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Case Report

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AST 17600 U/l after liver transplantation, What are you up to? – A case report

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Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Summary

Background: Miscellaneous clinical classifications of liver function after liver transplantation are rested upon elevation of transaminases which represent damaging of hepatocytes and with it of the liver.

Case Report: We report the case of a 35-year-old man suffering from hepatocellular carcinoma in the setting of alcoholic liver cirrhosis. The patient underwent liver transplantation and developed an extreme peak of transaminases due to prolonged cold ischemia time and additional extended donor criteria. On the first postoperative day the laboratory results showed peak transaminases as follows: AST 17577 U/l and ALT 9884 U/l. Frequent ultrasound revealed no signs of vascular complications. In spite of the dramatically elevated transaminases the liver showed a good primary function and the patient was cardiopulmonary stable. The entire postoperative course was uneventful. We discharged the patient after three weeks in a very good general state of health, with normal laboratory values.

Conclusions: Exclusive extreme elevation of transaminases after liver transplantation combined with adequate liver synthesis does not always require re-transplantation, if situation of the patient is stable. Nevertheless re-transplantation should be reconsidered in any case of clinical deterioration of the patient.

Key words: **elevated transaminases • liver transplantation • case report • extended criteria donor • clinical decision making**

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Background

Orthotopic liver transplantation is one of the most important treatment options for end-stage liver disease and unresectable hepatocellular malignancies. After liver transplantation a pattern of diagnostic tools is used for assessment of liver function due to a lack of more specific and sensitive assessment methods. Conventional laboratory data like transaminases AST and ALT represent damaging of hepatocytes and with it injury of the liver. The peak of transaminases in the first days after liver transplantation usually reflects the ischemic damaging of the transplanted organ. Miscellaneous clinical classifications of liver function after liver transplantation (e.g. early allograft dysfunction) are rested amongst other things upon elevated transaminases [1–4]. Cut-off values to differentiate between better and poorer prognosis are different in these classification systems. But an elevation of AST or ALT above 2000 U/l is commonly associated with a poor prognosis [5]. These classification systems are used to objectify the clinical course after liver transplantation and further important clinical decisions, maybe even retransplantation, are in part based on them.

Case Report

We here report the case of a 35-year-old man suffering from hepatocellular carcinoma in the setting of alcoholic liver cirrhosis. HCC lesions were located in segments II, IVa/b and V with a diameter of 4 mm, 24 mm and 8 mm, respectively, therefore being within Milan Criteria. Unfortunately resection of these lesions was not possible due to unfavorable position in both lobes of the liver. Extrahepatic co-morbidities were absent in the patients past medical history. Application of the Barcelona-Clinic Liver Cancer (BCLC) classification resulted in the BCLC stage A for this patient with liver transplantation as recommended treatment. The patient's medication consisted of beta blockers, proton-pump inhibitors, aldosterone antagonists, vitamin K and lactulose. At the time of liver transplantation the patient was listed with an exceptional MELD-Score of 22 points. The laboratory values resulted in a calculated MELD score of 9 points.

The donated organ had a donor risk index of 1.3. Donor age was 58 years and donor BMI was 24.7 kg/m^2. Cause of death was craniocerebral trauma and the donor had stayed in an ICU for three days with low vasopressor support (noradrenalin: 0.025 µg/kg/min) before organ procurement. Last laboratory values of the donor showed the following results: AST 156 U/l, ALT 38 U/l, Bilirubin 0.32 mg/dl, Sodium 147mmol/l, Creatinine 0.66 mg/dl. Organ quality of the liver was described as "good" by the procurement team. The result of a routine biopsy performed one hour after reperfusion during the recipient operation indicated 5% micro- and additional 5% macrovesicular steatosis (Figure 1). Cold ischemia time was 18 hours due to primary allocation to another patient, who was then judged non-transplantable at a different transplant center. Re-allocation as an organ rescue offer by Eurotransplant was accepted by our transplant center. Prior to transplantation the organ was treated by retrograde oxygen persufflation for revitalization.

Orthotopic liver transplantation was carried out with cava replacement and end-to-end anastomosis of hepatic artery, portal vein and bile duct. Warm ischemia time was 29 minutes. Blood flow measurements of hepatic artery and portal vein were performed 30 minutes after reperfusion and demonstrated an arterial blood flow of 345 ml/min and a portal blood flow of 640 ml/min. The course of the surgical procedure was uneventful and transfusion of blood components was not required. The perioperative immunosuppression regimen consisted of intravenous corticosteroids. Postoperative immunosuppression regimens consisted of a calcineurin-inhibitor (adjusted in accordance to the trough level of the drug) in combination with corticosteroids.

On the first postoperative day the laboratory results showed peak transaminases as follows: AST 17577 U/l and ALT 9884 U/l (Figure 2). Spontaneous INR was 1.41 and aPTT 30.9 seconds. Bilirubin showed a value of 1.6 mg/dl and GGT was 197 U/l. Frequently performed ultrasound displayed no signs of vascular complications at any time in the following clinical course. During the surgical procedure a routine liver biopsy was performed one hour after reperfusion. The result of this biopsy demonstrated a minor to moderate ischemic reperfusion injury. In spite of the dramatic elevation of transaminases the liver showed a good function of synthesis and the clinical course bore a cardiopulmonary stable patient. Therefore we abstained from a listing for retransplantation by high urgency status. Renal function was all-time excellent with normal laboratory values and stable diuresis. The patient was extubated on the second postoperative day and

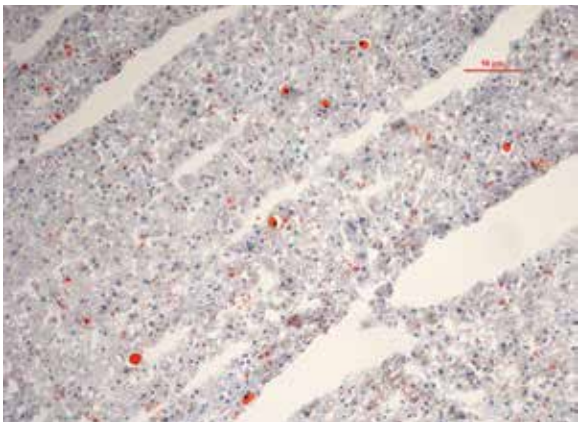

Figure 1. Routine biopsy of the liver taken 30 minutes after reperfusion. Oil Red staining for representation of liver steatosis.

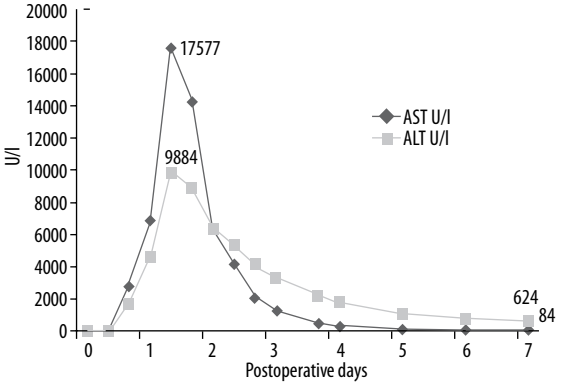

Figure 2. Laboratory course of the transaminases AST and ALT after liver transplantation.

was transferred to the regular ward on postoperative day five. The further clinical course was uneventful and the daily ultrasound revealed no abnormalities, especially no regional necrosis that could be responsible for elevated transaminases. The laboratory results demonstrated a constant decrease in transaminases in the following days. We discharged the patient after three weeks in a very good general state of health, with normal laboratory values, meaning AST 17 U/l, ALT 31 U/l, INR 1.02, aPTT 23.1 seconds, Bilirubin 0.3 mg/dl and gGT 49 U/l and without signs of liver dysfunction, particularly.

Six months after liver transplantation a routine CT-Scan and MRT-Scan of the liver were performed for follow up of hepatocellular carcinoma. These diagnostics showed a transplanted liver without any pathological findings, especially no signs of a past locoregional necrosis. Liver supplying vessels were entirely unremarkable as well as laboratory findings. The patient remained in a very good overall state of health without any signs of discomfort or liver dysfunction.

Discussion

The individual conditions of a liver transplantation originate in unpredictable environmental variables. The here presented case describes the liver transplantation of an extended criteria donor organ (defined by the cold ischemic time of 18 hours) into a young and relatively healthy recipient, who developed an extreme elevation of laboratory ischemic markers after liver transplantation. Such extreme elevations of ischemic markers after liver transplantation could be explained by locoregional necrosis through restricted blood supply in case of arterial thrombosis or by an overall ischemic damaging of the organ, frequently leading to subsequent liver failure. The former hypothesis of locoreginal necrosis of the liver was excluded by imaging diagnostics during the clinical course. The latter diagnosis would have resulted at least in short-term restricted liver function but our patient demonstrated a startlingly bland clinical course, other than expected.

In our opinion the uneventful clinical course of the here presented case might be due to the constellation of favorable variables combined in this transplantation procedure. Besides its extended criteria donor organ status the donated organ was accompanied by good overall properties with a donor risk index of 1.3 [6]. Furthermore only mild steatosis was described by liver biopsy. Since steatosis is known to be one of the major risk factors for graft dysfunction and graft failure the mild degree of steatosis might have yielded enough regeneration capability of the organ to compensate for an initial critical ischemic injury by a prolonged cold ischemia time [7]. Likewise, recipient details featured ideal properties for liver transplantation with a young recipient in a very good overall state of health and no known co-morbidities. Nonetheless liver transplantation was the preferential treatment for this recipient because of his unresectable liver malignancy [8]. The influence of the recipient's condition on the overall survival in turn is commonly known [9–11]. Matching the right recipient to the organ might be responsible for the unremarkable clinical course and the good outcome of this transplantation.

Rates of organ donation remain suboptimal in Germany [12], resulting in severe organ shortage while the attitude to organ donation rates might be increased by rather plain methods [13,14].

The persisting organ shortage in turn leads to acceptance of extended criteria donor organs on a regular basis (approximately 60% of organs in Germany) [15]. Thorough risk evaluation of these organs is required to minimize the risk for the particular recipient notably as it is suspected that current organ classifications lack accuracy [16]. Moreover, for optimal utilization and optimal outcome of these organs matching of donor and recipient factors seems to be pivotal [17,18]. Indeed, it still remains unclear whether organs of minor quality should regularly be allocated to healthier recipients with the capability to survive a potential initial phase of suboptimal graft function [19].

Definitions of early allograft dysfunction and other clinical classification systems have been developed to objectify the outcome of liver transplantation and therefore aid the transplant physician in the clinical decision making. Application of the most common classification systems in the presented case would have led to the prediction of an annihilating prognosis. Based on the transaminases which are usually part of these systems the patient would have been grouped to the worst classes. The limitations of these systems are underlined by this case report in a provocative manner: instead of focusing on usually representative variables, all available information must be taken into account for the rating of complex clinical situations. Classification systems should be regarded as additional information. Therefore assessment of liver quality and function after liver transplantation still requires a complex pattern of laboratory values and clinical parameters. New methods might be able to complete the current assessment methodology and differentiate with high specificity and sensitivity early allograft dysfunction with the need of intervention, even retransplantation. To our knowledge this is the first reported case of AST over 15.000 U/l after liver transplantation resulting in survival of organ and patient as well as an uneventful postoperative course.

Conclusions

In conclusion exclusive extreme elevation of transaminases after liver transplantation combined with adequate liver synthesis does not always require retransplantation. Clinical decision making is obliged to consider all available information.

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