CMV as a Cause of Multiple Liver Abscesses in an Immunocompetent Host: A Case Report and Review of the Literature

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We describe an unusual case of a previously healthy 50-year-old Caucasian female who developed multiple liver abscesses. CT guided aspiration of the hepatic cysts revealed rare polymicrobial organisms. A very uncommon anaerobe, *Fusobacterium necrophorum* was identified. Interestingly, a viral pathogen, *Cytomegalovirus* was additionally cultured. This combination of organisms and specifically a viral pathogen, has not been previously reported. The clinical synopsis and review of the literature are described.

**INTRODUCTION**

Pyogenic liver abscess is an uncommon clinical entity. Various studies report an incidence of 3–4 cases per year in a general hospital of 500 or more beds (1). A mortality of 40% has been described with a potential to reach as high as 79% in certain populations (2). In the pre-antibiotic era, liver abscesses were typically the sequelae of an unrecognized appendicitis. Today, however, the major cause of liver abscess is a complication of biliary disease (3). Progress has been made in the understanding of the microbiology of pyogenic liver abscesses. In 1972, Sabbaj identified anaerobic organism in liver abscesses (3). This is a case of an immunocompetent 50-year-old Caucasian female who developed multiple macroscopic hepatic abscesses containing *Fusobacterium necrophorum* and *Cytomegalovirus*. *Fusobacterium necrophorum* remains a rare cause of anaerobic liver abscess (4). A viral component of macroscopic hepatic abscesses has not been reported in the literature. Additionally, there have been no prior reports of hepatic abscesses caused by such a combination of organisms.

**CASE REPORT**

A 50-year-old Caucasian female with a history of cholecystectomy and appendectomy 20 years ago, pre-

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sented to an outlying hospital with complaints of fever, headache, anorexia, weight loss (10–15 lbs.), weakness, generalized malaise and cough for 4 weeks. Upon evaluation, the patient was found to be febrile (103 degrees F). Laboratory analysis revealed a WBC of 28.2 k/mm³ (bands 12%), Hct of 32.4% and sodium of 127 meq/L. Alkaline phosphatase was elevated at 200 U/L (30–136 U/L) and AST/ALT were normal at 48/47 U/L respectively. Urinalysis revealed 2+ protein, 100 WBC’s, positive nitrate, and large leukocyte esterase. The patient was subsequently admitted with a diagnosis of acute pyelonephritis and treated with ceftriaxone.

While on antibiotics, she continued to have Charcot’s type fevers and maintained a leukocytosis. A chest x-ray demonstrated a right pleural effusion and arterial blood gases revealed a PaO₂ of 53. Lower extremity doppler ultrasound was negative for deep venous thrombosis. Ultrasound of the pelvis depicted small fibroids. A computerized tomography (CT) of the abdomen and pelvis revealed multiple filling defects in the liver (Figures 1, 2). The patient underwent a CT guided liver aspiration of the largest cystic lesion. A yellowish-green, foul smelling, pus-like material was obtained and sent for cultures. The culture grew *Fusobacterium necrophorum*. The patient was treated with metronidazole 500-mg intravenous every eight hours.

There was little improvement after 10 days as she continued to have Charcot’s type fevers. Physical exam revealed decreased breath sounds at the right lower lung base and abdominal tenderness in the right upper quadrant and epigastrum. The laboratory data was as follows: WBC 23.8 k/mm³ (18% bands), serum albumin 1.2gm/dL (3.4–5.0 gm/dL), globulin 3.8 gm/dL (2.3–3.5 gm/dL), alkaline phosphatase 253 IU/L (30–136 IU/L) and lipase of 96 U/L. AST and ALT were normal. Additionally, HIV and hepatitis A, B, C were also negative. CT scans of the chest, abdomen and pelvis were repeated and revealed multiple ring-enhancing hepatic lesions with a 3.5 cm pocket adjacent to the lateral right hepatic lobe, a moderate to large right pleural effusion with underlying atelectasis of the entire right lower lung, para-aortic adenopathy, and anasarca.

Ultrasound guided thoracentesis was consistent with a transudate and cultures were negative. Subsequently, CT guided aspiration and percutaneous drainage was performed on two large hepatic abscesses. The drains were left in place for irrigation. The patient was switched to imipenem and clindamycin. Cultures for ova/parasites, acid fast bacillus, aerobic/anaerobic bacteria, and viral organisms were obtained. Viral cultures were positive for *Cytomegalovirus*. However, the patient’s serum IgG and IgM antibodies were negative. The patient began to improve clinically marked by res-
solution of her fever and leukocytosis. She was eventually discharged after a 28 day hospitalization.

**DISCUSSION**

Pyogenic liver abscesses have been recognized since the time of Hippocrates in 400 B.C. and remain an important diagnostic and therapeutic challenge (5). Although still relatively uncommon, the incidence has remained moderately stable in the last century. Mortality with multiple hepatic abscesses approached 95%-100% prior to the development of antibiotics (1). Since the development of potent antimicrobials, non-invasive drainage, and imaging advances, mortality has been reduced to 10%-25%, but remains high (6).

Liver abscesses occur when the initial inflammatory response fails to eradicate infectious insult from the liver (3). Spread of bacteria to the hepatic parenchyma may occur as a consequence of biliary tract disease. Direct extension from a contiguous source of infection, blunt or penetrating trauma and bacteremia are other means of developing hepatic abscesses.

Certain underlying conditions may also be associated with hepatic abscesses including diabetes mellitus, alcoholism, liver disease, colonic carcinoma, intrahepatic malignancy, immunodeficiency, and immunosuppression (4,7). Unfortunately 13%-35% of hepatic abscesses have no identifiable etiology (5).

The majority of organisms that invades the liver and cause hepatic abscesses are colonized in the gastrointestinal tract. Polymicrobial infections, including both aerobic and anaerobic flora of the gastrointestinal tract, occur in 22%-64% of cases (5). Specifically *Klebsiella pneumoniae* and *Escherichia coli* are by far the most common isolates accounting for 30% and 38%, respectively (1). Anaerobes are identified as an integral component of liver abscesses and account for approximately 45% of cases (8). However, others have suggested that this should be viewed as an over-estimate, as anaerobes are seldom collected consistently at this rate (4).

The most common anaerobic organisms identified include *Bacteroides fragilis*, *Microaerophilic streptococci*, *Clostridia*, and *Actinomyces* (9). *Fusobacterium necrophorum* has also been described as a rare cause of anaerobic liver abscesses (4, 10). This organism is part of the normal flora colonizing the human oropharynx, the gastrointestinal and urogenital tracts. The mechanism behind Fusobacterium’s invasive nature remains unknown (4).

**CYTOMEGALOVIRUS**

Cytomegalovirus (CMV) is a member of the human herpes virus family and is identified in a multitude of clinical settings (11). CMV is a significant pathogen in all age groups including both the immunocompetent and the immunocompromised; however, immunocompromised individuals are the most susceptible (12).

Congenital CMV infections are acquired transplacentally. CMV may also be contracted during delivery through an infected birth canal or via post-natal contact with maternal breast milk. Another clinical syndrome, CMV associated mononucleosis, is most often seen in young healthy adults (11,13).

CMV is found worldwide. In the United States, about 1% of neonates are infected with CMV (13). Statistics show that between 40%-80% of adults in the United States are sero-positive, indicating previous exposure (11,14,15). Most commonly, the virus is acquired early in life (14). In general, primary infection occurs by intimate contact with bodily fluids such as saliva, tears, semen, urine, stool and breast milk (13,14). Like other herpes viruses, CMV undergoes latency after primary infection and is carried for life (11,14,15).

CMV is typically reactivated when the T-lymphocyte mediated immunity is compromised. Consequently, CMV reactivation syndromes are identified in patients with human immunodeficiency virus (HIV), post solid organ transplant and bone marrow transplant. (11). Symptoms produced by CMV in immunocompromised patients include fever, malaise, myalgias, anorexia, fatigue and night sweats (13).

In immunocompromised patients, CMV causes a variety of syndromes. In the late stages of HIV, reactivation of CMV is the most common opportunistic infection and often causes retinitis, esophagitis and colitis (11,16). CMV may also cause encephalitis, polyarthritis, and multifocal neuropathy in HIV patients (13,16,17). CMV induced gastrointestinal ulcers are identified in the esophagus, stomach, small intestine, and colon of the immunosuppressed patients (14,18).
CMV as a Cause of Multiple Macroscopic Liver Abscesses

CONCLUSION

Fusobacterium necrophorum is an anaerobic gram-negative fusiform rod colonizing the human oropharynx, gastrointestinal and genital urinary tracts. The organism remains a rare cause of multiple pyogenic liver abscesses (4,7,10). Interestingly, our patient was not afflicted with trauma, sepsis, diabetes mellitus, alcoholism, immunodeficiency or immunosuppression. She had a remote history of a cholecystectomy and appendectomy. Additionally, colonoscopy revealed no evidence of malignancy, and endoscopic retrograde cholangiopancreatography revealed a normal appearing biliary tree. The patient’s thirteenth, fifteenth, and thirtieth teeth were extracted thus, identifying a potential source for Fusobacterium necrophorum.

The coinfection with CMV in our patient is rare. To our knowledge, there are no reported cases of CMV as a cause of macroscopic liver abscesses. CMV has only been reported as a cause of histologically defined microabscesses in transplanted liver recipients. Because the IgG and IgM antibodies to CMV were not detectable, the potential cause of CMV infection (primary or reactivation) in our patient is unknown. To our knowledge however, there have been no prior reports of hepatic abscesses caused by such a combination of organisms. We believe that our patient not only improved secondary to antibiotic therapy, but also because her immune system eventually eradicated the virus.

Since approximately 35% of hepatic abscesses have no microbiological identity, we recommend that viral pathogens be considered in patients who do not respond to initial antimicrobial therapy.

References