A puzzling case of Mycobacterium abscessus

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Learning Objective 1: The incidence of rapidly growing Non-Tuberculosis Mycobacterium (NTM) infection has been increasing worldwide. There is need for high degree of clinical suspicion in order to accurately diagnose rapidly growing Non-Tuberculosis Mycobacterium (NTM) as the cause for recurrent soft tissue swelling.

Learning Objective 2: It is equally important to distinguish M.abscessus from other NTM since the management and prognosis are different.

Case: A 50-year-old female presented with a progressive swelling between the first and second digits of her right hand of 4 months duration. 3 months after onset, she visited the Emergency Department, underwent an incision and drainage and took 7 days of Doxycycline. Within a month the swelling had recurred. Of note, she could recall a small cut on her right thumb while gardening, a week prior to symptom onset. Exam showed a firm 1.5 x 1 cm swelling between the interdigital space of her right first and second digits. There was no localized lymphadenopathy or limitation in range of movements. MRI of the hand reported a hyper vascular enhancing lesion adjacent to the first metacarpophalangeal joint, without any bony erosions or marrow enhancement. Preliminary report from samples sent from the Emergency Department showed gram-positive, auramine/rhodamine fluorescent and acid-fast positive rods. These organisms were difficult to culture. The sample was processed at 3 different laboratories before it was identified by nucleic acid analysis as Mycobacterium abscessus, later confirmed by standard culture and methodology. Surgical excision of the mass revealed necrotizing granulomatoid nodules with chronic inflammation, granulation tissue and dense fibrosis suggestive of granuloma annulare on histopathology. Patient was empirically initiated on Clarithromycin and Doxycycline. Inability to tolerate Doxycycline along with sensitivity patterns showing resistance to this antibiotic resulted in switching to a combination therapy of Clarithromycin and Ciprofloxacin which has been successful to date, with no further recurrences.

Discussion: Mycobacterium abscessus (formerly part of “M.chelonae-complex”) are the most pathogenic and chemotherapy-resistant of all rapidly growing Non-Tuberculosis Mycobacterium (NTM). Skin and soft tissue infections are often secondary to trauma or as a post surgical complication due to contaminated surgical instruments and supplies. They can occur in both immune competent and compromised hosts. Molecular tools such as the sequence analyses are preferred in the detection since methods based solely on microscopy, solid and liquid cultures, Bactec systems, and species-specific polymerase chain reaction may produce misleading results. M.abscessus is resistant to all first-line tuberculosis drugs. Early combination therapy is preferred to monotherapy with duration guided by clinical response. Surgery is indicated for abscesses, extensive disease, when drug therapy is limited by resistance or adverse effects, and in localized pulmonary disease poorly responsive to medical therapy. This particular case highlights the need for high degree of clinical suspicion even with absence of a pathognomonic clinical picture and variable histopathology findings in order to accurately diagnose rapidly growing Non-Tuberculosis Mycobacterium (NTM) as the cause for recurrent soft tissue swelling. It is equally important to distinguish M.abscessus since the management and prognosis is different from other NTM.
Learning Objective 1: Recognize the signs, symptoms, and pathophysiology of gastrointestinal sarcoidosis.

Learning Objective 2: Understand testing characteristics of CA-19.9

Case: A 53 year-old woman presented with abdominal pain and 30 pound weight loss over three months. Pain was dull, epigastric, with associated nausea and vomiting worse with oral intake. Cancer screening was up to date. An outpatient workup included an endoscopy, which showed mild atrophic gastritis, and a benign colonoscopy. She denied fever, dyspnea, cough, and chest pain. Vital signs were within normal limits, she appeared comfortable, and had mild diffuse epigastric tenderness. Labs revealed a hemoglobin of 10.5 G/dL, platelet count 440 K/uL, corrected calcium of 11.5 mg/dL, direct bilirubin 1.2 mg/dL, SGOT 78 U/L, SGPT 59 U/L, and alkaline phosphate of 546 U/L. Computed tomography revealed multiple bilateral pulmonary nodules, and innumerable small hypodense lesions measuring 1cm scattered throughout the liver, pancreas, and spleen. Differential diagnosis at the time included metastatic disease, primary pancreatic malignancy, lymphoma, or inflammatory process such as sarcoidosis. Due to concern for malignancy, tumor markers were ordered and CA-19.9 was elevated at 357 U/mL (normal <35 U/mL). Ultrasound guided liver biopsy was performed. Pathology showed non-necrotizing granulomas, negative for AFB, consistent with a diagnosis of gastrointestinal sarcoidosis.

Discussion: Sarcoidosis is a multi-system granulomatous disorder of unknown etiology, with the pathologic hallmark of non-caseating granulomas. The prevalence is 20 per 100,000 people per year. It is thought to arise from an exaggerated cellular immune response to self-antigens and subsequent accumulation of mononuclear inflammatory cells. Sacroid is a systemic disorder involving multiple organ systems. Ninety percent of patients have pulmonary involvement and present with cough, dyspnea, and classically have bilateral hilar adenopathy on chest xray. Common extrapulmonary manifestations include skin (erythema nodosum), eye (uveitis), and joint involvement. Gastrointestinal (GI) manifestations of sarcoid are rare and occur in only 0.5% of patients. When there is GI involvement, the stomach is the most commonly involved organ; patients present with epigastric pain, vomiting, and weight loss. Hepatic involvement is less common and usually asymptomatic, with differing case series reporting 20-95% incidence. Pancreatic involvement is rare and is often misidentified as pancreatic malignancy. Sarcoid, known as the “Great Imitator,” is often initially misidentified as malignancy and tumor markers ordered during the initial workup are frequently falsely elevated. CA19.9, a tumor marker elevated in GI cancers (pancreatic, hepatobiliary, gastric), is thought to be elevated in our patient due to chronic inflammation. CA19.9 has low sensitivity (80), specificity (85) and positive predictive value (72), and guidelines recommend against its use for cancer screening. Pancreatic sarcoidosis carries a good prognosis, with greater than 80% improvement in symptoms either spontaneously or with steroids, compared to the dismal prognosis of pancreatic cancer which carries a one year survival rate of 15-20%. This case of GI sarcoid, initially thought to be pancreatic cancer based on an elevated CA19.9 value, demonstrates that one should use caution in ordering tumor markers prior to having a tissue diagnosis.
Exudative pleural effusion in a Haitian Man

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Learning Objective 1: Diagnose tuberculous pleural effusion when all cultures are negative.

Learning Objective 2: recognize the features of a tuberculous pleural effusion.

Case: A 46-year-old previously healthy male presented with two weeks of subjective fevers, pleuritic chest pain, and worsened nonproductive cough with chills and night sweats. He denied hemoptysis, significant weight loss, or sick contacts. There was no significant past medical history or medications. He traveled to Haiti 6 weeks prior to presentation and reported having a purified protein derivative (PPD) 5 years prior to presentation but did not recall the results.

On exam, he had firm, fixed left axillary lymphadenopathy and dullness to percussion with decreased breath sounds in the right lung base. Chest computed tomography showed new bilateral pleural effusions and mediastinal lymphadenopathy. PPD had 10 mm of induration. Pleural fluid studies revealed an exudative effusion based on a total protein 6.8 g/dL (serum total protein 8.1 g/dL) and LDH 482 IU/L (serum upper limit of normal 210 IU/L). Other pleural fluid studies included total nucleated cell count of 34,300 cells/mm³ with 41% neutrophils and 33% lymphocytes, pH 7.4, glucose 105 mg/dL, albumin 3.4 g/dL, and adenosine deaminase 65.2 U/L with cytology negative for malignancy. Pleural acid fast bacilli (AFB) stain and culture were negative. Sputum AFB stain and culture were negative on three repeat examinations. PET-CT showed diffuse lymphadenopathy. HIV testing was negative. Left axillary lymph node biopsy revealed reactive lymphadenopathy. Pleural biopsy could not be obtained.

Discussion: Pleural effusions are commonly seen by the general internist with a wide differential. It is worthwhile for the general internist to be familiar with the features of tuberculous pleural effusion as it is the second most common manifestation of extrapulmonary tuberculosis and may be the first or only manifestation of tuberculosis in some individuals. Effusions are typically unilateral and located on the same side as the parenchymal disease. Pleural fluid is typically exudative with a protein concentration > 3.0 g/dL and LDH often greater than 500 IU/L, containing 1000 to 6000 cells/mm³ with a lymphocytic predominance. Pleural fluid cultures are positive in approximately 20% of cases, but pleural biopsy may increase the culture yield to 90%. An adenosine deaminase level greater than 45 U/L in pleural fluid has a 100% sensitivity and 80-97% specificity for the diagnosis of tuberculous pleural effusion. Neither PPD nor interferon gamma release assays are sensitive for the diagnosis of tuberculous effusion. Some features of our patient’s presentation were initially suggestive of malignancy, however, once this was excluded, though AFB and culture data were negative, tuberculous pleural effusion was the most likely diagnosis and empiric therapy was started with improvement in the patient’s symptoms. This case illustrates the utility of pleural fluid adenosine deaminase levels in establishing the diagnosis of tuberculous pleural effusion without positive AFB or culture data.
Luckily it is Not the Worst Case Scenario: Disseminated Histoplasmosis Presenting as a Wasting Syndrome with Hypercalcemia

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Learning Objective 1: Recognize that granulomatous diseases like sarcoidosis, tuberculosis, and disseminated fungal infections can cause severe hypercalcemia.

Case: A 65 year-old diabetic male presented with 2-month history of constipation, polyuria and unintentional weight loss. On examination, he was cachectic without rash, lymphadenopathy or organomegaly. Labs showed hemoglobin of 10.6 g/dl, creatinine of 3.23 mg/dl and serum calcium of 12.4 mg/dl. Liver function tests, parathyroid hormone level and serum protein electrophoresis were within normal limits. Body computed tomography showed 3 brain lesions, bilateral adrenal enlargement and a lesion at the base of the tongue. Biopsies of the tongue lesion and the left adrenal gland were identical and showed non-caseating granulomas and budding yeast forms consistent with histoplasmosis. After intravenous fluid hydration and improvement in his renal function, he was started on a 4-week course of liposomal amphotericin B followed by a long course of itraconazole with gradual improvement.

Discussion: Histoplasmosis is the most common endemic mycosis in the country. Infection is acquired after inhaling H. capsulatum microconidia. Most infections are asymptomatic or manifest as a mild self-limiting flu-like illness. Symptomatic disease has multiple manifestations including a chronic progressive disseminated infection. In this entity, the patient is classically a middle-aged or elderly man without a known immunocompromising illness. It usually presents like a wasting syndrome suspicious for an underlying metastatic malignancy. Hypercalcemia is a very rare presentation of this infection and results from increased vitamin D production in the infectious granulomas. Diagnosis hinges on isolating the fungus on cultures, identifying its characteristic yeast forms on histopathological exam, detecting histoplasma antigen in urine or serum which carries a sensitivity of 90% in disseminated infections or documenting a positive serology. The role of molecular methods in the diagnosis of histoplasmosis is still evolving. This infection is fatal if not treated. Cases that are mild to moderate in severity can be treated with itraconazole alone, whereas, more severe infections require an initial course of amphotericin B followed by a lengthy course of itraconazole. This case reminds Internists to consider disseminated granulomatous diseases including histoplasmosis in the differential of patients with hypercalcemia.
A case of erythema nodosum leprosum in a 23-year-old Marshallese man presenting with rash.

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Learning Objective 1: Lepromatous leprosy is a rare disease affecting the skin and peripheral nerves that should be considered in patients from endemic areas who present with a rash. Rarely, leprosy may present with erythema nodosum. Early recognition of this disease is important as early leprosy treatment is essential to avoid complications.

Case: A 23-year-old man presented to the emergency department with evolving rash over two weeks. The rash was non-pruritic and started on his lower limbs and gradually spread upwards to the rest of his body, including his face and ears. One week after the rash appeared, he developed fever and generalized pain in his hand and foot joints.

The patient had no allergies and no family history of skin disease. He was born in the Marshall Islands but had been living in the United States for the past five years. He had no known history of STDs. He had no recent history of international travel and none of his close contacts had a similar rash.

Physical examination revealed multiple erythematous nodules and papules on the head and neck, disseminated brown and erythematous macules and papules on trunk and limbs, including hands. Palpable purpura and hyperpigmented patches were present on his lower anterior legs. Mild synovitis of his finger joints and bilateral inguinal lymphadenopathy were present. There was no mucosal involvement.

Diagnostic testing revealed a white blood cell count of 3.0x10⁹/L and erythrocyte sedimentation rate of 80mm/hr. A skin biopsy was performed and was histologically diagnostic of lepromatous leprosy. Cytology also demonstrated neutrophilic infiltrate and karyorrhectic debris consistent with erythema nodosum leprosum. Fite stain demonstrated numerous intracellular acid-fast bacilli. A modified treatment protocol consisting of dapsone, rifampin and moxifloxacin was initiated. In addition, patient was also treated with prednisone for inflammatory symptoms.

Discussion: This case describes erythema nodosum with systemic symptoms as an atypical presentation of lepromatous leprosy. It illustrates the importance of maintaining a high clinical suspicion for leprosy in a patient who presents with a disseminated erythematous nodular and maculopapular rash. Although it is rare, it should be included in the differential for an unexplained rash in a patient from an endemic area.