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Listeria endocarditis in a patient with psoriatic arthritis on infliximab: Are biologic agents as treatment for inflammatory arthritis increasing the incidence of *Listeria* infections?

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Summary

The use of anti-tumor necrosis factor agents such as infliximab as treatment modalities of inflammatory joint diseases has widely spread over the past few years. However, increasing numbers of reports of infectious complications during TNF-a blockade have also highlighted the fact that an increased rate of sometimes life-threatening complications may be the price paid for superior therapeutic efficacy. We report the first case report of *Listeria* endocarditis associated with infliximab use and the second published case of *Listeria* infection associated with infliximab in patients with psoriatic arthritis. We also summarize the literature regarding the association of *Listeria* infection with use of infliximab. Further studies are needed to elucidate the contribution of anti-TNF-a therapy to development of listeriosis. Physicians should be aware of the possibility of *Listeria* infection in individuals receiving anti-TNF therapy.

Keywords

Listeria; Infliximab; Endocarditis

Introduction

The treatment of inflammatory joint diseases has changed dramatically over the past few years with the introduction of anti-tumor necrosis factor agents such as infliximab (Remicade®, Centocor), etanercept (Enbrel®, Wyeth) and adalimumab (Humira®, Abbott). Infliximab is a human/murine chimeric monoclonal antibody directed against tumor necrosis factor-alpha (TNF-α). TNF-a is a critical component of the host immune response, and anti-TNF therapy therefore increases in the rate of sometimes life-threatening complications,

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Ethical approval

Yes.

Conflict of interest statement

None.

including *Listeria* infection. However, the reported rate of listeriosis in patients who use infliximab is likely to be an underestimate of the incidence rate due to underreporting of *Listeria* infections. Except for the Food and Drug Administration (FDA) Adverse Event Reporting System (AERS) database, there are no reviews, to our knowledge, summarizing the available published scientific evidence regarding listeriosis induced by TNF-a inhibitors and more specifically infliximab. Herein, we report a case of *Listeria* endocarditis associated with infliximab use in a patient with psoriatic arthritis. We also review the literature regarding the association of infliximab with *Listeria* infection.

Methods

All previous cases included in our literature review were found using a PubMed search (1990–October 2009) of the English-language medical literature applying the terms "infliximab" and "*Listeria*". The references cited in these articles were examined to identify additional reports. We have also extrapolated available data (type of infection, mortality, age, sex) regarding cases of *Listeria* infections associated with use of infliximab from the Food and Drug Administration (FDA) Adverse Event Reporting System (AERS) database.

Case report

A 42 year old female with a history of psoriatic arthritis being treated with infliximab for the past 6 months, presented with one month history of fever, night sweats, anorexia, arthralgias and generalized malaise. She also complained of intermittent chest pressure during the peak temperature spikes. She had received 5 monthly infusions of infliximab in the dosage of 5 mg/kg at the time of presentation and reported considerable relief of her arthritic and skin symptoms. Prior to being started on infliximab she had been treated with methotrexate, etanercept and adalimumab, with incomplete clearance of skin lesions and persistent arthralgias. On presentation the patient was afebrile, with an unremarkable physical examination except for chronic changes of psoriatic arthritis. A white blood cell count was 9200 cells/mm^3 with 74% polymorphonuclear cells and other laboratory data were unremarkable with the exception of mildly elevated troponin I with otherwise normal cardiac enzymes. An EKG revealed sinus rhythm with non specific ST-T changes. Blood cultures were positive for *Listeria monocytogenes*. Whole body imaging with computed tomography scans failed to show any evidence of focal abscess formation. However, a computed tomography of the chest with intravenous contrast revealed localized infarction of the inter-ventricular septal wall (Fig. 1). A transthoracic echocardiogram showed presence of normal ejection fraction with anterior and septal wall motion abnormality. A transesophageal echocardiogram showed a hypokinetic anterior myocardial septum and vegetations on the aortic valve. A cardiac magnetic resonance imaging was also performed to evaluate for myopericarditis, which showed evidence of an acute infarct in the subendocardial region of the septal wall of the left ventricle and wall motion abnormalities (Fig. 2).

During her hospitalization, the patient made a quick recovery with resolution of her symptoms with initiation of intravenous high dose ampicillin 2 gm i.v q 4 h and was discharged to complete a 6 week course of antibiotic therapy. At follow up she continues to do well with resolution of all symptoms and negative blood cultures while a repeat

computed tomography of the chest revealed resolution of the aforementioned lesions (Fig. 3).

Results

We identified 92 cases of *L. monocytogenes* infections related to infliximab treatment in the Food and Drug Administration (FDA) Adverse Event Reporting System (AERS) database.[1] *Listeria* infections reported included meningitis in 69 cases (75%), sepsis in 20 cases (21.7%) and listeriosis in 3 cases (3.3%).[1] In 14/69 (20.3%) cases of meningitis there was also encephalitis and in 4/69 (5.8%) cases there was also coexistent listeriosis and sepsis. Among cases with available data, 51.7% were female and the average age was 48.6 years (range 12–80). Mortality was 17.4% (16/92 cases) and 15/16 (93.8%) of the fatalities had meningitis and one had sepsis. However, no further information was available regarding most of these 92 cases from the FDA AERS database.

We further identified 33 cases of *L. monocytogenes* infection related to infliximab treatment that have been published to date (Table 1).[2–20] Nine cases were excluded due to non-English language[2,5–7,9,12,14–16]and we included 24 cases in our review (Table 1). *Listeria* infections related with infliximab presented as meningitis in 14 cases (58.3%)[3,11,13,17–21]isolated bacteremia in 6 cases (25%),[4,8,10,20] cholecystitis with associated bacteremia in 2 cases[10,20] and septic arthritis in 2 cases.[10,20] Thirteen patients (54.2%)[10,17,20,21] had rheumatoid arthritis, 10 (41.7%) patients had Crohn's disease[8,20,4,11,13,19] and only one case of *Listeria* meningitis closely related to infliximab therapy has been reported in a patient with psoriatic arthritis.[18] With the exception of two cases of *Listeria* infection occurring after the sixth dose of infliximab,[4,10] the average number of infliximab doses prior to the *Listeria* infection was 2.5 (data from 21 available cases). These results are consistent with the data from the FDA AERS report where *Listeria* infections occurred early after the initiation of the therapy, with a median number of doses received of 2.5.[1,20] The most serious infections after infliximab treatment occur after three or fewer infusions.[20] In clinical studies there seemed to be no correlation between the number of infusions and the rate of infectious events.[22]Almost all of the reported patients were also concomitantly taking other immunosuppressive therapies including corticosteroids, azathioprine or 6-mercaptopurine.[8,11,17,20]

Discussion

Pathogenesis of infliximab induced listeriosis

The mechanism how TNF-a inhibitors such as infliximab predispose to *Listeria* infection is unclear. Infliximab is thought to neutralize the biologic activity of TNF-a by binding to the soluble and transmembrane forms of TNF-a, thereby preventing the interaction of TNF-a with its cellular receptors (TNFRs).[4,8,20] Infliximab binds and clears soluble TNF-α, thereby neutralizing its proinflammatory effects. It also binds to cell-bound TNF-α on macrophages and T cells, which interferes with direct cell-to-cell interactions and facilitates their destruction. Although host resistance to infection with *L. monocytogenes* is complex and likely involves multiple cell types,[23] TNF-a is critical in host defense against *Listeria*. The presence of this cytokine and its type I receptor, p55, seems to be critical for resistance

against primary infection by this intracellular pathogen.[23] TNF-a is produced within minutes of infection and its serum levels increase in parallel to the bacterial load, peaking before host death.[23] Animal studies have demonstrated that treatment with anti-TNF-a, both before or during *Listeria* infection resulted in premature host death with large numbers of bacterial copies per cell.[24,25] Moreover, TNF-α-deficient mice were highly susceptible to *Listeria* infection.[26] Anti-TNF-a therapy abolishes the activation of different cell lines including monocytes, macrophages, T lymphocytes and neutrophils.[23] Metalloproteinases have also been implicated in the modulation the immune response against *Listeria* infection.[27] The dysregulation of matrix metalloproteinases, produced by TNF-a blockers, has been linked to several infectious diseases, including bacterial meningitis, endotoxic shock, mycobacterial infection, and hepatitis B and human immunodeficiency virus (HIV) infection.[28] Effective therapy with anti-TNF-a in patients with psoriatic arthritis is associated with decreased levels of metalloproteinases and angiogenic cytokines in the sera and skin lesions.[29] Conclusively, further studies are needed to elucidate the mechanism of how infliximab may predispose to development of serious infections including *Listeria* infection.

Incidence of infections in infliximab treated patients

The treatment of inflammatory joint diseases has changed dramatically over the past few years with the introduction of anti-tumor necrosis factor agents. Anti-TNF-a is an emerging as well as a promising therapy in refractory rheumatoid arthritis, inflammatory bowel diseases such as active Crohn's disease, spondyloarthropathies such as psoriatic arthritis and ankylosing spondylitis.[30] One of these currently available agents is infliximab (Remicade®, Centocor) which is a human/murine chimeric monoclonal antibody directed against tumor necrosis factor-alpha (TNF-α). TNF-a plays an important role in host resistance against various microorganisms, particularly those that are intracellular,[4,8,20] and increasing number of reports indicate that sometimes life-threatening infections, including opportunistic infections, can be a high price to pay for these therapeutic options.[31,32] Although the incidence of opportunistic infections with use of infliximab is extremely low (Category C and D evidence),[32] infections whose containment is macrophage dependent, such as listeriosis, histoplasmosis or coccidiomycosis have been reported.[32]

In clinical studies the rate of serious infections after anti-TNF-a therapy ranged from 2 to 6.4%.[10,33–36] A meta-analysis showed an increased risk of serious infections in patients with rheumatoid arthritis treated with anti-TNF antibody therapy (pooled odds ratio for serious infection was 2.0; 95% CI, 1.3–3.1).[31] Pooled data from all Centocor sponsored clinical trials, involving 2292 patients, showed comparable death rates among placebo and infliximab treated patients (2% and 1%, respectively) and similar occurrence of serious infections.[37] A registry study (RABBIT) of German patients receiving anti-TNF therapy for rheumatoid arthritis found an increased risk of infection among patients treated with any biologic agents, but that addition of anti-TNF inhibitors further increased the risk after adjusting for other predictive factors of infection risk, including patient age and disease severity.[33]In a large retrospective study of 709 patients with rheumatoid arthritis, the incidence of serious infections in patients treated with TNF-a blockers was three times higher than controls[38] in contrast to placebo-controlled trials.[20,39,40] Discrepancies between different clinical trials[20,39,40] and meta-analyses[31] may be explained by the difference in

selection criteria of patients, lack of long term follow up in all studies, differences in sample size and rarity of infections.

However, the experience with infliximab remains limited in other rheumatic diseases such as psoriatic arthritis.

In contrast to patients with rheumatoid arthritis, there does not appear to be an increased rate of infections among patients with psoriatic arthritis receiving anti-TNF therapy. In a meta-analysis of randomized controlled trials assessing the risks and benefits of tumor necrosis factor-alpha inhibitors in the management of psoriatic arthritis,[41] there were no significant differences between TNF-a inhibitors and placebo in the proportions of patients experiencing serious adverse events (RR 0.98, 95% CI 0.55–1.77), or upper respiratory tract infections (RR 0.91, 95% CI 0.65–1.28). In two randomized, double-blind, placebo-controlled trials in patients with psoriatic arthritis treated with infliximab—the IMPACT (Infliximab Multinational Psoriatic Arthritis Controlled Trial)[42] and the IMPACT II[43,44] the investigators found no significant differences in the numbers or types of adverse events reported in infliximab treatment or placebo groups. In IMPACT I, 104 patients with psoriatic arthritis were followed for one year after starting treatment with infliximab, and the study failed to prove any difference in the incidence of infections between the infliximab treated and the placebo treated group.[45] In the 2 year follow up of the IMPACT study again there was no difference in the incidence of infections between the infliximab treated and the placebo group.[46]The IMPACT II study evaluated the safety of infliximab after 1 year of treatment in 200 patients with psoriatic arthritis. No difference in the incidence of infections between the infliximab, the infliximab plus methotrexate and the placebo group was found. [44] No reports of tuberculosis or opportunistic infection were reported in both IMPACT studies. Thus, although meta-analyses and controlled clinical trials have shown an increase in the incidence of serious infections in patients with rheumatoid arthritis treated with TNF-a blockers, there is limited experience with the use of infliximab in patients with psoriatic arthritis. One meta-analysis[41] and 2 randomized controlled trials[42–44] have shown that infliximab does not increase the incidence of infections between the infliximab treated patients with psoriatic arthritis and the placebo group. This may represent differences in the immunopathogenesis between different inflammatory disorders including psoriatic and rheumatoid arthritis. However, any comparison of data between different studies is very difficult in the setting of lack of long term controlled studies and is an important area for future research to assess the long term risk—benefit profile of these biological agents in treatment of inflammatory conditions including psoriatic arthritis.

Infliximab and listeriosis

Listeria infection is an opportunistic infection that has been reported in patients who undergo treatment with anti-TNF-a therapy. A confounding factor that may make comparison of the incidence of listeriosis between different studies difficult is the extent to which other immunomodulating drugs influence susceptibility to serious infections in patients on infliximab.[11] Reports from the AERS suggest that the number of patients with *Listeria* may be higher than those reported by post-marketing. Patients with predisposing conditions, such as older age (>75 years), pregnancy, diabetes mellitus, immune suppression,

liver failure, HIV infection, splenectomy may have an incidence of listeriosis as high as 210 cases per 100,000 (as compared with 0.7 per 100,000 cases in healthy individuals), and mortality that can reach 30%.[47]The estimated annual rate of reports to the FDA of listeriosis in infliximab-treated patients is greater than the FoodNet (the principal foodborne disease component of the Centers for Disease Control and Prevention Emerging Infections Program)-derived annual incidence rate of listeriosis.[17,20,21] There have been twice as many cases of serious *Listeria* infections in patients with rheumatoid arthritis treated with anti-TNF-α compared with patients with Crohn's disease. Infliximab-linked *Listeria* infections have also been reported in patients with ulcerative colitis, psoriatic arthritis and juvenile rheumatoid arthritis.[18,20]

However, *Listeria* endocarditis, a rare complication of bacteremia due to *Listeria*,[48] associated with use of infliximab has not been previously described, to our knowledge. According to the modified Duke criteria for endocarditis,[48] our patient had a major diagnostic criterion for endocarditis (presence of vegetation on echocardiogram) and 3 minor criteria (vascular pheonomena/septic emboli in coronary arterioles with subendothelial infarct, history of fever, and positive blood cultures for an atypical organism). This is also the second published case of *Listeria* infection associated with infliximab in patients with psoriatic arthritis. A unique feature of this case is that it was associated with use of infliximab without the simultaneous use of other immunosuppressive agents. However, underlying psoriatic arthritis would also increase her risk for a *Listeria* infection by impairing T lymphocyte/macrophage—mediated cellular immunity. It is not clear whether *Listeria* infections originate from ingestion of contaminated food or from chronic fecal carriage in these immunocompromised patients. A possible dietary source for the *Listeria* was identified in our patient since she admitted ingestion of soft cheeses and dairy products. Ingestion could have occurred up to 70 days prior to admission. Anti-TNF-a therapy may be a significant risk factor for the development of listeriosis, although most of the patients are immunocompromised due both to their chronic inflammatory illness and concurrent immune suppressive therapy. Patients starting infliximab therapy should be warned to avoid soft cheeses, non-pasteurized dairy products and undercooked meats during therapy, and physicians should be aware of the possibility of *Listeria* infection in such individuals. Early recognition of *Listeria* infection as a potential complication of treatment with TNF-a-neutralizing agents may decrease the high morbidity and mortality associated with this disease.

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References

1. http://www.fdable.com/aers/query/972d415847bf/7 [last visited 1/20/2010]. http://wwwfdablecom/aers/query/972d415847bf/7 [last visited 1/20/2010], 2010.
2. Yamamoto M, Takahashi H, Miyamoto C, et al. A case in which the subject was affected by Listeria meningoencephalitis during administration of infliximab for steroid-dependent adult onset Still's disease. Nihon Rinsho Meneki Gakkai Kaishi 2006;29(3):160–8. [PubMed: 16819265]

3. Williams G, Khan AA, Schweiger F. *Listeria* meningitis complicating infliximab treatment for Crohn's disease. Can J Infect Dis Med Microbiol 2005;16(5):289–92. [PubMed: 18159561]
4. Tweezer-Zaks N, Shiloach E, Spivak A, Rapoport M, Novis B, Langevitz P. Listeria monocytogenes sepsis in patients treated with anti-tumor necrosis factor-alpha. Isr Med Assoc J 2003; 5(11):829–30. [PubMed: 14650115]
5. Soderlin M, Blomkvist C, Dahl P, Forsberg P, Fohlman J. Increased risk of infection with biological immunomodifying antirheumatic agents. Clear guidelines are necessary as shown by case reports. Lakartidningen 2005;102(49):3794–800. [PubMed: 16408703]
6. Ramanampamonjy RM, Laharie D, Bonnefoy B, Vergniol J, Amouretti M. Infliximab therapy in Crohn's disease complicated by Listeria monocytogenes meningoencephalitis. Gastroenterol Clin Biol 2006;30(1):157–8. [PubMed: 16514404]
7. Osuna MR, Ferrer RT, Gallego GR, Ramos LM, Ynfante FM, Figueruela LB. Listeria meningitis as complication of treatment with infliximab in a patient with Crohn's disease. Rev Esp Enferm Dig 2006;98(1):60–1. [PubMed: 16555939]
8. Morelli J, Wilson FA. Does administration of infliximab increase susceptibility to listeriosis? Am JGastroenterol 2000;95(3):841–2. [PubMed: 10710107]
9. Keulen ET, Mebis J, Erdkamp FL, Peters FP. Meningitis due to Listeria monocytogenes as a complication of infliximab therapy. Ned Tijdschr Geneeskd 2003;147(43):2145. [PubMed: 14619208]
10. Kesteman T, Yombi JC, Gigi J, Durez P. Listeria infections associated with infliximab: case reports. Clin Rheumatol 2007; 26(12):2173–5. [PubMed: 17579802]
11. Kamath BM, Mamula P, Baldassano RN, Markowitz JE. *Listeria* meningitis after treatment with infliximab. J Pediatr Gastroenterol Nutr 2002;34(4):410–2. [PubMed: 11930099]
12. Joosten AA, van Olffen GH, Hageman G. Meningitis due to Listeria monocytogenes as a complication of infliximab therapy. Ned Tijdschr Geneeskd 2003;147(30):1470–2. [PubMed: 12908351]
13. Izbeki F, Nagy F, Szepes Z, Kiss I, Lonovics J, Molnar T. Severe Listeria meningoencephalitis in an infliximab-treated patient with Crohn's disease. Inflamm Bowel Dis 2008;14(3):429–31. [PubMed: 17973302]
14. Dederichs F, Pinciu F, Gerhard H, Eveld K, Stallmach A. Listeria meningitis in a patient with Crohn's disease—a seldom, but clinically relevant adverse event of therapy with infliximab. Z Gastroenterol 2006;44(8):657–60. [PubMed: 16902896]
15. de la Fuente PB, Marco PA, Riera MA, Boadas MJ. Sepsis caused by Listeria monocytogenes related with the use of infliximab. Med Clin (Barc) 2005;124(10):398.
16. Cabades OF, Vila FV, Arnal BM, Polo Sanchez JA. Lysteria encephalitis associated to infliximab administration. Rev Clin Esp 2005;205(5):250.
17. Bowie VL, Snella KA, Gopalachar AS, Bharadwaj P. *Listeria* meningitis associated with infliximab. Ann Pharmacother 2004;38(1):58–61. [PubMed: 14742795]
18. Aparicio AG, Munoz-Fernandez S, Bonilla G, Miralles A, Cerdeno V, Martin-Mola E. Report of an additional case of anti-tumor necrosis factor therapy and Listeria monocytogenes infection: comment on the letter by Gluck et al. Arthritis Rheum 2003;48(6):1764–5.
19. Ljung T, Karlen P, Schmidt D, et al. Infliximab in inflammatory bowel disease: clinical outcome in a population based cohort from Stockholm county. Gut 2004;53(6):849–53. [PubMed: 15138212]
20. Slifman NR, Gershon SK, Lee JH, Edwards ET, Braun MM. *Listeria monocytogenes* infection as a complication of treatment with tumor necrosis factor alpha-neutralizing agents. Arthritis Rheum 2003;48(2):319–24. [PubMed: 12571839]
21. Gluck T, Linde HJ, Scholmerich J, Muller-Ladner U, Fiehn C, Bohland P. Anti-tumor necrosis factor therapy and *Listeria monocytogenes* infection: report of two cases. Arthritis Rheum 2002;46(8):2255–7. [PubMed: 12209538]
22. Hanauer SB, Feagan BG, Lichtenstein GR, et al. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet 2002;359(9317):1541–9. [PubMed: 12047962]
23. Edelson BT, Unanue ER. Immunity to *Listeria* infection. Curr Opin Immunol 2000;12(4):425–31. [PubMed: 10899025]

24. Pfeffer K, Matsuyama T, Kundig TM, et al. Mice deficient for the 55 kd tumor necrosis factor receptor are resistant to endotoxic shock, yet succumb to L. monocytogenes infection. Cell 1993; 73(3):457–67. [PubMed: 8387893]
25. Rothe J, Lesslauer W, Lotscher H, et al. Mice lacking the tumour necrosis factor receptor 1 are resistant to TNF-mediated toxicity but highly susceptible to infection by Listeria monocytogenes. Nature 1993;364(6440):798–802. [PubMed: 8395024]
26. Mizuki M, Nakane A, Sekikawa K, Tagawa YI, Iwakura Y. Comparison of host resistance to primary and secondary *Listeria monocytogenes* infections in mice by intranasal and intravenous routes. Infect Immun 2002;70(9):4805–11. [PubMed: 12183523]
27. Bitar AP, Cao M, Marquis H. The metalloprotease of *Listeria monocytogenes* is activated by intramolecular autocatalysis. J Bacteriol 2008;190(1):107–11. [PubMed: 17965168]
28. Elkington PT, O'Kane CM, Friedland JS. The paradox of matrix metalloproteinases in infectious disease. Clin Exp Immunol 2005;142(1):12–20. [PubMed: 16178851]
29. Cordiali-Fei P, Trento E, D'Agosto G, et al. Decreased levels of metalloproteinase-9 and angiogenic factors in skin lesions of patients with psoriatic arthritis after therapy with anti-TNF-alpha. J Autoimmune Dis 2006;3:5. [PubMed: 17022813]
30. Schluter D, Deckert M. The divergent role of tumor necrosis factor receptors in infectious diseases. Microbes Infect 2000; 2(10):1285–92. [PubMed: 11008118]
31. Bongartz T, Sutton AJ, Sweeting MJ, Buchan I, Matteson EL, Montori V. Anti-TNF antibody therapy in rheumatoid arthritis and the risk of serious infections and malignancies: systematic review and meta-analysis of rare harmful effects in randomized controlled trials. JAMA 2006;295(19):2275–85. [PubMed: 16705109]
32. Wallis RS, Broder MS, Wong JY, Hanson ME, Beenhouwer DO. Granulomatous infectious diseases associated with tumor necrosis factor antagonists. Clin Infect Dis 2004;38(9):1261–5. [PubMed: 15127338]
33. Listing J, Strangfeld A, Kary S, et al. Infections in patients with rheumatoid arthritis treated with biologic agents. Arthritis Rheum 2005;52(11):3403–12. [PubMed: 16255017]
34. Salliot C, Gossec L, Ruyssen-Witrand A, et al. Infections during tumour necrosis factor-alpha blocker therapy for rheumatic diseases in daily practice: a systematic retrospective study of 709 patients. Rheumatology (Oxford) 2007;46(2):327–34. [PubMed: 16880188]
35. Furst DE, Breedveld FC, Kalden JR, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases. Ann Rheum Dis 2006;65(Suppl. 3):iii2–15. [PubMed: 17038465]
36. Kroesen S, Widmer AF, Tyndall A, Hasler P. Serious bacterial infections in patients with rheumatoid arthritis under anti-TNF-alpha therapy. Rheumatology (Oxford) 2003;42(5): 617–21. [PubMed: 12709536]
37. Stamm AM, Smith SH, Kirklin JK, McGiffin DC. Listerial myocarditis in cardiac transplantation. Rev Infect Dis 1990;12(5): 820–3. [PubMed: 2237124]
38. Giunta G, Piazza I. Fatal septicaemia due to *Listeria monocytogenes* in a patient with systemic lupus erythematosus receiving cyclosporin and high prednisone doses. Neth J Med 1992;40(3–4):197–9. [PubMed: 1603211]
39. Moreland LW, Cohen SB, Baumgartner SW, et al. Long-term safety and efficacy of etanercept in patients with rheumatoid arthritis. J Rheumatol 2001;28(6):1238–44. [PubMed: 11409115]
40. van de Putte LB, Atkins C, Malaise M, et al. Efficacy and safety of adalimumab as monotherapy in patients with rheumatoid arthritis for whom previous disease modifying antirheumatic drug treatment has failed. Ann Rheum Dis 2004;63(5):508–16. [PubMed: 15082480]
41. Saad AA, Symmons DP, Noyce PR, Ashcroft DM. Risks and benefits of tumor necrosis factor-alpha inhibitors in the management of psoriatic arthritis: systematic review and meta-analysis of randomized controlled trials. J Rheumatol 2008;35(5):883–90. [PubMed: 18381787]
42. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30(2):239–45. [PubMed: 7249508]
43. Antoni C, Krueger GG, de VK, et al. Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. Ann Rheum Dis 2005;64(8):1150–7. [PubMed: 15677701]

44. Kavanaugh A, Krueger GG, Beutler A, et al. Infliximab maintains a high degree of clinical response in patients with active psoriatic arthritis through 1 year of treatment: results from the IMPACT 2 trial. Ann Rheum Dis 2007;66(4):498–505. [PubMed: 17114188]

45. Antoni CE, Kavanaugh A, Kirkham B, et al. Sustained benefits of infliximab therapy for dermatologic and articular manifestations of psoriatic arthritis: results from the infliximab multinational psoriatic arthritis controlled trial (IMPACT). Arthritis Rheum 2005;52(4):1227–36. [PubMed: 15818699]

46. Antoni CE, Kavanaugh A, van der HD, et al. Two-year efficacy and safety of infliximab treatment in patients with active psoriatic arthritis: findings of the infliximab multinational psoriatic arthritis controlled trial (IMPACT). J Rheumatol 2008;35(5):869–76. [PubMed: 18381786]

47. Southwick FS, Purich DL. Intracellular pathogenesis of listeriosis. N Engl J Med 1996;334(12):770–6. [PubMed: 8592552]

48. Fernandez Guerrero ML, Rivas P, Rabago R, Nunez A, de GM, Martinell J. Prosthetic valve endocarditis due to *Listeria monocytogenes*. Report of two cases and reviews. Int J Infect Dis 2004;8(2):97–102. [PubMed: 14732327]

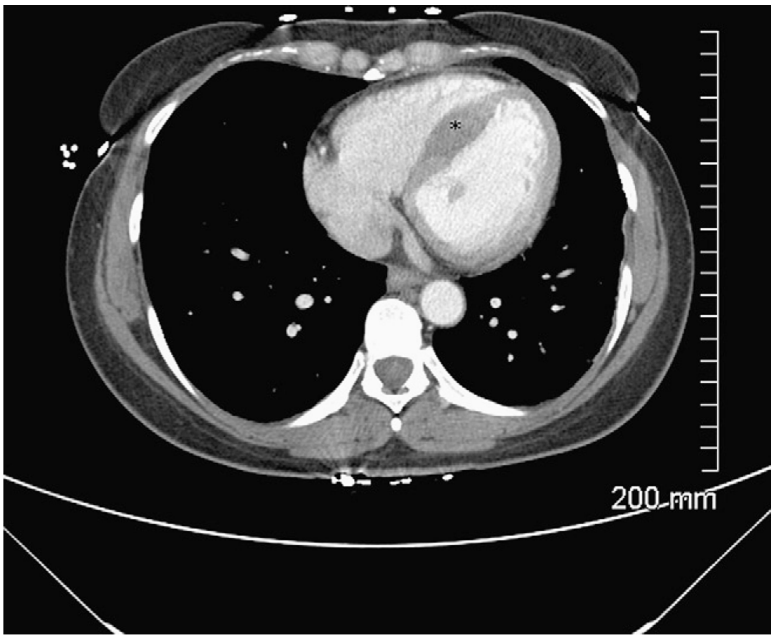

Figure 1.
Computed tomography of the chest with intravenous contrast showing septal infarction (asterisk).

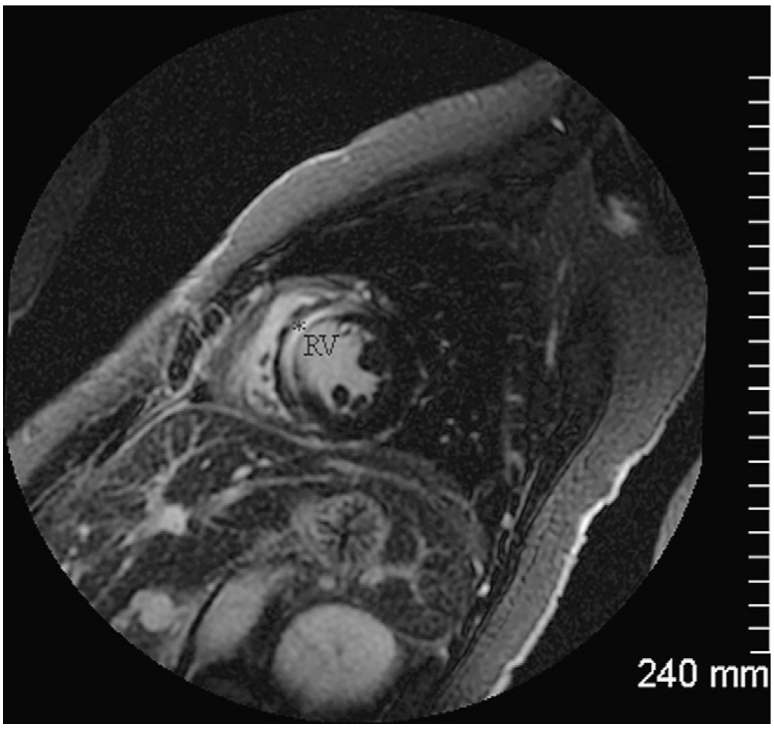

Figure 2.

Cardiac magnetic resonance imaging shows evidence of late gadolinium enhancement (asterisk) confined to the subendocardial portion of the septal myocardial wall of the right ventricle (RV) on inversion recovery images in the short-axis plane indicating myocardial damage.

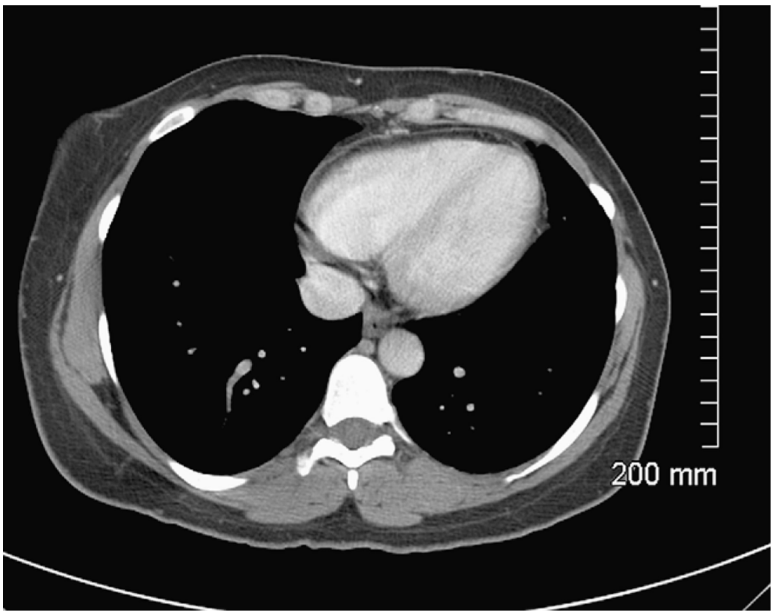

Figure 3.
Computed tomography of the chest with intravenous contrast showing resolution of septal infarction after treatment.

Table 1

Cases of Listeria infections associated with infliximab use.

Author	Year	Country	Age	Sex	Type of infection	Symptoms	Isolation of L. mono cytogenes	Underlying disease	Doses of infliximab	Concomitant drugs	Treatment	Outcome	Comments
Morelli et al[8]	2000	USA	67	M	Bacteremia	Fever, diarrhea, lethargy, weakness	Blood	Crohn's disease	3 (4 days after 3rd infusion)	Prednisone, AZA, 5-ASA	Broad spectrum antibiotics for 4 days (NR) and then augmentin for 2 weeks	Recovered	Ingestion of processed meat the week prior to the admission
Gluck et al[21]	2002	Germany	60	F	Bacteremia, cholecystitis meningoencephalitis	Fever, abdominal pain	Swab culture from the gallbladder obtained during surgery and a blood culture	Rheumatoid arthritis	6 (14 days after 6th dose)	Methotrexate, cyclosporin A, prednisolone	Cefriaxone, metronidazole	Death	Food NR
Gluck et al[21]	2002	Germany	62	F	Bacteremia, cholecystitis, brain abscess	Fever, abdominal pain and later hemiparesis, aphasia	Blood	Rheumatoid arthritis	2 (14 days after 2th dose)	Methotrexate	Ampicillin and gentamicin for a total of 18 weeks	Slow improvement of the neurologic symptoms	Food NR
Kamath et al[11]	2002	USA	17	F	Bacteremia/ meningitis	Fever, headache, malaise, abdominal pain	Blood, CSF culture negative (done 4 days on antibiotics)	Crohn's disease	1 (3 days after infusion)	Methylpredn isolone, 6-MP, 5-ASA	Ampicillin and cotrimoxazole for 6 weeks	Prolonged hospital course but fully recovered	Patient denied eating any suspicious food before symptoms
Aparicio et al[18]	2003	Spain	57	M	Meningitis	Headache, fever, confusion, vomiting	CSF	Psoriatic arthritis	6 (one month after 6th infusion)	Methotrexate, Prednisone	Ampicillin (duration NR)	Recovered	Food NR
Slifman et al (surveillance study)[20]	2003	USA, Canada, Sweden, Italy, Germany, France, Norway	Median age 69.5 years (range 17–80 years)	53% F (8/15)	Sepsis, meningitis, septic joint	NR	CSF, blood	9 patients with RA and 5 patients with Crohn's, one patient no data reported. 3 of thesecases have already been described in	Median number of doses was 2.5 (range 1–6).	All patients were on steroids. Of the 9 patients with RA, 7 were reported as receiving concomitant methotrexate, and 1 was receiving cyclosporine (in addition to methotrexate). Of	NR	5 deaths	Only one patient[7] was reported as having ingested processed meat in the week preceding the

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								the literature[7,10,20]		the 5 patients with CD, 1 was receiving mercaptopurine only, 2 were receiving mercaptopurine plus mesalamine, and 2 were receiving azathioprine plus mesalamine.			diagnosis of listeriosis.
Slifman et al[20]	2003	Canada	64	F	Blood	NR	Blood	Crohn's disease	1	Prednisone, 6-MP	NR	Recovered	NR
Slifman et al[20]	2003	Sweden	39	F	Blood/ meningitis	NR	Blood, CSF	Crohn's disease	3	Prednisone, 6-MP, 5-ASA	NR	Recovered, paralysis of one eye	NR
Slifman et al[20]	2003	Italy	20	M	Meningitis	NR	CSF	Crohn's disease	1	Methylpredn isolone, AZA, 5-ASA	NR	Death	NR
Slifman et al[20]	2003	USA	80	M	Blood/ meningitis	NR	Blood, CSF	RA	2	Prednisone	NR	Death	NR
Slifman et al[20]	2003	USA	74	F	Meningitis	NR	CSF	RA	6	Prednisone	NR	Death	NR
Slifman et al[20]	2003	USA	78	M	Meningitis	NR	CSF	RA	3	Methotrexate	NR	Remained comatose at time of report	NR
Slifman et al[20]	2003	USA	73	F	Blood, possible meningitis	NR	Blood	RA	2	Prednisone, methotrexate, nycophenolate mofetil	NR	Death	NR
Slifman et al[20]	2003	USA	74	F	Blood	NR	Blood	RA	5	Prednisone, methotrexate, hydroxychloroquine	NR	Recovered	NR
Slifman et al[20]	2003	USA	73	M	Meningitis	NR	CSF	RA	NR	Prednisone, methotrexate, leflunomide	NR	NR	NR
Slifman et al[20]	2003	Canada	60	M	Blood	NR	Blood	RA	2	Methotrexate	NR	NR	NR
Slifman et al[20]	2003	France	NR	F	Septic joint	NR	Synovial fluid	RA	NR	NR	NR	NR	NR

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Tweezer-Zaks et al[3]	2003	Israel	48	M	Blood, splenic abscess	Fever, rigors, headache	Blood	Crohn's disease	1 (9 days after infusion)	NR	Ampicillin, gentamycin and mertonidazole (duration NR)	Recovered	NR
Tweezer-Zaks et al[4]	2003	Israel	55	F	Blood	Fever, chills, malaise, mild dysuria	Blood	Crohn's disease	2 year history of infliximab use (2 weeks after last infusion)	Prednisone, methotrexate	Ampicillin, gentamycin (duration NR)	Recovered	NR
Ljung et al[19]	2004	Sweden	NR	NR	Meningitis	NR	CSF	Crohn's disease	NR	NR	NR	Recovered	NR
Bowie et al[17]	2004	USA	73	M	Meningitis	Decreased level of consciousness, headache, nausea, vomiting, and diarrhea for 3 days	CSF culture, blood	Rheumatoid arthritis	2 (3 weeks prior to symptoms)	Prednisone, methotrexate	Ampicillin for 21 days	Recovered	No change in food habits
Williams et al[3]	2005	Canada	37	M	Meningitis	Fever, tachycardia, diaphoresis, confusion	Blood cultures, CSF culture	Crohn's disease	2 (6 days after second infusion)	Prednisone, AZA, 5-ASA	Iv ampicillin and gentamicin, later switched to iv ampicillin and trimethoprime sulfamethoxazole for a total of three weeks	Recovered	NR
Kesteman at al[10]	2007	Belgium	52	F	Terminal ileitis and bacteremia	Fever, abdominal pain, diarrhea	Blood	Rheumatoid arthritis	3 (one week after infusion)	Prendisone, nethotrexate	sulfamethoxaz oletrimethoprim and gentamicin IVand then PO sulfamethoxaz oletrimethoprim for a total of 30 days	Recovered	
Kesteman at al[10]	2007	Belgium	79	M	Bacteremia associated with a prosthetic joint arthritis of the left hip	Fever, leg pain	Blood, intra-articular fluid from the left hip	Rheumatoid arthritis	4 years on infliximab (30 infusions)	Prendisone, nethotrexate	Ampicilliin for 2 weeks initially then ampicillin, rifampicin, gentamicin followed by a surgical arthrocentesis with debridement and combined	Recovered	The patient admitted consumption of soft cheeses some weeks before admission.

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											with a long term antimicrobial treatment with amoxicillin (exact duration NR).		
Izbeki et al[13]	2008	Hungary	50	M	Meningoencephalitis	Fever, headache, neck stiffness,	CSF	Crohn's disease	1 (one day after infusion)	Prednisone, 6-MP	Ampicillin, gentamicin	Residual unilateral weakness of eye movements	NR

Abbreviations: AZA: Azathioprine, CSF: cerebrospinal fluid F: Female, MP: Mercaptopurine, M: male, NR: Not reported, RA: Rheumatoid Arthritis.