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SM Journal of Pulmonary Medicine

Case Report

Mycobacterium szulgai and *Isospora belli* Dual Infection causing Chronic Diarrhea in an HIV Infected Individual

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Article Information

Received date: Aug 13, 2017
Accepted date: Sep 18, 2017
Published date: Sep 21, 2017

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Abstract

Non-Tuberculous Mycobacteria (NTM) are not obligate pathogens and generally do not cause disease or get transmitted from person to person they are opportunistic organisms that cause disease in immunocompromised individuals. They most commonly cause skin and soft tissue infections, lymphadenitis and lung infections.

Introduction

Tuberculosis is the most common opportunistic infection affecting HIV infected individuals. Clinical presentation of tuberculosis depends on the immune competence of the individual and the type of organism causing the disease. Around 8 to 10% of all tuberculous infections are due to atypical (NTM) mycobacteria. Diarrheal diseases are common manifestations of GI diseases in HIV infected individuals (0.9 to 14% in HIV infected and 60% with AIDS) [1]. Opportunistic infections of the GI tract that are commonly associated with diarrhea include parasites such as *Cryptosporidia, Giardia, Isosporiasis and Microsporidia.* Bacteria such as *Salmonella and Shigella* usually cause severe acute diarrhea. Mycobacterial diseases are a frequent cause of diarrheal disorders. MAC and CMV infections are observed in patients with CD4 cell count <100/mm^3. Malignancies causing diarrhea are an uncommon feature in patients with HIV infection.

Diarrhea may wax and wane over time, and in at least 30% of patients, an etiology cannot be determined. In such cases, the diarrhea is often attributed to HIV enteropathy in advanced cases.

Multiple opportunistic infections are common in late stages of HIV disease and cause intractable symptoms if not identified and treated appropriately on time.

We discuss here a case of *Mycobacterium szulgai* induced chronic diarrhea in an HIV infected individual co infected with Isosporiasis.

Case Report

A 35 year old male patient was being followed up at ARCON Centre, Sir J. J. Hospital since February'97. He was detected HIV 1 infected by ELISA (Genelavia, Sanofi, France) and rapid test (Serodia, Fujirabio, Japan).

In 1998 and 2000 he had sputum and culture positive pulmonary tuberculosis, which responded well to first line four-drug anti tuberculosis treatment on both occasions.

In November 2000, following chronic recurrent diarrhea, he was diagnosed as having *Isospora belli* infection and was started on TMP-SMX combination daily along with secretary inhibitors as and when required. With this treatment his symptoms were controlled. There were no other opportunistic infections during the subsequent follow up.

In February 2003, he presented with recurrent diarrhea for more than four months not responding to treatment. There was no vomiting, abdominal pain or discomfort or any other constitutional symptoms except weight loss. Appetite was normal.

Investigations

Routine tests were non-conclusive. Stool samples were concentrated and subjected to the following tests at the Department of Microbiology, Sir J. J. hospital:

- Ziehll Neelson Carbol Fuschin (ZNCF) staining which yielded a number of oocysts of *Isospora belli* and Acid Fast Bacilli (AFB).
- Culture on duplicate slants of Lowenstein Jenson (LJ) medium and incubated at 35° C, which yielded pigmented growth of AFB.

Table 1: Result of serial Immunophenotyping of CD_4 / CD_8 Lymphocytes.

Date	CD_4 Per cmm.	CD_8 Per cmm.	CD_3 Per cmm.	CD_4/CD_8 Ratio
21.11.2000	339	1095	1525	0.31
03.07.2001	498	1142	1164	0.44
08.04.2003	361	1054	1488	0.34
07.04.2004	542	1325	2025	0.41
29.09.2004	545	1177	1870	0.46

- Confirmation of the isolate was done by ZN stain and subculture on LJ medium.
- Photosensitivity test and the biochemical tests were carried out:
  - Niacin production – negative
  - Nitrate reduction – positive
  - Urease hydrolysis – positive
  - P-nitrobenzoic acid susceptibility resistant.
- The isolate was identified as *Mycobacterium szulgai*. Further tests to confirm the species could not be carried out due to resource limitations and non-availability of facilities locally.
- Anitimycobacterial susceptibility testing of the isolate - M. szulgai - to primary drugs was conducted using the proportion method. The strain was resistant to Streptomycin, Isoniazid, Rifampicin, Pyrazinamide and sensitive to Ethambutol.

Clinical course

Anti TB treatment was commenced with four first line drugs (HRZE) along with treatment for Isospora, pending stool culture reports. Therapy was changed to second line drugs including Clarithromycin, Ethambutol and Doxycycline in weight adjusted doses, and was given for one year. Anti Retroviral Therapy (ART) was commenced after he tolerated the anti TB medications, which were discontinued in August 2004. The patient was under regular follow up for two years post treatment completion and was asymptomatic except for ART related side effects in the form of peripheral neuropathy and lipodystrophy. CD_4 / CD_8 counts are shown in table 1.

Discussion

In the absence of antiretroviral therapy, diarrheal diseases are one of the most frequent presentations of HIV infections and AIDS and were responsible for 17% of new AIDS diagnosis [2]. Diarrhea has also been demonstrated to be an independent predictor of reduced quality of life in a multivariate analysis [3].

Diarrheal disease in HIV-infected individuals is frequently caused by infectious agents but may also be due to other opportunistic illnesses such as lymphoma or Kaposi's Sarcoma (KS) of the stomach, small bowel or large intestine [4-6]. Many medications used for HIV have been associated with gastrointestinal side effects or diarrhea, but the protease inhibitor, nelfinavir, is currently the drug most commonly associated with diarrheal syndromes [7].

HIV infection of the gastrointestinal tract is also well documented and may also play a role in the pathogenesis of diarrhea and gastrointestinal illness, though the exact mechanisms are not well understood.

Multiple opportunistic infections causing symptoms are commonly seen in severely immunocompromised HIV – infected individuals. Hence, search for infectious agents should continue, if symptoms persist despite identification and treatment of one source of infection.

Mycobacterium szulgai is an unusual pathogen that accounts for less than 1% of all cases of non-tuberculosis mycobacterial infections. *Mycobacterium szulgai* is a slowly growing *Mycobacterium* that has been associated with skin, joint, lymphatic, pulmonary, and disseminated disease [8]. Through 1986, only 24 cases of disease had been reported. A patient with SLE developed a cutaneous nodule caused by *M szulgai.* Another patient was on long-term corticosteroid therapy for sarcoidosis and exhibited multicentric, purely cutaneous infection [9]. Our case is the first report on gastrointestinal tract involvement with *M. szulgai*. Isolation of *M. szulgai* implies the presence of clinical disease, and when the organism is identified, treatment based on sensitivity testing should be initiated. The organism is usually susceptible to rifampin and higher concentrations of isoniazid, streptomycin, and ethambutol. Enhanced activity of rifampin, ethambutol, and streptomycin when used in combination has been shown *in vitro* [10,11]. Pulmonary infections caused by *M. szulgai* have been successfully treated with combinations of ethambutol, isoniazid, rifampin, and most recently clarithromycin [8,12]. Most patients treated with these drugs respond to therapy. Our case was sensitive to ethambutol and resistant to all other first line drugs and responded well to therapy with clarithromycin, ethambutol and doxycyclin.

The case highlights some important issues. Multiple infections should be considered in HIV / AIDS infected individuals especially when primary therapy to one causative organism fails to control the symptoms. Drug susceptibility testing should be carried out wherever possible to institute appropriate therapy.

The case under presentation is the first report of an HIV infected individual with chronic diarrhea due to dual opportunistic infection with *Isospora belli* and drug resistant *Mycobacterium szulgai*, which responded well to therapy.

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