A Case of Nodular Regenerative Hyperplasia with Rapid Progression To Liver Failure

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Introduction

Nodular regenerative hyperplasia (NRH) is a rare intrahepatic microvascular disorder in which an altered perfusion state transforms normal liver structures into nodules. Chronic use of thiopurines, chemotherapeutics, and antiretrovirals may contribute to development of NRH. NRH has also been linked to solid organ transplantation, autoimmune disorders, and diseases with recurrent vascular and infectious complications. Clinical presentation can be insidious as liver function tests can be normal. Though rare, NRH is an important disease process for clinicians to be aware of as it can cause significant symptoms of portal hypertension and liver failure in patients.

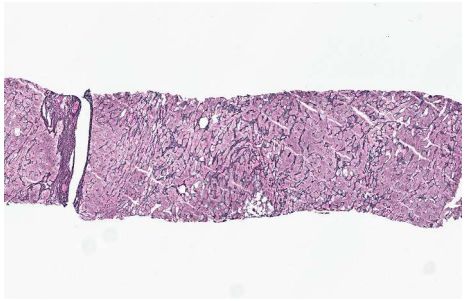
Description

57-year-old male with a history of end stage renal disease secondary to adenine phosphoribosyltransferase deficiency, status-post kidney transplant presents with abdominal distension and diarrhea. CT abdomen revealed ascites. He was diagnosed with campylobacter colitis and the ascites was thought to be reactive to the infection. He underwent paracentesis and improved with antibiotics. Unfortunately, his ascites reaccumulated multiple times in the following months despite confirmed campylobacter eradication. Serum-ascites albumin gradient was consistent with portal hypertension. A transjugular liver biopsy found an elevated hepatic portal venous gas and pathology consistent with NRH without cirrhosis. He also developed hematochezia, requiring multiple hospitalizations due to pan-colonic ulcers of uncertain etiology. Approximately 9 months after the initial onset of symptoms he presented with a GI hemorrhage and worsening liver function. He became encephalopathic and showed worsening synthetic liver function. Renal function deteriorated secondary to hepatorenal syndrome. He was urgently listed on the liver and kidney transplant list and successfully underwent simultaneous liver/kidney transplantation.

Description

Synthetic liver function is typically unaffected with NRH. The patient had completely normal liver function prior to his sudden decompensated liver failure. Previous CT imaging did not show any abnormalities with his liver prior to his diagnosis of NRH. MR elastography revealed stage 1-2 fibrosis. NRH can progress to significant fibrosis; however, there was none noted on his biopsy a month prior to the liver failure. A repeat biopsy prior to his transplant revealed ongoing NRH with pathology suggestive of suboptimal flow. CT abdomen showed prominent vessels in the cecum concerning for venous cecal extravasation which may represent a source of his hemorrhage along with the bleeding ulcers. Transplant was preferred over temporizing measure such as TIPS due to his decompensated liver/renal failure. He was listed to the transplant committee with a MELD of 40. He underwent transplant without significant complications and recovered well.

Figure 1



The lobular architecture of the liver is intact with alternating portal tracts and central veins with normal spacing. However, there is a vague nodularity of the hepatic parenchyma characterized by alternating hepatic plates with atrophy and hypertrophy. No significant fibrosis is identified

Table 1

Medications Associated with Nodular Regenerative Hyperplasia

Well-Described Agents	Other Reported Agents
Immunosuppressive agents	Bleomycin
Azathioprine	Busulfan
Mercaptopurine	Carmustine
Thioguanine	Chlorambucil
	Cyclophosphamide
Antiretroviral Agents	Cytosine arabinoside/daunorubicin
Didanosine	Doxorubicin
Stavudine	Gold and penicillamine
	Interleukin 2 therapy
Antineoplastic Agents	Isoplatin
Oxaliplatin	Methotrexate
	Oxymetholone
	Phenytoin
	Thorotrast
	Trastuzumab emtansine

Table 2

Diseases associated with the Development of Nodular Regenerative Hyperplasia

Autoimmune	Vascular
Antiphospholipid syndrome	Budd-Chiari syndrome
Behçet disease	Congestive heart failure
Celiac disease	Portal vein agenesis
IBD	Portal vein thrombosis
Myasthenia gravis	**Malignancy**
Polyarteritis nodosa	Carcinoid tumor
PBC	Castleman disease
Rheumatoid arthritis	Lymphoproliferative and myeloproliferative disorders
Sarcoidosis	
Scleroderma	**Other**
SLE	Common variable deficiency
	Kidney Transplant
	Sickle cell anemia
	Tuberculosis

Discussion

Treatment of NRH includes managing the stigmata of portal hypertension, addressing the underlying contributing disorder, and removal of etiologic agents. Liver failure from NRH is rare. The patient had been on mycophenolate and tacrolimus for his transplant, but these are not known to cause NRH. A review of records does not show a history of medications associated with NRH. There are case studies of patients developing NRH following renal transplant without the use of NRH-inducing medications which suggests an opportunity for research on NRH in transplant patients. NRH should be on the differential for renal transplant patients presenting with portal hypertension..

References

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