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REVIEW

Actinomycosis: a great pretender. Case reports of unusual presentations and a review of the literature

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Review

Summary Actinomycosis is a rare, chronic disease caused by a group of anaerobic Gram-positive bacteria that normally colonize the mouth, colon, and urogenital tract. Infection involving the cervicofacial area is the most common clinical presentation, followed by pelvic region and thoracic involvement. Due to its propensity to mimic many other diseases and its wide variety of symptoms, clinicians should be aware of its multiple presentations and its ability to be a 'great pretender'. We describe herein three cases of unusual presentation: an inferior caval vein syndrome, an acute cholecystitis, and an acute cardiac tamponade. We review the literature on its epidemiology, clinical presentation, diagnosis, treatment, and prognosis.

Introduction

Actinomycosis is a rare, chronic disease caused by a group of anaerobic Gram-positive bacteria that normally colonize the mouth, colon, and urogenital tract. Humans are the natural reservoir and there is no documented person-to-person transmission of the disease.[1]

Since these microorganisms are not virulent, mucosal disruption is needed to lead to infection, which in turn is characterized by a tendency to mimic malignancy due to its capacity to invade surrounding tissues and to form masses;[2,3] therefore clinical presentations are multiple.

We describe herein three patients with uncommon clinical presentations of actinomycosis compromising different organs and a short review of the literature on the topic.

Case 1

The first case is that of a 37-year-old man with a past medical history of pectoral actinomycosis diagnosed by biopsy in 2002, and chronic lower back pain of unknown etiology. He was admitted because of a 2-month history of progressive non-pitting swelling of both inferior extremities associated with genital and abdominal wall edema. He also was also suffering from weight loss, and there were multiple small painful nodules with purulent discharge on his lower back (Figure 1).

On examination he was afebrile and all lumbar movements were severely restricted by pain. There were multiple, and

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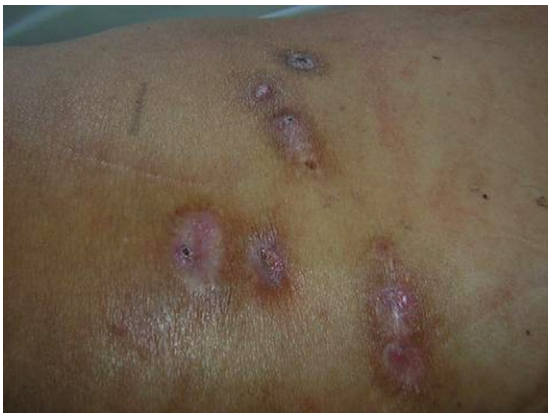

Figure 1 Multiple small nodules on the lower back of a patient with abdominal actinomycosis. Purulent discharge was noted.

not well circumscribed, tender nodules over the lumbosacral region. Pressure on these skin lesions produced pain that the patient described as radiating into the adjacent bones, and purulent discharge was noted. There was bilateral non-pitting leg edema associated with genital enlargement and abdominal collateral circulation. A neurological examination was normal. There were no palpable lymph nodes. The remainder of the examination was normal.

His hemoglobin level was 7 mg/dl and his serum iron concentration, transferrin level, and percent saturation of transferrin were consistent with anemia of chronic disease. His urea nitrogen level was 26 mg/dl and serum creatinine level was 1.2 mg/dl. Renal ultrasonography showed mild bilateral hydronephrosis, which was complemented by a computed tomography (CT) scan showing multiple paravertebral and retroperitoneal masses compressing structures such as both ureters and inferior cava vein. The CT scan also demonstrated images consistent with cava vein thrombosis. Vertebral involvement was seen mainly at the level of L5 with images of several osteolytic lesions (Figure 2).

A skin biopsy from the affected area on the back was consistent with actinomycosis involvement. He was anticoagulated for a period of 6 months. Concomitantly, he was treated with intravenous penicillin for 4 weeks and on an outpatient basis with oral amoxicillin for 12 months with an excellent response. Eight months later the patient had recovered his weight, had no back pain, and was fully ambulatory. A new CT scan showed a significant reduction in the abdominal masses.

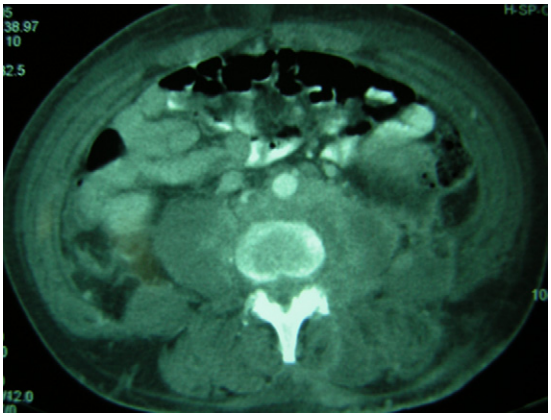

Figure 2 Abdominal computed tomography showing multiple paravertebral and retroperitoneal masses, a number of which are compressing some structures.

Case 2

The second case is that of a 41-year-old woman who presented to the emergency department with a 3-month history of intermittent severe epigastric pain, which became steady, radiating to the right upper quadrant.

Abdominal ultrasonography showed stones in the gallbladder and a laparoscopic cholecystectomy was performed. During the procedure the surgeon had to convert to an open operation due to intra-operative findings suggesting gallbladder cancer. The stomach and right colon were tightly attached to a scleroatrophic gallbladder and separation of these organs was extremely difficult.

Microscopic analyses of the gallbladder showed an acute inflammatory process with a suppurating focus and bacterial colonies consistent with actinomycosis.

She had no complications during the postoperative period and intravenous ceftriaxone for 4 weeks was indicated before changing to amoxicillin. She was discharged fully recovered to complete treatment on an outpatient basis.

Case 3

The third case is that of a 51-year-old man with an unremarkable past medical history who was admitted because of a 1-week history of productive cough, with small amounts of whitish sputum. The day before admission, he had an acute onset severe precordial pain, with no irradiation, and this was alleviated by leaning forward.

On admission, his vital signs were normal, the jugular venous pressure was not elevated, but heart sounds were diminished. No friction rub was found and cardiac enzymes were normal. An electrocardiogram showed diffuse ST elevation, and a chest X-ray showed an enlarged cardiac silhouette with clear lung fields (Figure 3). The echocardiogram showed mild pericardial effusion. Aspirin 500 mg was initiated, but four days later his temperature had increased to 38 °C. Tests for HIV and hepatitis B and C were all negative and rheumatologic blood tests were normal. An acid-fast stain on sputum was negative.

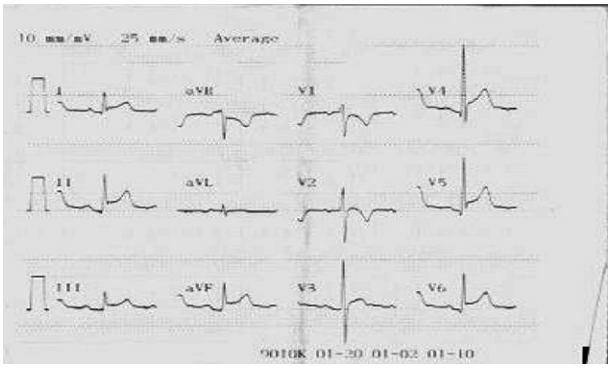

Figure 3 Electrocardiogram showing diffuse ST elevation consistent with the diagnosis of pericarditis.

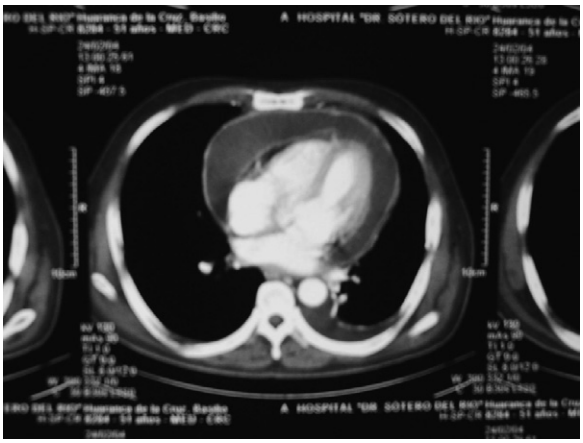

Figure 4 Thoracic computed tomography showing evidence of pericardial effusion in a patient with pericardial actinomycosis.

His condition worsened presenting severe dyspnea and an elevated jugular pressure, and pulsus paradoxus was noted. A new echocardiogram and a thoracic CT scan showed acute cardiac tamponade and pleural effusion (Figure 4).

On emergency thoracotomy, purulent pericardial fluid was drained and the pericardium appeared irregular and thickened with multiple nodules mimicking neoplastic lesions. Chemical analyses of the pericardial fluid revealed a leukocyte count of 30×10^9/l (94% neutrophils), glucose and total protein content of 1 mg/dl and 5.2 g/dl, respectively, and adenosine deaminase (ADA) of 67.4 U/l. No acid-fast bacilli were found in the pericardial fluid and results of culture were negative. Lung and pericardial histologic examination were consistent with lung and pericardial actinomycosis.

Intravenous penicillin was started, but dyspnea, elevated jugular pressure, and edema remained. Transesophageal echocardiography was consistent with constrictive pericarditis, but no surgery was needed. He was treated with intravenous penicillin for 4 weeks and amoxicillin thereafter. Following 4 months of treatment the patient was finally discharged in a stable condition and with minimal symptoms to complete 6 months of antibiotic treatment.

Discussion

Actinomycosis is an infection caused by anaerobic Gram-positive *Actinomyces* species, which belong to the natural flora of the oral cavity, gastrointestinal tract, and urogenital tract.[4,5] At least 30 species have been isolated, of which the most common microorganisms causing infections are *A. israelii*, *A. naeslundii*, *A. odontolyticus*, *A. viscosus*, *A. meyeri*, and *A. gerencseriae*.[6]

Actinomyces are closely related to *Nocardia* species, and both were once considered fungi because of their branching filaments,[1] but are currently classified as bacteria. Histopathologic examination of bones from individuals diagnosed with actinomycosis were recently evaluated by Rothschild et al.[7] Results from his work showed that actinomycosis has unique features that distinguish it from other microorganisms but, surprisingly, it has some amazing similarities to fungal infections, bringing into question its current classification as a bacterium.

Actinomycosis is endemic, occurring worldwide. It has no predilection for age, race, season, or occupation,[8] and although not considered an opportunistic infection, it has been described in patients with HIV[9,10] and leukemia,[11] and in patients with other causes of immunodeficiency. However no underlying disease or immunosuppression is found in most patients.[12]

These infections usually involve the cervicofacial, thoracic and abdominopelvic regions, and the CNS,[1] and no person-to-person transmission has yet been documented.

During the 1970s, an annual incidence of 1 case per 300 000 was found in the Cleveland area, however improved dental hygiene and the widespread use of antibiotic treatment have contributed to a decrease in this incidence.

Abdominal actinomycosis accounts for 20% of all actinomycosis[13] and is the most indolent and non-specific presentation, therefore diagnosis is quite difficult for clinicians. Clinical and laboratory findings are non-specific and a lot of conditions have been described as a possible initiating event, such as diverticulitis, appendicitis,[14] peptic ulcer disease, foreign body,[15] bowel surgery, and the utilization of an intra-uterine contraceptive device. Virtually all organs have been reported to be compromised.

Nevertheless, inferior cava syndrome is an uncommon manifestation or complication of actinomycosis. After a wide literature search in PubMed/Medline only one case was found of a patient with disseminated disease.[16] In our patient, the diagnosis was made by clinical examination, CT scan showing vascular involvement with thrombosis, and a good response to anticoagulation therapy. Actinomycosis complicated with ureteral compression is also an unusual presentation.[17]

Gallbladder actinomycosis is a rare presentation that can masquerade as a chronic cholecystitis but more frequently presents as an acute disease.[18] Because of the tendency to form masses and to invade other organs, cancer and actinomycosis are almost always confused, the latter being diagnosed only after a microscopic histopathologic examination.[19] However, there is one reported case of biliary actinomycosis associated with an adenocarcinoma of the gallbladder.[20] Gallbladder actinomycosis may spread to the liver,[21,22] but cholecystic or common bile duct involvement is very rare, being described only twice.[23,24]

There are no specific radiological features on ultrasound or CT scan to aid the diagnosis. Sometimes a CT can be helpful in the presence of a contrast-enhancing multicystic lesion in order to approach biopsy.[8] When the abdominopelvic actinomycosis involves the gastrointestinal tract, a bowel wall thickening and a peritoneal mass that tends to invade across tissue planes can be seen.[25]

Actinomycosis infection of the bone is mainly due to adjacent tissue infection, but it can also be seen in some fractures or hematogenous spread.[6] Involvement of the vertebral column has frequently been reported, and because of slow disease progression the lesions tend to be spheroid and surrounded by periosteal bone formation.[7] Vertebral collapse is not a common feature and osteolytic damage, as in our patient, is rare.[26] Cutaneous sinus tracts usually develop.

Thoracic actinomycosis may involve lungs, pleura, mediastinum, chest wall, or pericardium.[1] Pulmonary actinomycosis accounts for 15—45% of all cases reported and cardiac involvement only 2%. Of cases where the heart is involved, 80% have infection of the pericardium.[27] Mediastinal infec-

tion is uncommon usually arising from contiguous spread. Other forms of infection include transdiaphragmatic or rarely, hematogenous dissemination.

Chest pain, dyspnea, fever, weight loss, and cough are very common manifestations of thoracic and pericardial involvement.[6,28] Examination of pericardial fluid may reveal a polymorphonuclear leukocyte predominance, but detection of sulfur granules and culture of the *Actinomyces* organism are very difficult[29] with only 26% of cultures being positive.[28] Different cut-off values for ADA activity, ranging from 30 to 60 U/l, have been suggested as being indicative of tuberculous pericarditis,[30] however high levels have also been found in another infectious conditions with purulent fluid.[31] In endemic areas, an ADA cut-off value of 60 U/l has a 100% sensitivity and an 80% specificity for tuberculous pericarditis.[32] We found no data in the medical literature regarding ADA levels and actinomycosis. However our patient's pericardium biopsy did not demonstrate the presence of granulomas making the diagnosis of tuberculous pericarditis very unlikely.

Actinomyces species are susceptible to many antibiotics in vitro.[33] Clinical experience supports the use of penicillin G as the drug of choice, and in order to avoid relapse, prolonged treatment is advisable.[1] Therapy should be individualized, but high doses (18—24 million units/day) of penicillin over a long period of time (2—6 weeks) followed by oral therapy with penicillin or amoxicillin to complete 6 to 12 months seems reasonable.[6] However, there are some reports of successful short-term treatment with beta-lactam antibiotics in special circumstances.[34]

For penicillin-allergic patients, doxycycline, minocycline, tetracycline, clindamycin, erythromycin, and cephalosporins have been proven to be effective in case reports.[29,35—38] A recent in vitro study assessing the susceptibility of human clinical isolates of *Actinomyces* species to different antimicrobial agents showed that bacterial identification may be critical because of the resistance to some antibiotics.[33] Surgical treatment is controversial and may include incision and drainage of abscesses, resection of necrotic tissue, and curettage of bone.[1]

The prognosis for treated infections is excellent if it is recognized early. Hematogenous dissemination is a relatively frequent complication of actinomycosis, especially as a result of thoracic disease. It produces manifestations that can be easily mistaken for metastasic disease, with multiple nodules in virtually any organ or tissue. However, despite the extent of the disease, it has a good prognosis when discovered in time.[6,39]

Mortality ranges from 0 to 28% depending mainly on the site of infection and the time to diagnosis.[1,40—42] Actinomycosis of the central nervous system has the greatest mortality with neurologic sequelae being reported in half of these patients.[42]

Conclusions

Actinomycosis is still a disease that poses a great diagnostic challenge because of its insidious course and non-specific symptoms. Because of this wide variety of clinical presentations reported in the literature and its tendency to mimic different diseases, actinomycosis acts as a 'great pretender'.

We emphasize the importance of early diagnosis with a simple Gram stain, and that delayed treatment can lead to increased morbidity and even mortality.

Conflict of interest: No conflict of interest to declare.

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