

Tuberculosis: A Rare Cause of Peri-Anal Disease

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Pulmonary disease is the most common manifestation of tuberculosis. It was found that only a minority of patients with tuberculosis who are not infected with human immunodeficiency virus have gastrointestinal involvement [1,2]. The terminal ileum and ileocecal region are the most common sites, while isolated anal involvement is extremely rare [1,2].

Patients with intestinal tuberculosis may have clinical, endoscopic, radiological and histological features that simulate Crohn's disease, and differentiating between both conditions may be difficult [1,2]. We present the case of a man who suffered from severe peri-anal disease that was thought to be due to Crohn's disease. Atypical features of the peri-anal disease and the history of a recent visit to Vietnam raised the suspicion of tuberculosis infection, which was validated.

PATIENT DESCRIPTION

A 36 year old Israeli male presented to his family physician in early July 2010 with peri-anal pain and anal bleeding accompanied by fever of 39°C. Rectal examination revealed the presence of external hemorrhoids and an anal fissure. During the next 2 weeks an anal abscess developed along with a fistula from the

anus to the external skin. The patient continued to suffer from high fever as well as severe pelvic pain accompanied by anal bleeding and a pink-white purulent discharge. A month later he underwent peri-anal abscess drainage under general anesthesia. However, his symptoms persisted and he was readmitted twice in the same month for drainage of the peri-anal abscess. During the third drainage procedure it was noted that the abscess had spread to multiple sites in the perineum as well as the scrotum. A whole-body computerized tomography scan demonstrated the presence of hepatosplenomegaly and multiple small lymph nodes in the mesentery, retroperitoneum, mediastinum and the inguinal areas. Magnetic resonance imaging of the pelvic region revealed that the inflammatory process extended from the peri-anal into the gluteal regions. The patient was treated with repeated courses of broad-spectrum antibiotics.

In the following weeks additional fistulous tracts appeared and the purulent discharge persisted. The patient's pelvic pain worsened and he was unable to stay in a sitting position. Setons were inserted into the fistulous tracts. Endoscopic evaluation of the whole gastrointestinal tract by gastroscopy, full colonoscopy with endoscopic examination of the terminal ileum, and capsule endoscopy of the whole small intestine (Given Imaging, Yokne'am, Israel) did not show the presence of any mucosal lesions. Serological examination for the presence of anti-glycan antibody biomarkers for inflammatory bowel disease demonstrated only anti-chitobioside carbohydrate antibodies [3]. Throughout the disease course the patient lost 25 kg in weight. It was assumed that he had

Crohn's disease with severe peri-anal involvement. A decision was made to administer monoclonal anti-tumor necrosis factor antibodies. As routinely indicated, the patient underwent evaluation for past exposure to *Mycobacterium tuberculosis*. This included a chest X-ray examination and three consecutive subcutaneous Mantoux tests. All of these tests were interpreted as negative for past exposure to *Mycobacterium tuberculosis*.

At this stage it was decided to postpone the anti-TNF therapy, to culture the peri-anal discharge for atypical organisms such as *Actinomyces* species and *Mycobacterium* and to re-administer systemic antibiotics for the treatment of possible anaerobic pelvic infection. Direct stains of the discharge were negative for the presence of either *Actinomyces* or acid-fast *Bacillus*.

Six weeks later, while the patient was undergoing surgical drainage of the multiple peri-anal abscesses, *M. tuberculosis* grew from the culture plates that were inoculated with the patient's peri-anal discharge. Tests for HIV infection were negative. A course of combined anti-*Mycobacterium* treatment that included isoniazid, rifampicin, pyrazinamide and ethambutol was started. Within several weeks gradual healing with disappearance of the liquid discharge occurred. Several additional drainage procedures were performed and the pelvic pain gradually ceased. At the conclusion of 12 months of anti-*Mycobacterium* treatment the perineum was completely healed.

TNF = tumor necrosis factor
HIV = human immunodeficiency virus

COMMENT

Peri-anal tuberculosis is a rare condition in the western world [1,2]. This condition may manifest with peri-anal pain and discharge and the presence of multiple complex peri-anal fistulas. These fistulas may persist and have a long and relapsing course despite appropriate surgical management [4]. Also reported are inguinal adenopathy, peri-anal ulceration with purulent exudates, anal strictures, anal ulceration and fissures [4].

In patients with severe peri-anal pathology, as in our patient, the diagnosis is not straightforward. Additional disease conditions to be ruled out include Crohn's disease, hidradenitis and infection with either Actinomycosis or lymphogranuloma venereum or a neoplastic process (especially in patients with HIV) [1]. Culturing for these unusual pathogens and histological analysis of tissue samples from the diseased perineum may aid in reaching the correct diagnosis [2].

Distinguishing Crohn's disease from intestinal tuberculosis may be challenging. Both conditions have overlapping clinical, radiological, endoscopic and histological characteristics. Moreover, both conditions are chronic granulomatous diseases, and both trigger a potent adaptive TH1 cytokine response but tend to show impaired innate immunity [2]. Diagnostic algorithms to help resolve the diagnostic dilemma in endemic areas have been proposed [2]. This algorithm should probably also be applied in non-endemic areas, where active intestinal tuberculosis is rare.

Examination of the patient's serum for the presence of various anti-glycan anti-

body biomarkers revealed the presence of ACCA. Glycans are the predominant cell wall surface components in many saprophytic and pathogenic fungi, yeast and bacteria, as well as protozoa and viruses. In recent years it was reported that antibodies to glycans are effective markers for the disease phenotype, with a potential to predict the disease course [3]. However, the exact role of these antibodies and other serological tests in the differentiation from intestinal tuberculosis is unknown. Moreover, none of these tests is diagnostic and the exclusive use of one of the above-mentioned tests may be misleading and can delay the diagnosis of tuberculosis [4].

Our patient did not have evidence for pulmonary tuberculosis. The existence of pulmonary tuberculosis in Asian populations (mainly Indian) was reported to occur in < 50% of patients with intestinal tuberculosis [2]. In patients with peri-anal tuberculosis originating from Asia, pulmonary involvement was rare while in patients originating from European countries pulmonary involvement was more frequent [2,4].

The exact cause of the peri-anal localization of the tuberculosis infection in our patient is unknown. It was suggested that occurrence of tuberculosis infection in any specific region may occur through five possible mechanisms: a) hematogenous spread from the primary lung focus with later reactivation, b) ingestion of bacilli in sputum from an active pulmonary focus, c) ingestion of contaminated milk, d) direct spread from adjacent organs, and

ACCA = anti-chitobioside carbohydrate antibodies

e) through lymph channels from infected nodes (reviewed in [4]).

Our patient contracted the tuberculosis infection probably while visiting Vietnam. Loh et al. [5] reported that the tuberculosis infection rates are much higher in Asian than western countries. This should be remembered by clinicians encountering patients with various intestinal disease conditions who recently moved from an endemic area for tuberculosis to an area where tuberculosis is rare. Our case also emphasizes that a history of traveling to a tuberculosis-endemic country warrants a thorough examination to determine whether infection with *Mycobacterium tuberculosis*, rather than Crohn's disease, is the culprit.

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“The bitterest tears shed over graves are for words left unsaid and deeds left undone”

Harriet Beecher Stowe (1811-1896), American abolitionist and author. Her novel *Uncle Tom's Cabin* depicted the life of African Americans under slavery. It reached millions as a novel and play and became influential in the USA and Britain. It energized anti-slavery forces in the American North, while provoking widespread anger in the South

“Anyone who has ever struggled with poverty knows how extremely expensive it is to be poor”

James Baldwin (1924-1987), American novelist, essayist, playwright, poet and social critic, whose essays, such as the collection *Notes of a Native Son*, explore palpable yet unspoken intricacies of racial, sexual, and class distinctions in western societies, particularly in mid-20th century America