

Actinomycosis of the Gallbladder

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Actinomycosis of the gallbladder or major biliary ductal system is rare, and to our knowledge, there are fewer than 50 cases reported. We present a case with secondary perforation in a 48-year-old diabetic man who had no prior history of cholecystitis, or cholelithiasis. The diagnosis was made by demonstrating Actinomyces Israeli in the microbiology culture of gallbladder bile, and subsequently confirmed histologically in the cholecystectomy specimen. We reviewed the pathogenesis of abdominal and gallbladder actinomycosis, the diagnostic and therapeutic approaches of this rare disease.

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Cholecystitis is a common disease and most gallbladders are removed for cholelithiasis. Acute forms of cholecystitis are much less encountered and those due to infectious aetiology such as actinomycosis ‘a subacute to chronic infection caused by Actinomyces species’ are even rarer and fewer than 50 cases were reported¹. We report a case with secondary perforation in a 48-year-old diabetic Asian male who had no prior history of cholecystitis, or diabetes and review the literature of the pathogenesis of abdominal and gallbladder actinomycosis, the diagnostic and therapeutic approaches of this rare disease.

THE CASE

A forty-eight years old, diabetic, Asian male of unrecorded profession was admitted to the hospital complaining of fever, vomiting and vague colicky abdominal pain of three days duration. This pain was encountered especially after eating a heavy meal. He had constipation but was able to pass gasses. He denied any previous similar attack. Clinical examination revealed moderate dehydration, temperature of 39.9°C, tachycardia and blood pressure of 140/86 mm Hg.

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There was no jaundice and the abdominal examination showed mild tenderness over the right hypochondrium, positive Murphy's sign and reduced bowel sounds. Laboratory investigations revealed a normal WBC of $10 \times 10^9/L$, thrombocytopenia ($89 \times 10^9/L$) and neutrophilia ($1.5 \times 10^9/L$), high random blood glucose (14 mmol/L), low serum sodium (129.8 mmol/L), glucosuria and ketonuria⁹. All other laboratory tests were normal including alkaline phosphatase and a negative serology test for HIV. Ultrasound examination of the abdomen showed acute calculous cholecystitis and 2 cm stone impacted at the neck of the gallbladder. The wall of the gallbladder was thickened. Other abdominal organs including the liver were all normal. Chest X-ray was normal and the KUB demonstrated dilated transverse colon. The pre-operative diagnosis was acute calculous cholecystitis associated sepsis in a diabetic patient. He was started on septic work-up which included intravenous fluids, 4-units of Platelets' transfusion, intravenous antibiotics (Metronidazole and Cefuroxime) along with subcutaneous insulin injections. Blood culture showed Gram +ve diplococci sensitive to cephalosporins (Zinacef). After optimizing the patient's condition, he underwent trial of laparoscopic cholecystectomy which was converted to open cholecystectomy because of extensive adhesions. The operative findings showed a severely inflamed distended gallbladder with free pus at the substernal and pelvic region indicating perforation. No stone was identified. The omentum and parts of the small bowel were adherent to the liver covering the perforated gallbladder. Aspirated fluid from gallbladder was sent for bacterial culture and sensitivity. The gallbladder aspirate and blood culture results showed *Actinomyces Israeli*. The postoperative period was uneventful and the patient was discharged on the sixth postoperative day in good condition and was kept on Amoxicillin and Clavulanate (Augmentin) 375mg three times daily for three months.

Grossly, the gallbladder was enlarged measuring 6.5 X 4.0 X 3.0 cm, had marked serosal congestion and coarse granularity. The wall was oedematous and thickened up to 1.5 cm. The mucosal surface showed extensive ulceration covered by greenish hemorrhagic mucus. There were no apparent sulfur granules noted in the mucosal content, neither apparent mural perforation nor visible stones were found, which apparently had escaped through to the abdomen. Microscopic examination of the gallbladder showed extensive non-dysplastic mucosal ulceration and moderate to marked non-granulomatous, suppurative transmural neutrophil rich inflammation with multiple mural micro-abscesses. A focus of transmural necrosis was found and that was considered in line with the clinical diagnosis of gallbladder perforation. Individually dispersed and loose clumps of pleomorphic, filamentous, cotton wool-like actinomyces were seen both within the mural micro-abscess and the surface exudate (Figure1). Routine histochemical stains confirmed the mycelial and club characteristics of the organism (Table 1).

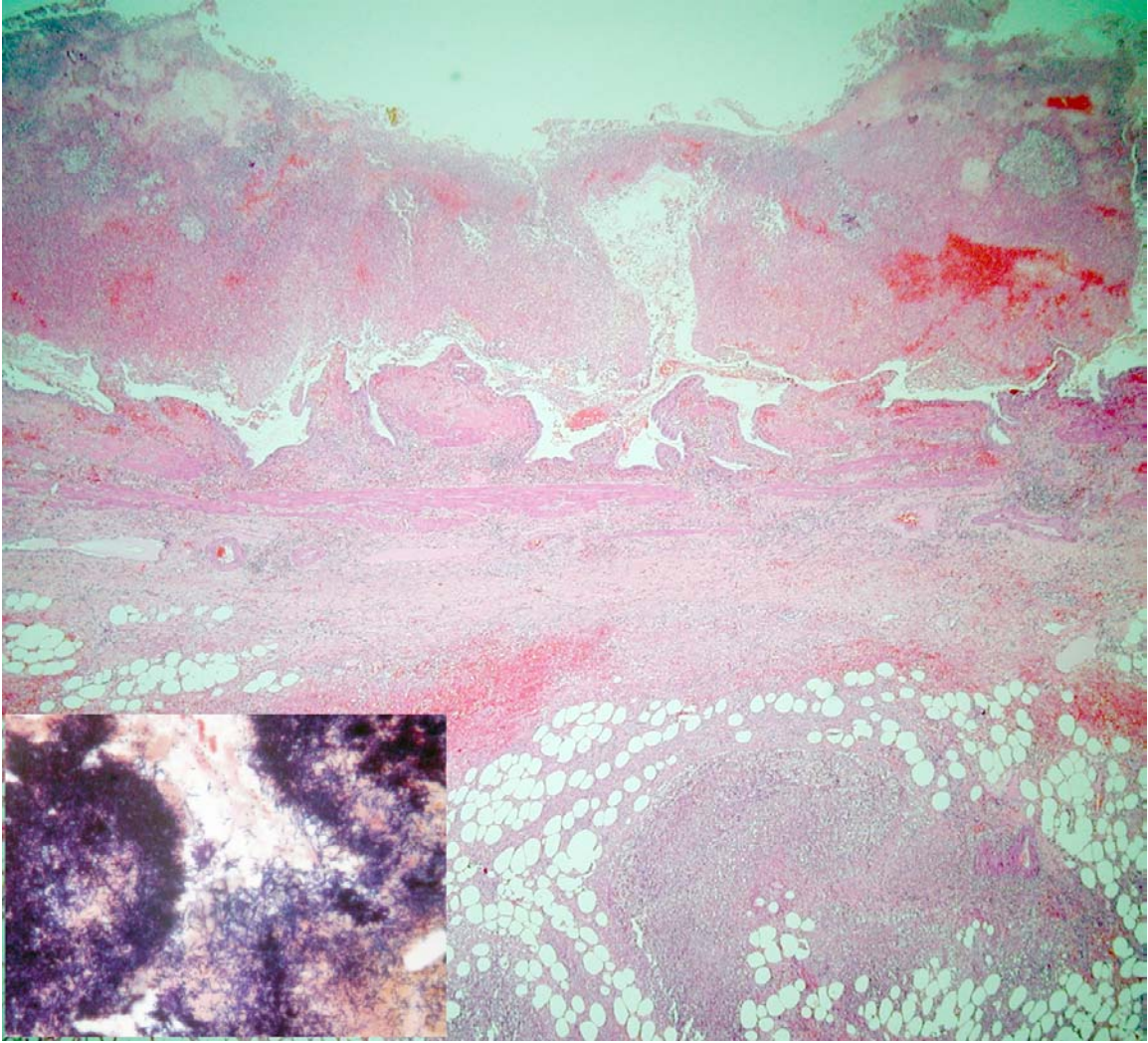


Figure 1: Photomicroscopic image of the gallbladder wall showing mucosal ulceration, transmural polymorphs inflammatory cells, and collection of mural micro-abscesses. Note the presence of filamentous, cotton wool-like Actinomyces at the surface exudate. (Medium power, Hematoxylin & Eosin stained) Insert: Close-up of Actinomyces.

Table 1: Histochemical staining characteristics of actinomyces, Table shows stains findings along with their correspondent reference guide. *PAS: Periodic acid-Schiff, ZN: Ziehl-Neelsen.

Stain	Mycelium		Clubs	
	Reference	Findings	Reference	Findings
H&E	Positive	Positive	Negative	Negative
PAS*	Negative	Negative	Positive	Positive
ZN*	Positive	Positive	Positive	Positive
Giemsa	Positive	Positive	Variable	Variable
Gram's	Positive	Positive	Negative	Negative
Grocott	Positive	Positive	Positive	Positive

DISCUSSION

Actinomycosis is a rare infection worldwide^{1,2}. The prevalence is higher in areas with low socio-economic status and poor oral hygiene. Affected people are usually young to middle-aged adults. No racial predilection exists and for unknown reasons, men are affected three times more commonly than women, with the exception of pelvic actinomycosis³. Actinomycosis is not a true fungus but rather more closely related to bacteria, it is composed of central mass of tangled hyphae (mycelium) and peripheral cub-shaped bodies. The genus *Actinomyces* contains obligatory anaerobic or microaerophilic gram-positive organisms that grow in the form of a vegetative mycelium which readily break up into bacillary and coccoid forms. There are several species of actinomyces that can infect animals and human; *Actinomyces Israeli*, *A. gerencseriae* and *A. naeslundii* are the causative agents of infectious actinomycosis in man². The organism is a common commensal in the mucous membrane of the nasopharynx, usually found in the crypts of tonsils and less prominently in the lower gastrointestinal tract and female genital tract. Actinomycetes are not virulent organisms but require two main factors to establish infection in man; a break in the integrity of the mucous membranes or presence of devitalized tissue and the presence of companion bacterial synergism in 65% of patients^{1,3}. This polymicrobial infection synergism participates in the production of infection by producing a toxin or enzyme or by inhibiting host defenses. The most important of these bacteria is *Actinobacillus actinomycetemcomitans*, followed by *Peptostreptococcus*, *Prevotella*, *Fusobacterium*, *Bacteroides*, *Staphylococcus*, *Streptococcus* species, and Enterobacteriaceae, depending on the location of actinomycotic lesions. Once infection is established, a state of subacute-to-chronic disease is produced characterized by contiguous spread of a markedly suppurative or granulomatous inflammation and frequent formation of multiple abscesses or sinus tracts that may discharge sulfur granules^{3,4}. As chronicity develops, fibrosis may develop subsequently. Hematogenous spread to distant organs, such as, the liver may occur at any stage of the infection leading to pyogenic liver abscess and portal hypertension⁵.

In man, actinomycosis of the abdomen and pelvis accounts for 10-20% of reported cases⁴. In the case of abdominal actinomycosis, the patient may have a history of recent or remote bowel surgery (perforated acute appendicitis) or ingestion of a foreign body (chicken or fish bone) inoculating the actinomycetes into the deep tissues. The ileocaecal region is involved most frequently, and the disease presents classically as a slowly growing tumour³. Involvement of any abdominal organ, including the abdominal wall, can occur by direct spread with eventual formation of sinuses discharging sulfur granules. Numerous non-specific presentations make pre-operative diagnosis of actinomycosis difficult. In the gallbladder, a diseased appendix is considered the primary source of actinomycosis, but infection may follow a penetrating abdominal wound, perforated intestinal ulcer or even a blunt trauma without apparent perforation. Retrograde spread of actinomycetes from the duodenum through the common bile duct has been considered as a possible route of infection^{3,4,6,8}. Isolated actinomycosis of the common bile duct without involvement of the liver or gallbladder has been reported⁴. Likewise, actinomycosis of the pelvis most commonly occurs by the ascending route from the uterus in association with intrauterine contraceptive devices extending to the uterus, omentum, parametrium, pelvic walls, colon, bladder and gallbladder^{4,9,10}. Lymphatic spread is uncommon because of the large filaments whereas hematogenous spread to the liver has been documented⁷.

The general predisposing factors for actinomycosis include diabetes mellitus, steroids, chemotherapy, current malignancy and history of previous surgery^{1,2-6}. As an opportunistic infection, it is one of the great imitators in clinical practice, particularly that of the abdominal and pelvic involvement and a high level of clinical suspicion is required until the organisms are demonstrated^{1-3,5,6,8,9}. There are no specific radiological signs of gastrointestinal actinomycosis. Ultrasonography and computed tomography usually reveals a tumour-like, infiltrative mass of decreased attenuation that enhances with contrast³. Laboratory investigations may show anaemia, mild leucocytosis, elevated erythrocyte sedimentation rate and in the case of hepatic involvement an elevated serum alkaline phosphatase^{3,7}. Serological tests have no role in the diagnosis¹. In the present case, the patient was discovered to be diabetic on admission and was accordingly classified as immunocompromised with septic shock considering his fever, thrombocytopenia and normal WBC count.

The pathological diagnosis of actinomycosis can easily be made by demonstrating the organisms in routine hematoxylin and eosin stained microsections and this can be confirmed with chemical and immunofluorescent antibody stains¹¹. Microbiology culture of aspirated gallbladder bile is also a standard test to identify the particular species and its sensitivity profile as in the present case². However, for immediate diagnosis and the initiation of therapy, the organisms can be demonstrated by examining cytological preparation of gallbladder bile collected intra-operatively¹².

The vascularity and indurations that result from actinomycosis emphasize the need for prolonged course of high-dose antibiotic therapy^{1-3,10}. Penicillin is the drug of choice for the treatment of all actinomycotic lesions including that of the gallbladder. For effective therapy, it is essential to excise the affected organ when possible and or the

accompanying abscess followed by antibiotic therapy started 1-14 days after surgery and continued for 6-12 months. A shorter course ranging from 3 to 6 months has been proposed for pelvic disease if the lesion is not associated with local complications^{1,3,10}. The risk of actinomycetes to develop penicillin resistance appears to be minimal and studies found that treatment failure is usually a good indicator of the presence of resistant companion bacteria as discussed above³. Bile leakage or dropped gallstones after accidental perforation of the extrahepatic biliary tract or perforated gallbladder is a frequent event during laparoscopic cholecystectomy and this practice has been regarded by some to be of no clinical importance. On the contrary, several studies have found that such dropped calculi which have been left in the abdominal cavity can produce late complications such as pelvic and retroperitoneal actinomycosis if the calculi or the bile contains the offending organism. In the present case, one impacted gallstone was demonstrated pre-operatively on ultrasonography, but later on, neither surgeons nor pathologist were able to identify it. This means that this gallstone has escaped through the perforated viscus along with the infected pus to the abdominal cavity. For this reason, Augmentin was given for three months to prevent future abdominal disease.

CONCLUSION

Actinomycosis of the gallbladder is a rare incidental finding and in no way can be predicted before microbiological, cytological or histology examination of the affected viscus. This case is not different from other previously reported cases; however, we wanted to alert the surgeons and pathologists alike about its possible unpredictable occurrence whether associated with background cholelithiasis or small perforations.

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