

Concomittant Liver Transplantation And Low Anterior Resection in Patient with Neuroendocrine Tumor and Chronic Hepatitis B Infection

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Abstract

Aim: The treatment of end-stage liver disease is liver transplantation. There are studies regarding liver transplantation in patients with colorectal cancer and neuroendocrine tumor liver metastasis indicating comparable results with patients who were transplanted for hepatocellular carcinoma. The aim of the present study is to present a case of a patient with Hepatitis B virus related chronic liver disease and rectal neuroendocrine tumor who underwent concomitant living donor liver transplantation and low anterior resection.

Case report: The patient was a 62 years old male patient with hepatitis B virus related end-stage liver failure and a rectal neuroendocrine tumor determined during colonoscopy surveillance. Model for end stage liver disease score was 21 and had two episodes of life-threatening variceal bleeding. We performed living donor liver transplantation and low anterior resection to the patient. Currently patient is doing well 2 years after the operation.

Conclusion: Our case is the first in literature showing concomitant liver transplantation for hepatitis B virus related liver failure and rectal resection for neuroendocrine tumor. These procedures can be performed synchronously provided that the etiology of liver failure is unrelated to neuroendocrine tumor and the primary tumor has favorable tumor biologic characteristics. We reviewed the English literature, we did not find any case who underwent rectal NET surgery and HBV-related liver transplantation in the same operation. We wanted to present this first case in the literature.

Introduction

Neuroendocrine tumors (NET) are epithelial neoplasms that originate from the enterochromaffin cells. They have various biologic behaviors, and they are usually located in pancreas and small bowel. Rectal localization is relatively uncommon. The incidence of gastro-entero-pancreatic NET (GEP-NET) is increasing together with extensive and elective use of upper gastrointestinal endoscopy [1, 2]. The NET has insidious behavior and therefore diagnosed at a later stage when the disease is metastatic. Liver is the most frequent site of metastasis for NETs' (46–93%) [1].

NETs' become symptomatic depending on the tumor burden and the level of hormone secretion. In United States, rectal NETs' make up 18% of all the NETs' and make up one third of all the gastrointestinal NETs [2]. Majority of these lesions are diagnosed in the early stages. The 5-years survival rates are reported to be 88% and the prognosis is relatively good [1]. Surgery is the only means of cure in GEP-NETs [3]. Various therapeutic options including liver resection can be applied for the treatment of liver metastasis of NETs'. Liver transplantation for unresectable liver metastasis of NETs' is an accepted therapeutic modality [4]. In the present study we present a case with NETs and hepatitis B virus (HBV) related cirrhosis who received synchronous living donor liver transplantation (LDLT) and low anterior resection (LAR) for rectal resection for NETs'. In our knowledge, this was the first case in the literature.

Case Report

A rectal mass was detected during colonoscopy in a 62-year-old male patient with chronic liver disease due to HBV (Fig. 1). Analysis of the biopsy specimen showed that it was a NET. The patient had a regulated diabetes mellitus. The patient had no history of intractable ascites, but his history showed that he suffered from two episodes of life-threatening variceal bleeding. The patient received antiviral treatment and his HBV DNA and hepatitis D virus RNA were negative. Physical examination was unremarkable. The clinical and laboratory characteristics of the patient is summarized in Table-1.

The abdominal tomography showed that the liver had shrunken with a heterogenous and lobulated liver parenchyma. Also, there was ascites that had 6.5 cm in thickness in tomographic sections. Also, there was a mural thickness in the rectum. Ga-68 DOTA scintigraphy was performed for surveillance of metastatic lesion which showed that only rectum was involved together with a lymph node in the mesorectum (SUV-Max: 44.5). There was no metastatic lesion in the liver either. Therefore, we decided to perform simultaneous LDLT and low anterior resection for the patient.

Intraoperatively, we initially performed LDLT which was followed by low anterior resection for NET. We decided to perform a sigmoid loop colostomy to provide protection for the colon anastomosis due to concomitant two major operations, prolonged operative duration, and coagulopathy. We performed our routine antibiotic prophylaxis to the patient. Immunosuppressive treatment included methylprednisolone (2x100mg) and mycophenolatemofetil (2x1000mg) which was started on postoperative first day. Tacrolimus (2x1 mg) was started on postoperative third day. The dose of tacrolimus was tapered according to the trough levels. Oral intake was started on postoperative 2th day after the discharge of the colostomy. The patient was discharged on postoperative 11th day.

The explant pathology showed that liver was nodular and advanced fibrosis but had no malignant metastasis. Histopathology of the hilar lymph node showed reactive hyperplasia. The rectal resection material was 12.5 cm. The dimensions of the rectal mass was 1.8x1.2x1.3 cm and the proximal and distal surgical margins were negative. The tumor was grade II rectal NET. The tumor infiltrated perirectal adipose tissue and also had lympho-vascular and perineural invasion. The meso-rectal lymph node showed reactive changes. Synaptophysin, chromogranin A and CD56 immunostaining was extensively positive. CEA staining was patchy positive and Ki 67 proliferative index was 15–20%.

The patients was followed monthly for the first postoperative 6 months. In the second postoperative 6-months the follow up was once in every 3 months. Later the follow up routine was two times a year. The closure of the loop colostomy was delayed to postoperative 20th month due to the COVID-19 pandemic. The patient is now in good condition without any recurrence 24 months after the surgery.

Discussion

The treatment of end-stage liver disease is liver transplantation. The studies have shown patients transplanted for NET liver metastasis had comparable outcome to the patients with HCC within Milan

criteria [5]. The patients are required to have at least 2 years following primary surgery for NET and the disease should be confined to liver at the time of liver transplantation [6].

Majority of the rectal NET are small and localized to the mucosa and submucosa. Majority of the cases are dormant and symptomatic. However, as the tumor size and invasion depth increases, the risk of metastasis and aggressive biologic behavior increases. This has an effect on the postoperative outcome of these tumors and therefore. Early diagnosis has paramount importance for a favorable postoperative prognosis [7]. The definitive treatment of rectal NET's are resection. European Society of Medical Oncology guidelines state that surgery is the primary treatment of gastrointestinal NETs [8]. The 5-years survival rates of patients with rectal NET is 80–100% [9, 10]. Smaller tumors can be treated with endoscopic mucosal resection, transanal minimally invasive surgery. However larger tumors (> 2 cm) or tumors that penetrate and extend through muscularispropria require low anterior resection and abdominoperineal resection [11].

In the present study we performed concomitant LDLT and low anterior to patients with HBV related end stage liver disease and rectal NET. The majority of early postoperative infective complications (30–40%) observed following liver transplantation is intraabdominal sepsis. This is due to the fact that biliary and gastrointestinal surgeries are contaminated surgeries [12]. We took every necessary precaution to prevent abdominal sepsis in a dismal surgical environment. The patient is now in postoperative second year with and uneventful postoperative follow-up. Our literature search has shown that there is only one reported case with concomitant liver transplantation and resection [13]. This was the case for our patient and only rectal resection may lead to decompensation of the patient due to surgical trauma. On the other hand, performing LDLT would be contraindicated due to high risk of tumor progression due to immunosuppressive therapy. For this reason, we performed both LDLT and LAR in the same session. Portal clamping during liver transplantation causes edema in the colon. Since this edema will affect the anastomosis safety, we first performed LDLT and then LAR.

In conclusion, the present study shows that concomitant liver transplantation and resection for gastrointestinal NET can be performed under strict selection. The characteristics of the patient in the present study showed that if the tumor has favorable biological characteristics, localized to primary site and the liver failure is unrelated to the NET; than synchronous operations can be performed to the patients because staged procedure has definitive risks that would preclude definitive treatment and survival.

Authors' contributions

Tuncer A, Ogut Z and Usta S conceived and designed research. Akbulut S, Sahin TT and Yilmaz S conducted the research. Tuncer A, Usta S, Ogut Z, and Akbulut S contributed to data extraction. All authors wrote the manuscript. All authors read and approved the manuscript.

Declarations

Authors' contributions

Tuncer A, Ogut Z and Usta S conceived and designed research. Akbulut S, Sahin TT and Yilmaz S conducted the research. Tuncer A, Usta S, Ogut Z, and Akbulut S contributed to data extraction. All authors wrote the manuscript. All authors read and approved the manuscript.

Availability of Data and Material: Data sharing is not applicable to this article as no new data were created.

Code Availability: Not applicable

Informed Consent

Informed consent including publication of photographs in medical journals was obtained from the participant of this study

Compliance with Ethical Standards

Ethical Approval

All procedures performed in the report were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare that they have no conflict of interest

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Tables

Table-1 The preoperative clinical and laboratory characteristics of the patient is summarized.

MELD score	21	AST (IU/mL)	38
BMI (kg/m²)	29	ALT (IU/mL)	21
HBSAG	2396	ALP (IU/mL)	266
HBV DNA PCR	Negative	GGT (IU/mL)	55
HDV RNA PCR	Negative	CA-125	142
ANTI-HAV	Positive	Na (mmol/L)	128
Hgb (g / dL)	9,9	Albumin (g / dL)	1,9
INR	1,32	Total Bilirubin(mg/dL)	2,2
Creatinine	0,81		

Abbreviations: **MELD:** Score The Model For End-Stage Liver Disease Score, **BMI:** Body mass index, **HBSAG:**Hepatitis B surface antigen,**HBV DNA PCR:**Hepatitis B Virus DNA Polymerase Chain Reaction,**HDV RNA PCR:**Hepatitis Delta Virus RNA Polymerase Chain Reaction, **ANTI-HAV:**Hepatitis A Virus Antibody,**Hgb:**Hemoglobin, **INR:**International Normalized Ratio,**AST:** Aspartate aminotransferase, **ALT:** Alanine amino transferase, **ALP:**Alkaline phosphatase, **GGT:**Gamma glutamyl transferase, **CA-125:**Cancer antigen 125, **Na:** Sodium

Figures



Figure 1

Axial pelvic computed tomography shows that a small lesion compatible with tumor originating from left rectal wall.