown by many authors that reported smaller time intervals from preneoplastic lesions to carcinoma such as Barrett esophagus, skin lesions and colonic polyps in liver graft recipients [18-22].

PTLD are the most common malignancies associated with immunosuppressive agents [13-15], probably because of the rapid cellular "turn-over" found on this tissues promoting mutation to tumoral cells. It is assumed that a higher cell proliferation in the gastric mucosa could increase the incidence of gastric cancer incidence among these patients but there´s no relevant data to prove this. Apparently, other factors such as smoking, immunosuppressive drugs and viral infections have a bigger role in gastric cancer carcinogenesis than simple accelerated cellular "turn over" found in some tissues [1,10-12,26].

Immunosuppressants undoubtedly have decreased acute rejection in transplant recipients therefore increasing the overall survival of this population and it is a proven fact that malignancy onset is closely related to the time and type of immune modulation. This relation allow us to classify this patients as a high risk population, with a three to fourfold risk of developing tumors when compared to normal populations [9] and is important to asses this immune therapy and it is actual cost when diagnose and screening tools for cancer are necessary increasing overall values and gaining relevance in public health policies and health funding destination.

Still considering the costs, early detection of these malignancies could be translated to a better prognosis with less invasive therapies and less expenses to society. From this point of view, certain eastern countries authors appeal to aggressive screening programs with EGD and contrast imaging studies in transplant recipients, mainly because of higher rates of gastric cancer at these countries, whether for the transplanted and for the non-transplanted populations [13,23,24].

An incidence rate of gastric cancer in seven thousand solid organ transplant recipients in the United States was of 486 cases in 100.000 transplantations [13]. Nevertheless if we compare those results to the incidence among normal population in the US, of approximately 10 cases in 100.000 [14], it is quite evident the importance of surveillance and analysis of the risks that this patients are submitted and also the impact of a neoplasm in the overall medical costs. This rate is more than half of the overall incidence of gastric cancer in the population of Japan: 78 cases in 100.000 people where massive investments are made in this type of cancer screening and treatment [14].

There is an estimated gastric cancer rate of 1,2% of all the malignant neoplasm in the transplanted patients, and it is a fact that when cancer it is detected at an early phase there is a chance of survival and even cure. It is an interesting fact that in Japan, even among renal transplant recipients, gastric cancer stands as the second most common malignancy; therefore justifying health politics in that country and the importance of aggressive screening programs for this tumor in all types of patients [23,24].

Conclusion

The renal and liver transplant recipients may course with aggressive neoplastic diseases with an elevated mortality. Early detection, accurate staging and treatment of tumors is imperative for these patients, specially for gastric malignancies where an objective, fast and aggressive multidisciplinary approach could bring higher overall survival rates and the best quality of treatment available.

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