Case report

Colonic perforation due to invasive amebic colitis during anti-TNF therapy for spondyloarthritis

Juan Pablo Restrepo\textsuperscript{a,}*, Maria del Pilar Molina\textsuperscript{b}

\textsuperscript{a} Universidad Quindío, Quindío, Colômbia
\textsuperscript{b} Universidad Libre, Quindío, Colombia

\textbf{Abstract}

TNF blockade has been successful in the treatment of some rheumatic diseases such as spondyloarthritis. Many infectious complications have been reported with anti-TNF therapy, mainly bacterial, mycobacterial, viral and fungal infections. \textit{Entamoeba histolytica} is an extracellular protozoan parasite that mainly causes colitis and hepatic abscess; bowel perforation is an uncommon complication with high mortality. TNF is considered the principal mediator of cell immunity against amebiasis. Initially, it is chemotactic to \textit{E. histolytica}, enhancing its adherence to enterocyte via galactose inhibitable lectin, and then activating macrophages to kill ameba though the release of NO, so that TNF blocking could be harmful, increasing amebic virulence. We describe the case of a 46-year-old woman with spondyloarthritis who presented a colonic perforation due to invasive amebic colitis during anti-TNF use.

\copyright 2014 Elsevier Editora Ltda. All rights reserved.

\textbf{Resumo}

O bloqueio do TNF tem tido sucesso no tratamento de algumas doenças reumáticas, como a espondiloartrite. Relatam-se muitas complicações infecciosas com a terapia anti-TNF, principalmente infecções bacterianas, micobacterianas, virais e fúngicas. A \textit{Entamoeba histolytica} é um protozoário extracelular que causa principalmente colite e abscesso hepático, sendo que a perfuração intestinal é uma complicaçã o rara, com alta mortalidade. O TNF é considerado o principal mediador da imunidade celular contra a amebiase.Inicialmente, é quimiotático para a E. histolytica, potencializando sua adesão ao enterócito por meio da lectina galactose-inhibível, e depois ativando os macrófagos para matarem a ameba pela

\textsuperscript{*} The case was originated in Servicio Occidental de Salud, Rheumatology section, Cali, Colombia.
\textsuperscript{#} Corresponding author.
E-mail: jprestrep@lycos.com (J.P. Restrepo).

DOI of original article: \url{http://dx.doi.org/10.1016/j.rbr.2013.09.004}

2255-5021/\copyright 2014 Elsevier Editora Ltda. All rights reserved.
Introduction

TNF (tumoral necrosis factor) is a major cytokine involved in the pathogenesis of rheumatoid arthritis and spondyloarthriti-
s. TNF inhibitors have been showed to be effective in the
treatment of axial and peripheral spondyloarthritis and in
some extraarticular manifestations, however some infectious
complications have been reported. These included bacterial,
mycobacterial, viral and fungal infection. Amoebic infection
has not been described during anti-TNF inhibitor. We describe
a 46-year-old woman with spondyloarthritis who presented a
colonic perforation due to invasive amoebic colitis during anti-
TNF use.

Case report

A 46-year-old female with a previous diagnosis of spondy-
loarthritis based on ASAS criteria,1 who was been treated
with subcutaneous adalimumab 40 mg every other week dur-
ing 4 months and good disease control activity. She presented
diffuse abdominal pain and mucous diarrhea for 2 weeks.
Physical exam revealed distended abdomen without bowel
sounds and diffuse rebound tenderness, so a diagnosis of
acute peritonitis was done. Laboratory tests gave the fol-
lowing results: leucocyte count: 11,980/mm³ with 73% of neutrophils,
hemoglobin: 9.6 g/dL, CRP: 55 mg/L. Emergency laparotomy
showed multiple and small colonic perforations and severe
peritonitis; right hemicolecctomy, mucous fistula of ileon
and intraperitoneal drainage were performed. Metronidazole,
erapenem, teclozan were administered during her hospital-
ization in intensive care unit. Histopathological examination
of the resected gut revealed extensive areas of ulceration with
abundant trophozoites of E histolytica (Figs. 1 and 2). One
month later the patient was discharged without other com-
plication. At this time the patient is being medicated with
naproxen 250 mg BID with partial response, while ileostomy
closure is done to resume adalimumab.

Discussion

Entamoeba histolytica is an extracellular protozoan para-
site that causes mainly colitis and hepatic abscess and it is
responsible of 100.000 deaths worldwide every year. Bowel perfor-
ation occurs between 1%-6% of the patients with amebiasis
but its mortality is extremely high ranging from 55% to 100%.2

TNF plays an important role in the pathogenesis of parasitic infection14 and it is considered the principal medi-
ator of cell immunity against amebiasis. Gamma interferon,
colony-stimulating factor 1 act synergistically with TNF in
macrophage activation using a murine mode.5 TNF produced
by macrophages can kill E histolytica in vitro.6

Oppositely, Blasquez et al demonstrated that TNF
can enhance amebic virulence and is chemotactic for E
histolytica.7 Amebic adherence to colonic mucosa is medi-
ated by galactose inhibitable lectin8 which is a potent stimulant of TNF production. Nitric oxid (NO) is a major
effector molecule produced by activated macrophages for
in vitro toxicity against E histolytica trophozoites and its
production is increased by TNF.9 Macrophages isolated from
amoebic liver granulomas are defective for the production of

Figure 1 – Histological examination of the resected colon
demonstrated extensive mucosal ulceration.

Figure 2 – High power view of trophozoites of E histolytica
in right colon (40×).
TNF, NO, H$_2$O$_2$. Finally anti-TNF antibodies inhibit TNF release, NO production, and amebicidal activity by activated murine macrophages.

In conclusion TNF has a dual role, initially is chemotactic to E histolytica, enhancing its adherence to enterocyte via galactose inhibitable lectin and then activating macrophages to kill ameba though the release NO so that TNF blocking could be harmful increasing amebic virulence. From our knowledge this is the first case of colonic perforation due to invasive amebic colitis during anti-TNF therapy. We recommend deworming against E histolytica in endemic areas prior the beginning of anti-TNF therapy and regularly during its use.

**REFERENCES**