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Case Presentation

- 85 year old female with past medical history including paroxysmal atrial fibrillation, hypertension, colon cancer, COPD, and rheumatoid arthritis

- In October 2012, the patient was taken to an OSH for intense left wrist pain
  - Underwent surgical repair
  - Given Dilaudid after several complications, including hematoma
  - Discharged home after 10 days

- Two days after the patient was discharged, she was found unconscious by her daughter

- The patient was taken to the hospital and was found to be hypotensive. Over the next 4 days, she subsequently developed new onset abdominal pain and jaundice
The patient underwent an extensive work-up and labs revealed the following:

- Elevated total bilirubin (9.2)
- Elevated liver function tests (AST, ALT in the 300-500s)
- Elevated lipase (466)
- Elevated alk phos (449)

The patient’s course was complicated by pneumonia and a UTI.

The patient was transferred to UCLA for higher level of care for acute liver failure of unclear etiology.
ERCP performed on November 14th was consistent with intrahepatic disease.

Labs were negative for:
- ANA, AMA, SMA, ANCA, Hepatitis A IgM, Hepatitis B sAg, Hepatitis B core IgM, Hepatitis C IgG Ab

A liver biopsy was performed on 11/15...
Microscopic Findings
Diagnosis??
Diagnosis:

Subacute Nonsuppurative Cholangitis
Subacute Nonsuppurative Cholangitis

- An unusual type of cholangitis, characterized by ductular reaction with inspissated bile plugs in dilated ductules and sparing of native bile ducts

- An uncommon histopathological finding in liver biopsies in any clinical setting
Subacute Nonsuppurative Cholangitis
Terminology

- Described as “subacute” because the lesion evolves over weeks to months, and was first used in association with subacute endocarditis.

- Termed “cholangitis lenta” in septic patients and in patients with subacute bacterial endocarditis.

- The histologic lesion has been termed “bile ductular cholestasis”.

Cholangitis lenta was first described by Schottmuller in 1921, and was considered to be a hepatic analogue of an indolent cardiac infection by Streptococcus viridans

Originally thought to be the result of mechanical biliary obstruction
- Disproved in the 1980’s

Proposed correlation between SNC and sepsis
- Potentially life threatening condition
In 1981, Lefkowitch published a case series, showing the following observations:

- In no instance was bile ductular cholestasis due to mechanical obstruction of the bile ducts

- The intrahepatic cholestasis was a late (preterminal or terminal) phenomenon, and presumably due to a functional alteration of bile flow in some manner associated with severe febrile illness or infection

- Identification of this lesion on liver biopsy may signify the patient has a potentially life threatening illness
Proliferation of bile ductules at the edges of portal tracts

Inspissated bile within dilated bile ductules

Absence of acute inflammation within ducts or ductules

Normal non-reactive structure of interlobular bile ducts
Clinical Significance

- Few studies have been conducted correlating clinical parameters and histologic findings in liver biopsy.
- The limited number of cases have suggested an association between SNC and sepsis and/or intra-abdominal infection.
- Thus, our goal was to conduct a large scale retrospective study to identify liver biopsies that carried the potential diagnosis of SNC and to correlate these findings with detailed clinical parameters.
### Patient Demographics and Clinical Variables

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Low</th>
<th>High</th>
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<tbody>
<tr>
<td>Age, years</td>
<td>49.2 +/-  20.6</td>
<td>28 (days)</td>
<td>85</td>
</tr>
<tr>
<td>Male</td>
<td>60%</td>
<td></td>
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<tr>
<td>Female</td>
<td>40%</td>
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<tr>
<td>Temperature</td>
<td>38.0</td>
<td>36.9</td>
<td>39.1</td>
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<tr>
<td>WBC</td>
<td>19.2</td>
<td>3.75</td>
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<tr>
<td>AST</td>
<td>473.4</td>
<td>47</td>
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<tr>
<td>ALT</td>
<td>308.7</td>
<td>43</td>
<td>1744</td>
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<tr>
<td>Bilirubin, Total</td>
<td>17.3</td>
<td>1.7</td>
<td>42.5</td>
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<tr>
<td>Alkaline Phosphatase</td>
<td>428.0</td>
<td>68</td>
<td>2152</td>
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# Infectious Disease Work-Up and Clinical Outcomes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Sepsis</td>
<td>23/27</td>
<td>85.2%</td>
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<tr>
<td>Intraabdominal abscess</td>
<td>9/27</td>
<td>33.3%</td>
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<tr>
<td>Positive culture</td>
<td>22/27</td>
<td>81.5%</td>
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<tr>
<td>Liver transplant</td>
<td>23/27</td>
<td>85.2%</td>
</tr>
<tr>
<td>Biliary obstruction</td>
<td>0/27</td>
<td>0%</td>
</tr>
<tr>
<td>Vascular thrombosis</td>
<td>0/27</td>
<td>0%</td>
</tr>
<tr>
<td>Mortality</td>
<td>14/27</td>
<td>51.9%</td>
</tr>
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</table>
Our study examined the largest number of SNC cases and our findings support the notion that SNC in a liver biopsy is associated with the presence of sepsis and/or intraabdominal infection.

In addition, our data shows that patients with SNC bear a poor prognosis.

Familiarity with this entity and recognition of the association with sepsis / intraabdominal infection may help avoid unnecessary clinical work-up or incorrect management.
Patient Follow Up

- Thorough evaluation for underlying source of infection
  - No occult infection of the chest, abdomen, or pelvis was detected by CT
    - CT revealed only scattered small pulmonary nodules and postinflammatory lung collapse
    - Thoracentesis with cultures, gram stain, and fungal serologies negative
  - Possible source of infection being in her biliary tract versus spontaneous bacterial peritonitis
    - Diagnostic paracentesis was not performed due to patient becoming acidotic
  - Endocarditis was on the differential
    - Cultures all remained negative

- The patient was continued on broad spectrum antibiotics and given supportive care

- Patient’s transaminases and bilirubin began to improve somewhat, but she developed worsening renal function, increasing WBC, cholestatic jaundice, and delirium

- Patient was discharged home on comfort care with a very poor prognosis, where she passed away a few weeks later
Subacute nonsuppurative cholangitis is an uncommon but important histological finding in liver biopsies.

Prior studies on a limited number of cases have shown an association of SNC with sepsis or intraabdominal infection.

Our study supports this association, and underlines the need for clinical management of the patient when such a lesion is found on biopsy.
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