Splenic Abscess Caused by *Streptococcus gallolyticus* Subspecies *pasteurianus* as Presentation of A Pancreatic Cancer: A Case Report and A Brief Review

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Abstract:

Splenic abscess caused by *Streptococcus bovis* are rarely reported in the literature and are mainly seen in patients with endocarditis and associated colonic neoplasia/carcinoma. We report the first case of splenic abscess caused by *Streptococcus gallolyticus* subspecies *pasteurianus* (*S. bovis* biotype II/2) as presentation of a pancreatic cancer.

Keywords: *Streptococcus gallolyticus* subspecies *pasteurianus*, Splenic abscess, Pancreatic cancer
A 55-year-old man was referred to the Department of Infection and Critical Care Medicine, Beijing Friendship Hospital, Capital University of Medical Sciences (Beijing, China) because of persistent fever over 40 °C for 9 days, with shaking and chills. He also complained of general fatigue and loss of appetite, but had no abdominal pain, vomiting, weight loss or other symptoms. His previous medical history was unremarkable. On physical examination, fever was present (39.3 °C); lung fields were clear; heart sounds were regular without murmur; abdomen was soft, non-distended, and with no palpable mass.

Initial laboratory studies showed a white blood cell count of 16.7×10⁹/L with 83.6% neutrophils. Stool occult blood test was negative. Inflammatory tests showed the following results: C-reactive protein > 160 mg/dL (normal 0.0-0.8 mg/dl) and procalcitonin (PCT) 2.32 ng/ml (reference range: 0-0.05 ng/ml). Tumor markers CA125 and CA19-9 increased greatly: CA19-9 >1200 U/mL (reference range: 0-37 U/mL), CA125 247.9 U/mL (reference range: 0-37 U/mL). But the carcinoembryonic antigen level was normal. The results of pancreatic amylase test and creatinine, glucose, and liver function tests were all within normal limits. Blood cultures were collected.

A chest radiograph was unremarkable; however, a chest computed tomographic scan (CT) showed lobar consolidation in the left lower lobe with associated pleural effusion. An abdominal ultrasound exam demonstrated a hypoechoic area in the spleen with unclear margin, suggestive of a splenic abscess. An enhanced abdominal CT further
revealed a nonenhancing hypodense lesion in the tail of the pancreas with invasion into
the spleen and multiple hypodense lesions in the liver, along with the splenic lesion
(Figure 1a and 1b). The splenic artery was slender without obvious filling of the contrast
agent. These findings were also demonstrated on magnetic resonance imaging studies.
Together, the imaging studies, constitutional presentation, and laboratory test results
suggested a working diagnosis of an occult pancreatic cancer and a splenic abscess.
Empirical antibiotic therapy with intravenous Piperacillin-Tazobactam and
Azithromycin was started. However, the patient’s fever persisted, up to 40.5 °C, which
required switch of antimicrobials to imipenem-cilastatin and vancomycin in order to
broaden the coverage. On the 4th hospitalization day, an endoscopic ultrasound-guided
percutaneous drainage of the splenic abscess was performed, which aspirated 50 ml
odorous pus, leading to a decrease of the patient's temperature. The aspirate was stained
and cultured. Numerous white blood cells were found and the Gram-positive coccus was
isolated and identified as *Streptococcus gallolyticus* by VITEK 2 compact GP systems
(bioMérieux, France). On the 5th hospitalization day, the isolate from initial blood culture
was also identified as *S. gallolyticus*. Subsequently on the 7th day, the patient underwent
EUS-guided percutaneous drainage again, 100 milliliters of pus were obtained, and the
culture was the same *S. gallolyticus*. The isolate was tested by a microdilution method
according to the published CLSI standard (1) and proved sensitive to vancomycin and
Cefotaxime, resistant to erythromycin, clindamycin, Levofoxacin. Treatment with i.v.
vancomycin was continued. The isolate was further subspeciated by partial sequencing of
16S rRNA gene (Institute for Biological Product Control, National Institutes for Food and Drug Control, Beijing, China). Bacterial genomic DNA was extracted with the DNeasy Blood & Tissue Kit (QIAGEN). The 16S rRNA gene was amplified by PCR with the universal primers 27F (5’-AGAGTTTGATCMTGGCTCAG-3’) and 1492R (5’-TACGGYTACCTTGTTACGACTT-3’). The PCR amplification program was followed by 95 °C (30 S), 55 °C (30 S), and 72 °C (90 S) for 30 cycles and a final extension step at 72 °C (10 min). The products were purified and submitted for nucleotide sequencing (Shanghai Songan Biological Engineering Technology & Services Co., Ltd., Shanghai, China). The 16S rRNA gene sequences were compared by using the BLASTN program at the U.S. National Center for Biotechnology Information website (http://www.ncbi.nlm.nih.gov/BLAST/), and showed 100% (1,414/1,414 bp) homology with *S. gallolyticus* subspecies *pasteurianus* (EU163502, GenBank).

Considering the association between *S. bovis/gallolyticus* bacteremia and colonic carcinoma, the patient underwent colonoscopy, but no significant lesions were found. The surgical service was consulted, but eventually the patient refused an operation for the pancreatic cancer. After treatment with antibiotics and EUS-guided PCD, the culture of drainage turned negative, and the patient was discharged 3 weeks later in stable condition.

The patient was followed up after discharge. He was advised to go to the Beijing Cancer Hospital where the same diagnosis of pancreatic tail cancer was made. But the patient also refused an operation or chemotherapy. His condition deteriorated in the next
several months, including development of abdominal symptoms, ascites, and others. He
died six months later.

Splenic abscess is a rare clinical entity, occurring in 0.14% to 0.7% of autopsy studies
(2). It generally occurs in patients with neoplasia, immunodeficiency, trauma, metastatic
infection, splenic infarct or diabetes (3). Splenic abscess is often misdiagnosed, because its
signs and symptoms are nonspecific. Sarr and Zuidema suggested the triad of fever, left
upper quadrant pain and a tender mass for diagnosing splenic abscess (4). However, fever
was the only symptom observed in our patient.

The pathogenesis of splenic abscess is multifactorial, including metastatic infection,
contiguous infection, noninfectious splenic embolism with ischemia and secondary
infection, trauma and immunodeficiency (5). And the metastatic infection of spleen is
often caused by a different primary site of infection, especially endocarditis. In our case,
the patient’s echocardiography was normal, which essentially ruled out endocarditis as the
source of splenic abscess. Instead, the occult pancreatic cancer was the probable cause of
the large abscess, which caused persistent fever with positive blood culture.

A variety of microorganisms have been isolated from splenic abscesses (6,7). The
frequently isolated aerobic and facultative isolates were *E. coli*, *Proteus mirabilis*, *S. bovis*,
*K. pneumoniae* and *S. aureus*. Anaerobes were *Peptostreptococcus spp.*, *Bacteroides spp.*, *Fusobacterium spp.* and *Clostridium spp.* (6,7). The organisms isolated often reflect the
underlying pathogenesis i.e., *S. aureus* and *S. bovis* were associated with endocarditis, *K.
pneumoniae with respiratory infection or liver abscess, E. coli with urinary tract and abdominal infection, Bacteroides spp. and Clostridium spp. with abdominal infection (6).

Splenic abscess caused by S. bovis are rare and usually due to septic emboli from endocarditis in patients with colonic cancer (8,9). To our knowledge, our case is the first report of a splenic abscess in association of pancreatic cancer along with subspecies identification.

S. gallolyticus subspecies pasteurianus belongs to the group D streptococci, and was previously recognized as S. bovis biotype II/2. S. bovis, is found as part of the human gastrointestinal microbiota in 5 to 16% of individuals (10). Using the scheme proposed by Schlegel et al (11) on the basis of DNA studies, there are two species of principal interest: S. gallolyticus, with the subspecies gallolyticus (formerly biotype I), pasteurianus (formerly biotype II/2) and macedonicus; and S. infantarius (formerly biotype II/1), with the subspecies coli and infantarius. Each biotype has somewhat different pathogenicity. S. gallolyticus subspecies gallolyticus (biotype I) has been associated frequently with underlying colorectal cancer (12). S. infantarius (biotype II/1) could be associated with noncolonic cancers (13). S. gallolyticus subspecies pasteurianus (biotype II/2) has been reported recently to cause neonatal and adult meningitis (14-16), and bacteremia and peritonitis (17, 18), but not solid organ infections.

The association between S. bovis bacteremia and pancreatic carcinoma was first reported in 1980 (20) and has been reported in only a few case reports to date (13,19-22). But molecular genetic characterisation of strains was not described in the studies. One of
them described the association with *S. infantarius* (13), but there is no reported case associated with *S. pasteurianus*. Our case of *S. gallolyticus* subspecies *pasteurianus* bacteremia with splenic abscess and underlying pancreatic cancer reminds clinicians that malignancy might be a potential feature to search for.

Splenic abscess as a complication of pancreatic cancer has been reported in only a few cases to date (23-27). This may be due to the location of the tumor in the pancreas. As we all know, pancreatic carcinoma occurs most commonly in the head, and as such, usually presents with obstructive jaundice. Conversely, the least common location for pancreatic carcinoma, as seen in our patient, is in the tail. These cancers tend to present later and are larger at presentation than pancreatic head tumors, with signs of advanced disease, such as contiguous organ extension, vascular invasion and distant metastases (24), and splenic involvement can include infarction, abscess, intrasplenic pseudocysts, and hemorrhage (28).
ACKNOWLEDGEMENT

We acknowledge financial supports from the Capital Medical Development Fund sponsored by the Beijing Municipal Bureau of Traditional Chinese Medicine (SF-2009-I-11) and the Scientific Research Fund of the Beijing Friendship Hospital. We thank Prof. Qiang Ye, director of Institute for Biological Product Control, National Institutes for Food and Drug Control, for subtype determination of *Streptococcus gallolyticus.*
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Figure 1. (a) CT scan (portal phase) image of hypodense area, which invaded hilum of spleen in the tail of pancreas (white arrow) and irregular hypodense area with unclear margin in the spleen (black arrow). (b) CT scan (arterial phase) image of nonenhancing hypodense area, which invaded hilum of spleen, in the tail of pancreas (white arrow 1) and irregular nonenhancing hypodense area in the spleen (black arrow). Splenic artery is slender (white arrow 2).