



## CASE REPORT

# Liver Transplant with a Donor after Bothropic Accident - Case Report

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## Abstract

**Background:** Orthotopic Liver transplantation is the primary treatment for most end-stage-liver diseases. Victims of snakebite are potential organ donors since the venom's ability to induce irreversible brain damage. However, in the literature, reports of liver transplants obtained from victims of these accidents, their outcome and follow up are practically non-existent. Our purpose is to report a case of a donor with brain death following complications of a bothropic accident, and the patient who receives the liver with cirrhosis due to Hepatitis B.

**Case report:** A 40-year-old male patient was admitted to Fortaleza General Hospital (HGF) to perform a liver transplant. The 67-year-old donor, who, after a snakebite of the species *Bothrops jararaca*, developed coagulopathy and progressed with a hemorrhagic stroke. There was confirmation of encephalic death. In the laboratory examinations, the donor presented AST of 17 U/L, ALT of 20 U/L, total bilirubin 2,4 mg/dL and platelets of 80,000/μl. Hepatic transplantation was performed, which occurred without complications. On the first postoperative day (PO), there was an AST peak of 2885 U/L and ALT of 1497 U/L, followed by progressive reduction. In the eighth PO, ultrasonography with Doppler showed a graft without alterations.

**Conclusion:** There were no complications that compromised the graft or the life of the recipient, being, this case, an example of the possibility that the organs from deceased snakebites donors can be transplanted.

## Keywords

Liver transplantation, Bothrops, Donor selection

## Background

Over the past 50 years, liver transplantation has emerged, evolved and is now the primary treatment for end-stage-liver disease [1,2]. Since the incorporation of the Model for End-Stage Liver Disease (MELD) system, there has been an effective reduction in the mortality of candidates on the liver waiting list [1-3]. The lack of organs for donation is the main issue for a liver transplant, and the number of organs is still lower than patients on the waiting list. Therefore, scientific evidence that any given condition does not disable a liver from being donated is most welcomed.

Literature is practically nonexistent in records of a liver donation from patients who died from contact with venomous snakes and lizards, although there is evidence of successful transplantation involving deceased kidney donors from snakebites [4]. Although in Brazil alone there are about 100 deaths per year due to this cause [5], *Bothrops jararaca* and *Bothrops atrox* account for 90% of snake poisonings. The mortality rate is 0.5% and is related to the amount of venom inoculated, time of care (ideally < 6 hours) and intrinsic factors of the patient [6,7].

This case report is about a rare occasion in which a liver is donated for transplantation after the donor is declared with encephalic death due to snakebite of the *Bothrops jararaca* species.

## Case Report

A 67-year-old female patient, after an ophidian accident by the snake of the *Bothrops jararaca* species, developed consumption coagulopathy. She received the protocol treatment for the cases of a bothropic accident, which consisted of the administration of antithrombotic serum, drainage of the bite segment, analgesia, and hydration. The patient presented only mild swelling in the bite site, the distal segment of the left limb, with no clinical evidence of cellulitis or necrosis. However, in the first 24 hours after the admission, the patient progressed to a hemorrhagic stroke (HS) and died.

After confirmation of brain death, it was determined that the patient's liver had not been compromised by the snake venom. The liver had approximately 30% of steatosis and had the presence of a cyst in the left lobe. In laboratory tests, the donor presented aspartate aminotransferase level 17 U/L, alanine aminotransferase level of 20 U/L, prothrombin time of activity 12.7 seconds, total bilirubin of 2.4 mg/dL (direct bilirubin 0.8 mg/dL), platelets 80,000/ $\mu$ l and the serologies for hepatitis B and C, syphilis, Chagas' disease, HIV, CMV (IgM and IgG) were all negative. There was no evidence in laboratory tests that showed any suspicion for hemolysis or disseminated intravascular coagulopathy (DIC). Laboratory investigations also revealed normal renal function with a serum creatinine of 0.8 mg/dl, blood urea of 38 mg/dl and a urine output of 1.3 Liters per 24 hours. The patient maintained a blood pressure of 130/90 mmHg, a temperature of 35 °C and a heart rate of 87 per minute. Hence, it was laboratory and clinically determined that the venom did not compromise the liver nor the kidneys, and both of the organs were donated.

The liver was donated in May 2017 for transplantation, for a 40-year-old male patient from the city Fortaleza of the state Ceará-Brazil, who had cirrhosis due to Hepatitis B (Anti-HBc and Anti-HBs positive). The patient had a MELD of 16, but was prioritized after hepatic encephalopathy and had a readjusted MELD to 29. In his preoperative studies, the recipient had an AST of 43 U/L and an ALT of 22 U/L. Also, his serum sodium was 138 mEq/L, and potassium was 4.8 mEq/L. His INR was 1.9 and the activated partial thromboplastin time (aPTT) was 1.69 times the standard value. The transplant underwent with no complications, the cold ischemia was 4 hours and 9 minutes, and the warm ischemia time was 45 minutes. The patient received tacrolimus and everolimus followed by prednisone for three months, according to the institution immunosuppressive protocol. On the first postoperative day, there was an increase in transaminases, with a peak of aspartate aminotransferase level of 2885 U/L and alanine aminotransferase level of 1497 U/L, followed by progressive reduction of these levels down to AST 32 U/L and of ALT 137 U/L on the eighth postoperative day. Ultrasonography with

Doppler showed a graft without alterations. The INR and aPTT were also elevated on the first postoperative day, with a maximum value of 2.15 and 3.5 times the normal range, respectively, followed by a progressive decrease to normal. Finally, there were no complications that compromised the graft, and the transplantation was successful. Currently, approximately 22 months after transplantation, the patient who received the liver is alive and in good health.

## Discussion

In cases of bothropic accidents, the venom of the *Bothrops jararaca* acts in the body of the victim through three known pathophysiological mechanisms. The first is the proteolytic action with complex pathogenesis, but probably involves the activity of proteases, hyaluronidases, and phospholipases, as well as the release of mediators leading to an acute inflammatory process. This process is responsible for local changes in the site of the bite and nearby, such as phlogistic signs, ecchymoses, blisters and necrosis [8].

The second mechanism involves a coagulant action since the venom has both substances capable of activating factor X and prothrombin, as well as having a thrombin-like action when converting fibrinogen to fibrin, resulting in the consumption of coagulation factors and increase in the degradation of fibrin products. This mechanism has, as a consequence, the development of consumption coagulopathy, characterized by a state of blood non-coagulability associated with thrombocytopenia [6,7,9].

The third mechanism is hemorrhagic action. The venom has proteins capable of breaking the integrity of the vascular endothelium. The union of hemorrhagic action and coagulation disorders can cause detectable bleeds, such as bleeding gums, blood in the urine and hemorrhagic stroke, as well as other potentially life-threatening complications [9,10].

Among these pathophysiological processes involved, there is the direct action of metalloproteinases present in the ophidian venom on the endothelium, a mechanism that occurs independently of the one that affects the coagulation cascade. Among these proteins, bothropasin has been described and is capable of fragmenting the basal endothelial membrane, breaking the capillary integrity and, thus, leads to the appearance of hemorrhagic conditions [11]. Because it is a systemic mechanism, any organ can present this complication, including parenchymal organs (liver and kidney). The discovery of this mechanism justifies the occurrence of hemorrhagic processes in patients who do not present significant coagulopathies or in cases in which bleeding precedes the changes in coagulation [12].

As reported in the case, even with adequate medical care, the donor evolved with a hemorrhagic stroke. Local hemorrhagic manifestations are common in patients

after the snakebite of the *Bothrops jararaca* species, but hemorrhagic manifestations in organs of the gastrointestinal tract, cerebral parenchyma, and respiratory system are rare.

Although there are few reports on the prognosis and evolution of patients who received organs from donors who died of snakebites, there are some reported cases, mainly in the renal transplantation scenario. The outcome varies according to the patient's previous laboratory and clinical status, regarding renal function, liver function and, coagulation parameters. In cases in which the donor presented normality of these parameters, or slight changes, and absence of hemolysis, better prognosis was observed in the follow-up, and safe transplantation has been reported [13]. Unfavorable outcomes have been associated with more significant coagulopathies including, DIC and thrombocytopenia [12], but it is essential to take into account the species of the cobra involved and not to define the post-transplant outcomes as common to all species. More studies are needed to evaluate the follow-up of these patients with snakebite, although there is already evidence of their inclusion in donors with extended criteria [14].

Acute renal injury is the most common systemic complication and the leading cause of death from *Viperidae* poisoning [10]. Involvement of the liver by the venom of the bothropic species has also been associated with complications such as the formation of a subcapsular hematoma [15]. However, it is not clear if the parenchymal hemorrhagic condition is associated with a pre-existing vascular malformation or comorbid condition such as Diabetes Mellitus or hypertension [15]. Despite the systemic involvement reported in the case, the liver was preserved, remaining well perfused and able to be transplanted.

The AST peak between 2000 U/L and 3000 U/L presented in the case classifies it as a mild early graft dysfunction [16]. However, in the follow-up, there was no impairment that required emergency intervention or resulted in graft loss.

## Conclusion

Reports of organ transplants obtained from deceased patients after an ophidian accident are practically non-existent in the literature. In this case, we highlight the absence of complications that could compromise the graft or the life of the patient who received the organ in the postoperative period. This case is evidence of the possibility that organs from this type of donor, when appropriated selected and with no significant coagulation or hepatic involvement, can be transplanted.

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