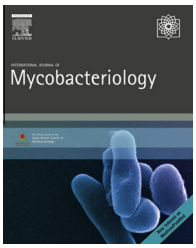
Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/IJMYCO



Full Length Article

Nontuberculous mycobacteria in fistula-in-ano: A new finding and its implications

Pankaj Garg *

Department of Colorectal Surgery, Indus Super Specialty Hospital, Mohali, Punjab, India
Department of Colorectal Surgery, Garg Fistula Research Institute, Panchkula, Haryana, India

ARTICLE INFO

Article history:
Received 20 April 2016
Received in revised form
11 May 2016
Accepted 14 May 2016
Available online 1 June 2016

Keywords:
Fistula-in-ano
Histopathology
Mycobacteria
Polymerase chain reaction
Tuberculosis

ABSTRACT

Objective/background: Nontuberculous mycobacteria (NTM) are not known to be associated with fistula-in-ano. NTM was detected in three fistula-in-ano patients in our series. In this study, related data was reviewed to find the mycobacterial disease in patients in our database. Methods: In this study, 311 consecutive fistula-in-ano patients operated over 2 years were analyzed. The histopathology of anal fistula tract epithelial lining of every operated patient was analyzed and other tests (real-time-polymerase chain reaction [RT-PCR], GeneXpert, and mycobacterial culture) were conducted in patients with high index of suspicion of having mycobacterial disease. Results: Two patients had histopathological features suggestive of mycobacterial disease. Of these, one patient had NTM and the other had Mycobacterium tuberculosis (MTB) on RT-PCR. Four patients had normal histopathology features but tested positive on RT-PCR (2 each for NTM and MTB). Therefore, a total of six patients were tested for mycobacterial disease (3 each for NTM and MTB). Mycobacterium culture was performed in two patients (both NTM) but the result was negative. Five of six patients (NTM = 2, MTB = 3) presented with delayed recurrences after operation (6–18 months after complete healing). Conclusion: NTM can cause fistula-in-ano. It could be an undiagnosed contributory factor in fistula recurrence. Mycobacterial disease (both tuberculous and nontuberculous) may be associated with delayed recurrence of fistula. RT-PCR is highly sensitive and can differentiate between NTM and MTB. It should perhaps be performed in all recurrent and refractory cases.

Introduction

Although *Mycobacterium tuberculosis* (MTB) infection is considered to be a diminishing clinical problem in industrialized countries, it continues to be a dominant public health concern in many developing ones [1]. However, the incidence of nontuberculous mycobacteria (NTM) infections has increased in developed countries with the global human

* Address: 1042, Sector 15, Panchkula 134113, Haryana, India.
E-mail address: drgargpankaj@yahoo.com

Peer review under responsibility of Asian African Society for Mycobacteriology.
http://dx.doi.org/10.1016/j.ijmyco.2016.05.001

immunodeficiency virus/acquired immunodeficiency syndrome epidemic and the use of immunosuppressive agents [1]. Unlike MTB, which is transmitted from one person to another, NTM are abundant in nature, soil, and water, and are believed to be acquired by environmental exposure. Different species of NTM prefer different environmental conditions, and thus, they are also known as *environmental bacteria*.

Extrapulmonary TB is responsible for 3–46% of all types of TB cases worldwide [2]. Of these, perianal TB is a rare type accounting for only 0.7% of these cases [3]. However, it is very likely that the prevalence of perianal TB is underestimated as it remains undiagnosed or gets misdiagnosed as Crohn's disease or other granulomatous diseases [4]. NTM is not known to be associated with perianal or fistula-in-ano disease.

NTM was detected in three fistula-in-ano patients in our series. The data were reviewed to find the mycobacterial disease in patients in our database.

Materials and methods

A retrospective analysis of 311 consecutive fistula-in-ano patients operated in a referral fistula center between August 2013 and October 2015 was performed.

The protocol of our center was to send the histopathology of anal fistula tract epithelial lining of every operated patient for further analysis. Because NTM was not known to be associated with fistula-in-ano, patients with histopathological features suggestive of mycobacterial disease (granuloma formation, caseation necrosis, epithelioid cells, or Langhans giant cells; Figs. 1 and 2) were assumed to be suffering from MTB and standard antitubercular therapy was started in these patients. This practice was continued until NTM was detected on real-time-polymerase chain reaction (RT-PCR). Since then, RT-PCR was performed in cases in which mycobacterial disease was suspected clinically. However, it was not performed in all operated fistula cases due to cost constraints. RT-PCR is highly sensitive and can differentiate between TB and NTM but has low specificity (due to false positives and contamination) [5]. By contrast, both histopathological analysis and mycobacterial culture have low yield [6,7]. Therefore, RT-PCR positivity and the overall clinical picture were correlated to arrive at a diagnosis. Other related tests (chest X-ray, Mantoux test, GeneXpert, *Mycobacterium* culture) were performed as deemed necessary.

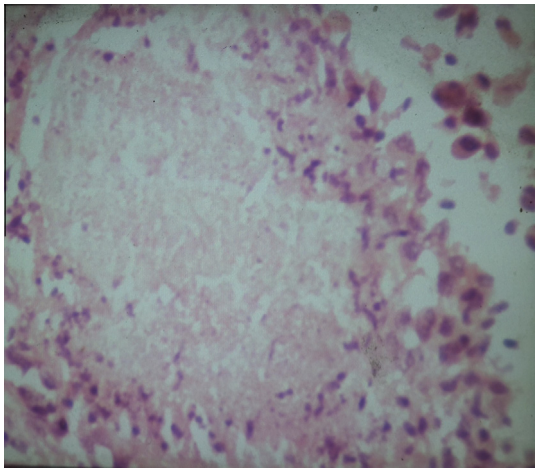


Fig. 1 – Epithelioid cell granuloma with early cessation necrosis in a 37-year-old male patient with recurrent fistula-in-ano with nontuberculous mycobacteria on real-time-polymerase chain reaction.

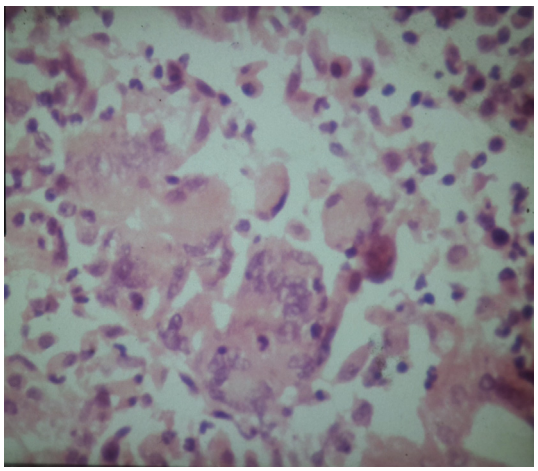


Fig. 2 – Langhans giant cell in a 37-year-old male patient with recurrent fistula-in-ano with nontuberculous mycobacteria on real-time-polymerase chain reaction.

Delayed recurrence of fistula-in-ano was defined when a patient with fistula-in-ano was completely cured after the fistula surgery but had a recurrence 6–18 months after the operation.

Results

Histopathology of anal fistula tract epithelium was analyzed in 311 fistula-in-ano patients and only two patients had features suggestive of mycobacterial disease. Of these, one patient had NTM and the other had MTB on RT-PCR. A total of six patients were tested for mycobacterial disease (3 each for NTM and MTB) on RT-PCR (Table 1). Four (2 each for NTM and MTB) of these six patients had normal histopathology features. *Mycobacterium* culture was done in two patients (NTM positive on RT-PCR) but the result was negative. Five of the six patients (NTM = 2, MTB = 3) presented with delayed recurrences after the operation (6–18 months after complete healing; Table 1). All patients diagnosed with NTM received an oral antibiotic combination (clarithromycin + sulfona mides/faropenem/doxycycline), which empirically covered all common skin and soft-tissue infections causing NTM (*Mycobacterium fortuitum* group, *Mycobacterium abscessus*, *Mycobacterium chelonae*, and *Mycobacterium marinum*) [8]. The two-drug combination was given for 3 months and all the patients responded well with complete healing of their fistula.

The study clearly indicated that histopathology had lower sensitivity as compared with RT-PCR. It would have been interesting to compare the sensitivity of histopathology and RT-PCR. As we know, the sensitivity of a test is the probability that a test will indicate *disease* among those with the disease. Because there is no gold standard test to diagnose