Title: Fulminant Hepatic Failure as the Initial Presentation of Hodgkin's Disease and Liver Transplantation: A Case Report.

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Highlights:
- Currently, receiving a liver transplant having a neoplasm is a contraindication.
- The presentation of Hodgkin's disease with hepatic infiltration is extremely rare.
- There are only a few reported cases of liver transplantation at the time the patient has a neoplasm.

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Discussion Points:
- Did you know that receiving a transplant if you have a neoplasm is an absolute contraindication? This has been the rule for years and is still the case today, however, it could be an ideal treatment for patients who need it.

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Background: Hodgkin's disease, a B-cell neoplasm, primarily impacts lymph nodes or extranodal lymphoid tissue. It includes two distinct entities: classical (95%) and lymphocyte-predominant nodular. While the disease commonly manifests as the growth of cervical and intrathoracic lymph nodes in 60-90% of cases, there are rare instances where Hodgkin’s disease has been linked to fulminant liver failure, carrying a very poor prognosis.

The Case: We present the case of a 13-year-old Hispanic female, who started with an insidious condition that evolved to fulminant hepatic failure of unknown etiology with an AST of 770 mg/dl. It was decided to perform an orthotopic liver transplant, the histopathological analysis of the explant and a lymph node reported mixed cellularity Hodgkin's disease. Subsequently, the hematology service requested a lumbar puncture, with no evidence of infiltration. It was decided to initiate six cycles of chemotherapy (CTX) with BEACOPP (bleomycin, etoposide, adriamycin, cyclophosphamide, vincristine, procarbazine, and prednisone) scheme, evolving without complications and achieving a complete response eleven months later; currently, she has been free of disease for three years.

Conclusion: The etiology of Hodgkin's disease in our 13-year-old patient remains elusive, emphasizing the importance of early diagnosis and diverse treatment approaches. Despite limited hospital resources, the decision to proceed with the transplant was driven by the potential fatal outcome if left untreated. Future considerations may necessitate individualizing each case, and carefully assessing the risks and benefits associated with transplantation.

Key Words: Hodgkin disease, liver failure, transplantation, case report
INTRODUCTION.
Hodgkin's disease is a neoplasm of B lymphocytes, that affects the lymph nodes and has a bimodal distribution, with the first peak between 15 and 30 years of age and the second around 55 years of age. Moreover, the World Health Organization classifies this neoplasm into two types: predominantly lymphocytic nodular Hodgkin's disease (5%) and classical Hodgkin's disease with the presence of Reed-Sternberg cells (95%).

It affects different parts of the body, leading to variations in its clinical presentation. The most common presentation involves cervical and intrathoracic lymph node growths in 60-80%, contrasting with the rare initial presentation through hepatic infiltration, since it constitutes approximately 0.44% of all cases, the clinical presentation is usually nonspecific, leaning more towards one consistent with fulminant hepatic failure, which is defined as the development of coagulopathy and encephalopathy within eight weeks of the onset of hepatic dysfunction in patients without the pre-existing liver disease, many of these cases with fatal outcomes, however, for years it has been an absolute contraindication to receive a transplant to have an untreated active neoplasm, and it is still maintained to this day. We present a case of a 13-year-old female who received a liver transplant at the time she had Hodgkin's disease.
THE CASE

A 13-year-old Hispanic female, previously healthy, who began 6 weeks earlier with fatigue, nausea, and fever, went to the doctor for evaluation and requesting laboratory tests, iron deficiency anemia was diagnosed, being managed with acetaminophen at adequate doses for her weight and oral supplemental iron at conventional doses, remaining asymptomatic for six weeks. Afterwards she restarted with asthenia, intermittent fever, nausea and vomiting, going again for medical evaluation, finding data of pancytopenia, jaundice, abdominal pain, nausea, vomiting, hyperlipidemia and hyperthermia for which she was sent to the local emergency department, on admission in poor general condition, with evidence of grade I encephalopathy, generalized icteric tinge, hepatosplenomegaly, paraclinical data included anemia, transaminase elevation, cholestasis, alterations in coagulation times test and findings suggestive of acute liver failure (Table 1). Supportive management was initiated, and the patient was admitted to the pediatric intensive care unit, broadening the diagnostic approach to determine the etiology. Upon questioning family members, there was no reported ingestion of herbal medicine, illicit substances, or others.

She was evaluated by the transplant service of the hospital (Table 2), fulfilling the criteria for liver transplantation, classifying the case as UNOS status 1A. The next day, a cadaveric liver transplant was performed, and the explant with a lymph node was sent to pathology for histopathological studies. The report indicated a liver weight of 1.160 kg, measures 21x17x5cm, irregular surface, rough, greenish color with purplish areas. The lymph node measures 1.1x0.6cm, grayish-brown, irregular, and soft. The pathology report shows a hepatic hilum lymph node consistent with Hodgkin's disease of mixed cellularity and hepatic infiltration; immunohistochemistry is positive for CD15, CD30, CD45, and fascin in neoplastic cells. A week later, a bone marrow biopsy was performed, without evidence of neoplastic infiltration. Afterwards, the Hematology service classified the lymphoma as stage IV.

Due to the diagnosis, management with chemotherapy BEACOPP (Bleomycin, Etoposide, Adriamycin, Cyclophosphamide, Vincristine, Procarbazine and Prednisone) scheme of six cycles was started, which lasted for nine months; during her management a cervical lymph node was found in Computed Tomography, which was kept under follow-up, and a biopsy of the lymph node was performed without finding infiltration. The rest of the clinical evolution was towards improvement, maintaining stable liver enzyme levels throughout the CTX sessions, complying with immunosuppressive management, achieving complete response, currently free of disease for three years and in her last consultation with good general condition and adequate hydration, as well as steady laboratory levels (Table 3).
DISCUSSION.

It can be seen in the case as the patient evolved satisfactorily achieving a complete response and remaining free of disease at present, even though different guidelines mention that it is a contraindication to perform a liver transplant in fulminant hepatic failure secondary to neoplasms, some cases have been reported in the literature of favorable evolutions after undergoing liver transplantation.

Kirsten M. et al. reported a case involving a seven-year-old male with fulminant hepatic failure requiring emergency liver transplantation, during surgery, enlarged lymph nodes were located around the portal vein, and Hodgkin's disease was later diagnosed, the patient had a relapse when an enlarged cervical lymph node was located, so chemotherapy was performed, achieving a complete response, even some time later he needed a retransplantation at 13 months due to chronic graft rejection.

Brannigan et al. reported the case of a 12-year-old pediatric patient who developed fulminant hepatic failure, initially, parvovirus was considered as the main cause, a living-donor liver transplant was performed with his mother; when the explant was examined, Hodgkin's disease was diagnosed, the patient up to the date of publication remains in remission at one year.

There are other cases in which a liver transplant was performed despite a previous diagnosis of Hodgkin's disease, which is also considered a contraindication at present.

Frank S Hong et al. reported two cases of fulminant hepatic failure, one of a 19-year-old male with a pre-transplant diagnosis of Hodgkin's disease who achieved a complete response to the disease; the other 55-year-old patient died without having received a transplant due to posterior fossa hemorrhage.

Also, Hope et al. reported a similar case of a five-year-old pediatric patient with a history of Hodgkin's disease diagnosed at the age of two, who developed fulminant hepatic failure, a percutaneous biopsy was performed in which areas of portal infiltration by lymphocytes were found without detection of cells suggesting cancer, It was decided to perform the transplant, during surgery a plaque was located in the patient's liver, and a intraoperative biopsy was performed with a high possibility of being Hodgkin's disease, it was decided to continue with the transplant as it was not entirely diagnostic; histopathologic examination was performed diagnosing Hodgkin's disease, sometime later there was a recurrence of cancer, which was successfully treated with rituximab, the patient is in remission five years later with no apparent complications.

Although it is not intended that all patients with hepatic infiltration by undiagnosed Hodgkin's disease who evolve to fulminant hepatic failure receive a transplant, due to the scant information available to date, it is important to observe how the reported cases have achieved favorable results, likely due to the fact that this type of neoplasm has good survival rates depending on the stage.

We believe it would not be appropriate to dismiss this hypothesis. Therefore, we might consider, in the future, individualizing each case to evaluate whether receiving the transplant would be beneficial or not.
In addition, given the limited resources in many hospitals to obtain an early diagnosis meeting the criteria for Hodgkin's disease, it was decided to perform the transplant since, it had not been performed, it is very likely that the patient would have a fatal outcome.

Conflict of Interest Statement & Funding
The Authors have no funding, financial relationships, or conflicts of interest to disclose.

Declaration of patient consent
The authors certify that patient consent has been taken for participation in the study and for publication of clinical details and images. The patient understands that the name and initials would not be published, and all standard protocols will be followed to conceal their identity.
Falla hepática fulminante como la presentación inicial de enfermedad de Hodgkin y trasplante hepático: Reporte de un caso.

Desde hace tiempo es una contraindicación recibir un trasplante al tener una neoplasia diagnosticada y se mantiene hasta nuestros días, sin embargo, ha habido casos reportados en la literatura sobre pacientes que recibieron un trasplante hepático en esas mismas circunstancias. En este caso presentamos a una paciente femenina la cual inicio con un cuadro insidioso, posteriormente progreso a falla hepática fulminante de etiología desconocida, decidiéndose realizar un trasplante hepático de receptor cadavérico no emparentado al cumplir con criterios del King’s college. Posteriormente se reporto enfermedad de Hodgkin en el hígado y un ganglio peri hepático, iniciándose quimioterapia con esquema BEACOPP, evolucionando favorablemente y estando libre de enfermedad en la actualidad.

Es importante ver como la paciente evoluciono de manera favorable y que, en el caso que se hubiera diagnosticado primero la neoplasia, no hubiera recibido el trasplante y probablemente hubiera fallecido por complicaciones mismas de la falla hepática fulminante. Por lo cual pudiera ser de importancia a futuro para individualizar cada caso y decidir si se beneficiaría de recibir un trasplante o no.
REFERENCES.


FIGURES AND TABLES.

Table 1. Blood test results after admission.
<table>
<thead>
<tr>
<th>Paraclinical Report</th>
<th>Value</th>
<th>Normal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>10.6</td>
<td>12.2-18.1 g/dL</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>3.8</td>
<td>4.2-10.2 K/uL</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>2.4</td>
<td>2.0-6.9 K/uL</td>
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<tr>
<td>Lymphocytes</td>
<td>0.1</td>
<td>0.6-3.4 K/uL</td>
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<tr>
<td>Platelets</td>
<td>94.7</td>
<td>142-424 K/uL</td>
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<tr>
<td>HBV</td>
<td>Negative</td>
<td>N/A</td>
</tr>
<tr>
<td>HCV</td>
<td>Negative</td>
<td>N/A</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>12.04</td>
<td>0.1-1.2 mg/dl</td>
</tr>
<tr>
<td>Direct bilirubin</td>
<td>8.86</td>
<td>&lt;0.3 mg/dl</td>
</tr>
<tr>
<td>Indirect bilirubin</td>
<td>3.18</td>
<td>0.2-1.2 mg/dl</td>
</tr>
<tr>
<td>ALT</td>
<td>1144</td>
<td>4-36 U/L</td>
</tr>
<tr>
<td>AST</td>
<td>770</td>
<td>8-33 U/L</td>
</tr>
<tr>
<td>HIV</td>
<td>Negative</td>
<td>N/A</td>
</tr>
<tr>
<td>Lupus anticoagulant</td>
<td>Normal</td>
<td>&lt;1.2</td>
</tr>
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</table>
Table 2. Blood test results to evaluation for transplantation department.
<table>
<thead>
<tr>
<th>Paraclinical Report</th>
<th>Value</th>
<th>Normal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bilirubin</td>
<td>17</td>
<td>0.1-1.2 mg/dl</td>
</tr>
<tr>
<td>Direct bilirubin</td>
<td>11.9</td>
<td>&lt;0.3 mg/dl</td>
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<tr>
<td>Indirect bilirubin</td>
<td>5.6</td>
<td>0.2-1.2 mg/dl</td>
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<td>ALT</td>
<td>1014</td>
<td>4-36 U/L</td>
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<td>AST</td>
<td>716</td>
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<td>LDH</td>
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<td>105-333 U/L</td>
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<tr>
<td>INR</td>
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<td>1</td>
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<tr>
<td>Ammonium</td>
<td>285</td>
<td>15-45 μg/dl</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>&gt;10</td>
<td>&lt;0.5 ng/ml</td>
</tr>
</tbody>
</table>
**Table 3.** Last consult blood test results.
<table>
<thead>
<tr>
<th>Paraclinical Report</th>
<th>Value</th>
<th>Normal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>13</td>
<td>12.2-18.1 g/dl</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>3.9</td>
<td>4.2-10.2 K/uL</td>
</tr>
<tr>
<td>Platelets</td>
<td>126</td>
<td>142-424 K/uL</td>
</tr>
<tr>
<td>INR</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>0.30</td>
<td>0.1-1.2 mg/dl</td>
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<tr>
<td>ALT</td>
<td>19</td>
<td>4-36 U/L</td>
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<tr>
<td>AST</td>
<td>24</td>
<td>8-33 U/L</td>
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<tr>
<td>Sirolimus levels</td>
<td>6.8</td>
<td>5-15 ng/ml</td>
</tr>
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