

## Case Report

# From Benign Liver to the Worst Nightmare: High Risk Resection and Attempt to Rescue with Transplant in a Hepatic Localization of Alveolar Echinococcosis

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## Abstract

**Introduction:** Alveolar Echinococcosis is a chronic infection with primary hepatic involvement that can eventually progress to a severe invasive disease with MOF. The standard treatment in hepatic involvement is early surgical resection associated with albendazole or mebendazole.

**Case Report:** A 26 years old man presented with hepatic lesion with an extension above the diaphragm through the vena cava foramen with vascular involvement and previous hepatic resection of a cyst.

During the challenging resection, a lesion of the supra-hepatic left vein was made and this event led to a difficult outflow of the remaining hypertrophic liver. A total hepatectomy was performed and the Transplant System was activated.

The patient suffered two failures of transplant, and during the third transplant, which was ABO incompatible and needed a boost immunosuppression, he developed sepsis and he died.

**Conclusion:** In case of extremely complex hepatic AE it's important to consider as possible solutions liver transplantation or ex-vivo resection have to be evaluated as possible therapeutic solutions. The surgeon experience and background in hepatic resection and transplant are important in this kind of surgery due to the high risk of morbidity and mortality, and for this reason this kind of surgery should be performed in specialized centers: a complete study of the lesion should be made, using US and color-Doppler, CT, MRI (especially when micro cyst presence is suspected), and a multidisciplinary team should create an individualized approach to the patient.

**Keywords:** Alveolar Echinococcosis; Transplant; Liver resection

## Abbreviations

AE: Alveolar Echinococcosis; MOF: Multiorgan Failure; OLT: Orthotopic Liver Transplant; CT: Computed Tomography; MELD: Model for End Stage Liver Disease; MRI: Magnetic Resonance Imaging; WHO: World Health Organization; OR: Operating Room; HCV: Hepatitis-C Virus; HBV: Hepatitis-B Virus; HDV: Hepatitis-D Virus; HIV: Human Immunodeficiency Virus; T-L: Termino-Lateral; IVC: Inferior Vena Cava; T-T; Termino-Terminal; PV: Portal Vein; VOD: Vein Occlusive Disease

## Introduction

Alveolar Echinococcosis (AE) is usually a chronic infection with primary hepatic involvement after a long incubation period, but it can eventually progress to a severe invasive disease with MOF and high mortality rate (75-90% at 10-15 years if untreated [1]). The usual approach to AE, when there's hepatic involvement, is early surgical resection that must be supported by a medical treatment with albendazole or mebendazole for two years after radical resection [2]. However, it is also possible to consider more radical solution, as transplantation, in anatomically challenging situations.

In this case report we want to share how a high-risk hepatic resection for AE had to be converted to urgent OLT and how complications lead to further procedures on the same patient.

## Case Report

A 26 years old Caucasian male came to our attention for abdominal pain and tenderness associated with dyspnea caused by hepatic and left lung localization of Alveolar Echinococcosis.

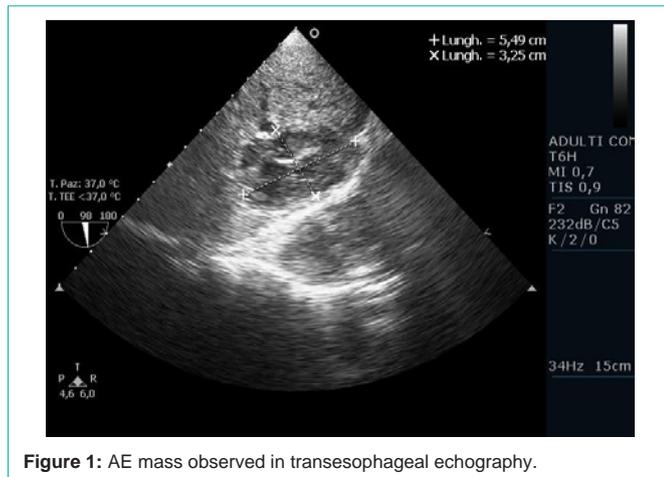
The man was HBV positive, HDV, HCV, HIV negative, his clinical history reported a previous surgical excision of hepatic AE cyst at the age of 16 done in his home country.

He provided us a CT-scan done in another hospital showing a hepatic localization with a diameter of 11cm, and a left lung metastasis with a diameter of 2cm in the inferior lobe.

His liver function was normal (MELD score = 8) and he showed no sign of portal hypertension.

After an infectious disease consult he was prescribed with antifungal therapy with Albendazole 10-15 mg/kg daily.

An MRI was performed, which described a central multiloculated



**Figure 1:** AE mass observed in transesophageal echography.

lesion with an extension above the diaphragm through the vena cava foramen. The right and middle hepatic vein and of the right portal branch were also involved. The hepatic anatomy was distorted by the previous excision, which caused left lobe hypertrophy and hypotrophy of the right one due to the localization of the original cyst.

A brain MRI was also requested for staging, showing no involvement of the cranial structures.

According to the WHO classification [3] the disease was classified as a P4N0M1, requiring an antifungal treatment associated with surgery.

The operation was planned in consultation with thoracic surgeons as a wedge inferior left lung resection and hepatic resection.

In the OR the patient was studied by the anesthesiologist with Trans esophageal echography and he was able to observe the mass (Figure 1).

After opening the abdominal cavity, the cyst appeared to be adherent to the supra-hepatic and para-cardiac IVC with involvement of right and middle hepatic veins and adhesions to the left hepatic vein. The right portal branch was also involved. Decision was made to proceed with a right hepatectomy.

During the dissection of the vascular structures from the AE lesion, a lesion of the supra-hepatic left vein was made, with prompt repair. Unfortunately, this event lead to a difficult outflow of the remaining hypertrophic liver, resulting in an uncontrollable bleeding from the cleavage area and coagulopathy.

To control the bleeding, we resolved to perform a total hepatectomy with a P-C shunt and we activated the emergency system (status 1) for liver transplantation.

The OLT was performed after 24 hours. The whole ABO identical liver was collected from a 49 years old brain death donor and the transplant was performed with a standard procedure: T-L anastomosis between supra-hepatic vena cava of the graft and IVC of the recipient, T-T anastomosis of the PV and T-T anastomosis of the hepatic artery, duct to duct anastomosis over T-tube.

On day 15 a worsening of graft function was observed, with hyperbilirubinemia and coagulopathy.

A CT-scan was performed, revealing edema of the graft with suboptimal vascularization compatible with outflow obstruction. Patient was relisted for urgent re-OLT.

The second transplant was performed 5 days later (post-operative day 20), with a 53 years old whole graft ABO identical with 20% macro-steatosis.

During the procedure we observed thrombosis of the hepatic artery and partial thrombosis of the portal vein with histology compatible with VOD (vein occlusive disease) in the previous transplanted liver. We proceed with OLT performing a T-L cavocavostomy, a T-T portal vein connection and an aorto-hepatic conduit. Intraoperative ultrasound was performed at the end of the procedure to ensure normal flow in the supra-hepatic and portal veins and hepatic arteries.

The graft suffered a primary non function and on the 11<sup>th</sup> post-operative day we urged for a third liver. On day 13 a 40 years old ABO incompatible (A to 0) whole liver graft was available.

Decision was made to accept the liver and to perform a boost immunosuppression, due to the critical condition of the patient. MMF, Basiliximab and Rituximab were added to the patient immunosuppressive standard therapy (Tacrolimus and steroids). We also performed a pre-transplant plasmapheresis and provided the patient with intravenous IgG 0.8 g/kg and programmed a repeated post-transplant plasmapheresis to obtain an anti-A IgM and IgG titer <1:8.

The procedure was performed without complication and a proper antibody titer was reached but in the following days the lymphocytes count fell subthreshold and the patient developed sepsis.

After a CT-scan showing intestinal perforation, we performed an explorative laparotomy finding perforations of the small bowel and the sigmoid colon. We performed a resection of the affected tracts and a hepatic biopsy. The biopsy showed focal vascular damage with no signs of rejection. The intestinal biopsy showed an invasion of *Aspergillus*.

The patient was shifted from the standard antifungal prophylaxis with Fluconazole to Amphotericin-B but after 3 days his condition worsened, leading to MOF and death.

The autopsy showed pulmonary invasive *aspergillus*'s with vascular invasion and embolisms, leading to cerebral and intestinal spread.

## Conclusion

AE can be a very challenging disease, because lesion progression may be silent for years before diagnosis and relapse can after treatment go unnoticed for long periods of time, so the immune status of the patient is of crucial importance.

The invasion of bile ducts and vessels is common and represent the main issue in the surgical planning, paired with the considerable risk of dissemination to other organs. It is also important to look for stem cells in the germinal layer, which are resistant to therapy and may remain unnoticed and persist in the liver. Clearly, all these characteristics of the AE lesions have lead us to compare them to a malignant tumor: safety margins to perform an R0 resection (no

parasitic residue) were found to be around 2cm and were reached in Japanese centers in 18-75% patients [4]. With specialized teams, intra and early postoperative mortality of liver resections for AE ranges from 0 to 2% [5].

Palliative partial resection (R2) have also been studied but it didn't provide better results than medical treatment alone. R1 resection (microscopic remnants) with a 1cm safety margin may achieve almost equal overall survival rates as R0 if associated with albendazole treatment. This solution may be chosen in high-risk resection with invasion of hepatic vessels, vena cava and diaphragm [6].

Liver transplantation as an option for AE lesions emerged in 1980s both as curative and palliative treatment. However, the risk of recurrence after liver transplant is high: a large multicenter European series of 45 cases treated with OLT showed a curative treatment in only 50% of cases, with an overall 5-years survival rate of 71% [7]. More recent studies show similar overall survival rates [8,9].

Even if WHO enlists metastatic disease as absolute contraindication to OLT, experts prefer to consider only brain involvement as an absolute contraindication [7]. Obviously, the presence of metastasis requires more aggressive surgical treatment and a stronger immunosuppression.

The new and probably most interesting solution is the auto-transplantation after ex-vivo resection. This technique may be an even more effective alternative to liver allo-transplantation, remembering that AE lesions are very sensitive to anti-rejection therapy. An interesting Chinese analysis on 15 cases showed that this treatment is very effective on critical invasion of retro-hepatic vena cava, hepatic veins, portal and arterial branches. In that study patients were carefully selected, and a 3D model of the site of resection and the FLR of the auto graft was used [10].

In case of extremely complex hepatic AE with major vessels or biliary structures involvement, especially if repeated liver resections have been made, it's very important to proceed with a careful evaluation before additional liver resections, due to high risk of technical failure. Liver transplantation or ex-vivo resection have to be evaluated as possible therapeutic solutions. The surgeon experience

and background in hepatic resection and transplant are important in this kind of surgery due to the high risk of morbidity and mortality, and for this reason this kind of surgery should be performed in specialized centers: a complete study of the lesion should be made, using US and color-Doppler, CT, MRI (especially when micro cyst presence is suspected), and a multidisciplinary team should create an individualized approach to the patient.

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