Mycobacterium mucogenicum Isolated From a Patient With Granulomatous Hepatitis

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**Mycobacterium mucogenicum** is a recently characterized, rapid-growing mycobacteria rarely seen in human infections. We describe the case of a 51-year-old man with rapidly progressive granulomatous hepatitis caused by *M. mucogenicum*. Although premortem evaluation failed to identify an etiologic agent, autopsy liver cultures produced smooth, rapid-growing mycobacterial colonies. Biochemical, growth, and cell wall fatty acid characteristics were consistent with the identification of *M. mucogenicum*.

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Hepatic granulomas are often seen as part of the pathologic findings in liver biopsies. The most probable cause of granulomatous hepatitis is dependent on patient demographics. There are many causes for granulomatous hepatitis, including bacterial, mycobacterial, fungal, chlamydial, parasitic, viral, and rickettsial infections, as well as hypersensitivity reactions, autoimmune disorders, foreign material, neoplasms, unknown etiologies, and other less common agents. Mycobacteria are often implicated as infectious causes of granulomatous hepatitis; reports have cited *Mycobacterium tuberculosis*, *Mycobacterium avium-intracellularure* complex, *Mycobacterium leprae*, bacillus Calmette-Guérin, *Mycobacterium kansasi*, and *Mycobacterium fortuitum*. This case represents the first documented case of granulomatous hepatitis associated with *Mycobacterium mucogenicum*.

**REPORT OF A CASE**

The patient was a 51-year-old, male, retired anthracite coal miner who initially presented to an outside hospital complaining of right upper quadrant pain, nocturnal fevers, and night sweats of a few months’ duration. His social history was significant for a 90 pack/year history of tobacco abuse and remote alcohol use. His past medical history was significant for hypothyroidism, arthritis, and a questionable diagnosis of coal worker’s pneumoconiosis. His medications included multiple nonsteroidal anti-inflammatory agents, narcotics (propoxyphene and oxycodone), muscle relaxants, and levethroxine. His admission laboratory evaluation included the following values: albumin, 26 g/L; alkaline phosphatase, 1148 U/L; alanine aminotransferase, 232 U/L; aspartate aminotransferase, 176 U/L; total bilirubin, 2.93 mg/dL (50.1 μmol/L); direct bilirubin, 2.29 mg/dL (39.2 μmol/L); lactate dehydrogenase, 196 U/L; white blood cell count, 3.9 × 10⁹ cells/μL; hematocrit, 112 g/L; platelet count, 99 × 10⁹ platelets/μL; serum iron, 38 μg/dL; and serum ferritin, 181 μg/mL (9569 μg/L). Bone marrow biopsy showed normocellular bone marrow with rare small clusters of epithelioid histiocytes. Liver biopsy showed noncaseating granulomatous hepatitis with portal inflammation and necrosis. An endoscopic retrograde cholangiopancreatography was unremarkable, showing no evidence of sclerosing cholangitis. Chest radiography showed evidence of old healed pulmonary granulomas. Computed tomographic scans of the abdomen and chest showed hepatosplenomegaly with mottled hypodensity of the liver parenchyma and a hypodense lesion in the spleen. There was no significant periaortic or perihilar adenopathy, and the portal vasculature appeared normal.

The patient was then transferred to our facility, having developed significant lower extremity edema and ascites, along with worsening liver function. He developed mental status changes and acute gastrointestinal bleeding. Esophageal, gastric, and duodenal endoscopy found no evidence of esophageal varices, but did identify a gastric ulcer and a duodenal bulb erosion. Laboratory evaluation included testing for autoimmune diseases, as well as bacterial and viral infections. The following studies were negative: hepatitis A, B, and C profiles; p-antineutrophil cytoplasmic antibodies, c-antineutrophil cytoplasmic antibodies, antineutrophil cytoplasmic antibodies, anti-Smith antibodies, anti-exosome antibodies, Coxsackie, Epstein-Barr, cytomegalovirus, Mycoplasma, and rat heat shock protein 65. Serum and urine tests for *Mycobacterium tuberculosis*, *Mycobacterium avium-intracellularure* complex, *Mycobacterium leprae*, *Bacillus Calmette-Guérin*, *Mycobacterium kansasi*, and *Mycobacterium fortuitum* were negative. Tests for *Mycobacterium mucogenicum* were negative as well. A purified protein derivative skin test for tuberculosis was negative (0 mm of induration), while an anergy panel demonstrated an adequate immune response. The patient was treated empirically with broad-spectrum antibiotics, fluconazole, and prednisone for suspected bacterial and fungal infection, as well as sarcoidosis.

A second liver biopsy performed 3 days after the initiation of steroids showed extensive acute and histiocytic inflammation, focal moderate cholestasis, mild fatty change, and a few scattered, poorly formed epithelioid cell granulomas (Figure, B). Stains and cultures for bacteria, fungi, and mycobacteria were negative. There was no polarizable or refractile material in the granulomatous lesions. His liver function studies remained abnormal (albumin, 17 g/L; alkaline phosphatase, 965 U/L; alanine aminotransferase, 228 U/L; aspartate aminotransferase, 261 U/L; total bilirubin, 8.7 mg/dL [148.8 μmol/L]; direct bilirubin, 5.9 mg/dL [100.9 μmol/L]; and lactate dehydrogenase, 196 U/L).

The patient's general course continued to worsen, and he eventually developed respiratory distress that required intubation. Terminal events included the development of gram-negative sepsis with *Acinetobacter calcoaceticus var anitratus* and disseminated intravascular coagulation. Despite appropriate antibiotic therapy, the patient became anuric and was placed on continuous venovenous hemodialysis. An emergency laparotomy was performed for an acute abdomen. Surgical findings revealed no evidence of tissue ischemia. The liver was markedly enlarged, thus preventing examination of the spleen. The patient died in multiorgan failure secondary to gram-negative sepsis. Permission for a limited autopsy was obtained.
(A) Gross morphology of fixed liver shows a nutmeg appearance with areas of infarction.
B and C, Liver biopsies (hematoxylin-eosin, original magnifications ×20). Approximately 1 week before death (B) tissue demonstrates discrete foci of granulomatous inflammation within intact parenchyma. At death (C), more than 50% of the tissue is involved, with extensive necrosis noted. D, Gross colony morphology of Mycobacterium mucogenicum on Middlebrook agar.

**PATHOLOGIC FINDINGS**

The autopsy consisted of an external examination with biopsies of the liver, spleen, kidneys, heart, and lungs through the previous laparotomy incision. The external autopsy examination revealed anasarca with ascites, jaundice, diffuse petechiae and purpura, and a presacral decubitus ulcer.

The peritoneal cavity contained blood-tinged serosanguinous fluid; all the abdominal organs were in their normal anatomic position. The liver measured 12 cm at the midclavicular line and had a nutmeg appearance. The cut surface appeared granulated and tan with multiple areas of hemorrhage and infarction (Figure, A). Hematoxylin-eosin–stained sections of the liver revealed extensive centrilobular necrosis; 50% of the liver parenchyma appeared nonviable. These changes were consistent with hypotension and sustained septic shock (Figure, C). Elastic trichrome and trichrome stains of the liver tissue failed to show evidence of fibrosis. Fite and Gomori methenamine-silver stains were negative for acid-fast and fungal organisms. The splenic capsule had a speckled appearance with a soft clot adherent to its surface; sections demonstrated a 2.6-cm, soft yellow lesion consistent with infarct. Histologic sections showed congestion, acute hemorrhage, and infarction; Fite, Gomori methenamine-silver, and Gram stains showed no organisms.

Hematoxylin-eosin–stained sections of the lungs demonstrated foci of anthrasilicosis and moderate emphysematous change. There was an organizing alveolar exudate along with extensive alveolar hemorrhage. Peribronchial tissue in the right lung demonstrated 2 nodular lesions with calcification and hyalinization; Fite and Gomori methenamine-silver stains failed to show the presence of any organisms. There were no metallic or foreign body deposits in the mediastinal lymph nodes, liver, spleen, or abdominal lymph nodes.

Routine fungal and mycobacterial cultures were performed on postmortem blood samples and tissue biopsies.
membrane fatty acid composition performed by the Ken-
mance liquid chromatography analysis of the isolate’s
chemical characteristics are summarized and compared
with undulating edges (Figure, D). The organism’s bio-
terium chelonae-
terial colonies were smooth, nonpigmented, and tan-white
with the patient’s premortem septic state. The mycobac-
tum was also recovered from both liver and blood, consistent
bacterial culture.

*Mucogenicum* was iatrogenic. It is more prob able that acq uisition
with granulomatous hepatitis 1 month prior to his hospi-
tal setting. It is unknown what sources of drinking water
were used by the patient prior to his illness.

Members of the *M fortuitum-chelonae* complex are rapid
ners (group IV) in Runyon’s mycobacterial classifica-
tion scheme. This complex contains a number of different
species and subspecies of organisms. Rapid growers are
differentiated from the traditional slow-growing organ-
isms such as *M tuberculosis* based on their growth rate. All
members of this group must demonstrate the following 5
characteristics: (1) acid fastness, (2) lack of pigment pro-
duction, (3) growth on subculture in less than 7 days at
an optimal temperature, (4) production of arylsulfatase
within 3 days of growth, and (5) growth at 28°C on crystal
violet–negative MacConkey agar. 

*Mycobacterium mucogenicum* was designated as a new
species in 1995 owing to its unique 16s rRNA nucleotide
sequence and may be specifically identified by ribosomal
sequencing. It may also be definitively identified by my-
cobacterial membrane fatty acid composition, as in our
case. *Mycobacterium mucogenicum* tends to show resistance
to the traditional antimycobacterial agents, such as isoni-
azid and rifampin, but is susceptible in vitro to amikacin,
imipenem, cefoxitin, clarithromycin, ciprofloxacin, and the
new fluoroquinolones, as well as to trimethoprim/sulfa-
methoxazole.

In conclusion, this report represents the first document-
ed case of *M mucogenicum*–associated granulomatous hep-
atitis. Although most often encountered in environmental
water sources, this organism has been demonstrated to
cause disease in humans. The scope of human disease
caused by *M mucogenicum* has now expanded to include
granulomatous hepatitis, as in this patient.

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lipooligosaccharides of *Mycobacterium mucogenicum* spn. (formerly *Mycobacte-
rrium chelonae*-like organisms): identification and chemical characteriza-

**Comments**

*Mycobacterium mucogenicum* was formerly classified as *M
celonae*-like organism and is a member of the *Mycobacte-
rium fortuitum-chelonae* complex. This organism has been
identified as a water contaminant in the hospital setting. *Mycobacterium chelonae*-like organism has been implicated
in numerous nosocomial infections. These infections in-
clude postsurgical wound infections, soft tissue infections,
catheter-related sepsis, peritonitis following peritoneal di-
alysis, bacteremia in patients undergoing hemodialysis,
central venous line–associated sepsis, meningitis, pneu-
monia, and lymphadenitis. Since this patient presented
with granulomatous hepatitis 1 month prior to his hospi-
talization, it is unlikely that the infection with *M mucogenic-
icum* was iatrogenic. It is more probable that acquisition
was instead through water ingestion or contact with a con-
taminated environmental water source outside the hospi-
tal setting.