American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2021; 22: e929892
DOI: 10.12659/AJCR.929892

Received: 2020.11.16
Accepted: 2021.04.13
Available online: 2021.04.19
Published: 2021.05.25

Pott's Puffy Tumor in an Inflammatory Bowel Disease Patient on Anti-TNF Therapy

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

AE 1,2 Ahmad Miri
EF 3,4 Alice I. Sato
E 5,6 Ryan K. Sewell
AE 1,2 Andrew Huang-Pacheco

1 Department of Pediatric Gastroenterology, Hepatology and Nutrition, University of Nebraska Medical Center, Omaha, NE, U.S.A.
2 Department of Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital and Medical Center, Omaha, NE, U.S.A.
3 Department of Pediatrics Infectious Disease, University of Nebraska Medical Center, Omaha, NE, U.S.A.
4 Department of Pediatrics Infectious Disease, Children's Hospital and Medical Center, Omaha, NE, U.S.A.
5 Department of Otolaryngology – Head and Neck Surgery, University of Nebraska Medical Center, Omaha, NE, U.S.A.
6 Department of Ear, Nose and Throat, Children's Hospital and Medical Center, Omaha, Ne, U.S.A.

Corresponding Author: Ahmad Miri, e-mail: ahmmiri@gmail.com
Conflict of interest: None declared

Patient: Male, 14-year-old
Final Diagnosis: Pott's puffy tumor
Symptoms: Face swelling
Medication: —
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology • Infectious Diseases • Otolaryngology • Pediatrics and Neonatology

Objective: Unusual clinical course

Background: Anti-TNF-α therapies were the first class of biologics to be used in treatment of moderate to severe IBD. Immunosuppression status that develops from using anti-TNF-α therapies increases the risk of serious and opportunistic infections. We present here a rare case of serious infection that developed in an IBD patient while on anti-TNF therapy.

Case Report: Our patient was a 14-year-old boy with a history of chronic sinusitis and ulcerative colitis who had been on infliximab therapy for the last 3 years. He presented with facial swelling and worsening constant frontal headache. Imaging showed frontal scalp subgaleal abscess, mild frontal calvarial early osteomyelitis, bilateral preseptal cellulitis, and acute and chronic paranasal sinus disease. He was treated with intravenous antibiotics and underwent sinus surgery with incision and drainage of the forehead abscess. He recovered well and resumed his infliximab infusions 3 weeks after the surgery.

Conclusions: PPT is a serious complication of untreated sinusitis. IBD patients on biologics can have higher risk of developing such complications because of their decreased ability to fight infections. Although the risk of serious infections declines significantly after the first year of using biologics, physicians should keep a low threshold for investigating symptomatic patients for serious infections, as they require prompt intervention. Despite the potential complications from using biologics, the benefits of this therapy in IBD patients outweigh the risks.

Keywords: Inflammatory Bowel Diseases • Pediatrics • Pott Puffy Tumor • Tumor Necrosis Factor-alpha

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/929892

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Background

Anti-TNF-α therapies were the first class of biologics to be used in treatment of moderate to severe inflammatory bowel disease (IBD) [1]. Immunosuppression status that develops from using anti-TNF-α therapies increases the risk of serious and opportunistic infections. We present here a rare case of serious infection that developed in an IBD patient while on anti-TNF therapy [2]. This case report sheds light on this unusual complicated sinus infection and raises awareness of the need for prompt sinusitis treatment in immunosuppressed patients.

Case Report

The patient was a 14-year-old boy who presented to the Emergency Department with 2 days of worsening constant frontal headache and a 1-day history of forehead swelling. His past medical history was significant for ulcerative colitis diagnosed 5 years ago and he had been receiving infliximab infusions for the past 3 years. In addition to ulcerative colitis, his past medical history was positive for recurrent acute suppurative otitis media, recurrent methicillin-sensitive *Staphylococcus aureus* (MSSA) nasal infection, and episodes of facial cellulitis for the last 3 years. He was seen by his primary care physician 2 weeks prior to presentation, with symptoms of subjective fever, malaise, headache, and mild cough. At that time, a respiratory viral panel was positive for influenza B. His symptoms continued to progress to high-grade fever, chills, and body aches. A physical exam was positive for diffuse forehead swelling extending to the mid-brow, doughy to palpation, with mild tenderness. He had bilateral eyelid edema, nasal vestibule with dried blood and excoriations, nasal septal perforation, and edematous and erythematous nasal mucosa. The initial blood work-up showed elevated c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). The initial non-contrast brain and facial bone computed tomography (CT) scan showed pansinusitis and abnormal density of subcutaneous tissue in the frontal region extending inferiorly to the left, which indicated an inflammatory process with possible developing abscess. Magnetic resonance imaging (MRI) for the brain and orbit with and without contrast was obtained (**Figure 1A, 1B**). It showed frontal scalp subgaleal abscess, mild frontal calvarial restricted diffusion compatible with early osteomyelitis, mild frontal dural enhancement and thickening consistent with meningitis, bilateral preseptal cellulitis, and acute and chronic paranasal sinus disease.

Given his sinus involvement and being immunocompromised, which put him at higher risk for methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas* infections, he was started on broad-spectrum antibiotics (cefepime, vancomycin, and metronidazole) due to the risk of polymicrobial infection. His next infliximab infusion was held during treatment of acute infection and he was started on oral mesalamine.

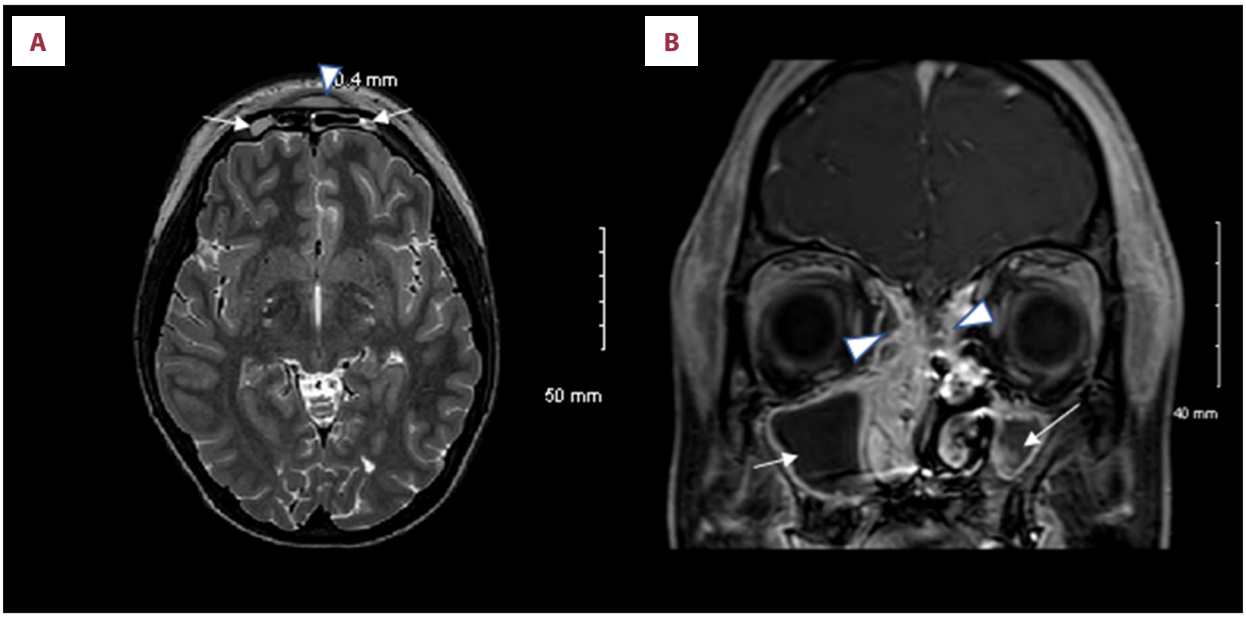

Figure 1. (**A**). Orbit and brain MRI with contrast shows 5×0.8×4 cm of frontal scalp subgaleal rime enhancing fluid collection, showing subgaleal abscess (arrow head) with mild restricted diffusion within the frontal calvarium, compatible with early changes of osteomyelitis. Moderate fluid collection is shown in underlying frontal sinuses (arrows). (**B**) MRI brain and orbit shows fluid throughout maxillary sinuses, with mild mucosal thickening bilaterally (arrows). Fluid and mucosal thickening within ethmoid air cells is shown (arrow heads). The findings show acute and chronic sinusitis.

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

IBD History

The patient had been diagnosed with ulcerative colitis 5 years prior to the current presentation. Histology showed pancolitis. He failed mesalamine and 6-Mercaptopurine (6MP). He had 3 flares in less than 1 year after infliximab induction. His flares were under better control after adding methotrexate to infliximab. He remained asymptomatic despite recurrent positive inflammatory markers for the past year, which were attributed to recurrent sinus, nasal, and ear infections. His methotrexate was tapered off 6 months prior to this presentation.

Hospital Course

The patient underwent bilateral maxillary antrostomy, right total ethmoidectomy, left anterior ethmoidectomy, bilateral frontal sinusotomy, and incision and drainage of Pott's puffy tumor at day 1 of hospital admission. Culture of drainage from the frontal abscess and maxillary sinus showed moderate growth of MRSA and group A *Streptococcus*. Cefepime was stopped and the patient was discharged after improvement on oral metronidazole and i.v. vancomycin. After discharge, CRP normalized 2 weeks after starting treatment with antibiotics. ESR continued to trend down. He finished a total of 7 weeks of antibiotics, with brain and orbit MRI showing resolution of dural enhancement and abscess. Infliximab was resumed 3 weeks after surgery (10 weeks after the last infliximab infusion). His maintenance infliximab infusion plan prior to infection was scheduled every 7 weeks, so his treatment was delayed by 3 weeks. He developed stomach pain and dark stool color 2 weeks after presentation.

Discussion

Pott's puffy tumor (PPT) is a frontal subperiosteal abscess associated with underlying frontal osteomyelitis. It was first described by Sir Percival Pott in 1760 [3]. PPT usually develops after untreated frontal sinusitis, head trauma, surgery in the frontal region, methamphetamine or cocaine abuse, insect bite, mastoiditis, fibrous dysplasia, or dental infections [4,5]. The incidence of PPT decreased after the start of the antibiotic era.

PPT is very rare in young children because the pneumatized frontal sinus above the orbital ridges does not appear until approximately 6 years of age, and it does not develop completely until late adolescence [6]. As in our patient, PPT is seen more frequently in adolescents and young adults. The flow rate of the diploic veins increases during adolescence; these vessels are responsible for draining the mucosa of the frontal sinuses, facilitating the spread of infection to the bones and brain. The infection is also known to spread directly through the sinus wall [7].

Clinical features include headache, swelling in the periorbital or scalp regions, fever, and nasal discharge. Fluctuant swelling in the midline of the forehead is typical [8]. CT scan is the criterion standard for diagnosis of PPT [6], and it usually shows involvement of bone and paranasal sinuses. MRI is more useful in detecting intraorbital or intracranial involvement, leptomeningeal enhancement, small extra-axial collections, bone marrow edema, and venous sinus thrombosis [6]. In our patient, we proceeded with MRI due to the extension of infection on CT scan to assess for meningeal and orbital involvement.

Management usually focuses on the use of intravenous antibiotics and surgical drainage. Empiric broad-spectrum antibiotics are used initially, then the antibiotic choice is tailored based on culture results. In our patient, the abscess culture was polymicrobial, a common finding in cases of PPT. The most frequently found pathogens in PPT include *Streptococcus* species (such as *Streptococcus milleri*, viridans group *Streptococci*, *Streptococcus pyogenes*, and *Streptococcus pneumoniae*), *Staphylococcus aureus*, anaerobic microorganisms, and (rarely) *Hemophilus* influenza [9,10].

Surgery is the cornerstone treatment for PPT [9]. The main goals of surgery are debriding infected tissue from the sinus and drainage of the subperiosteal collection. The surgical approach can be external, endoscopic, or a combination. Although the external approach provides direct visualization of the frontal sinus and ensures immediate drainage of subperiosteal abscesses, endoscopic intranasal frontal sinusotomy (ESS) has replaced external approaches due to lower morbidity, shorter recovery period, and no visible scarring [11].

Anti-TNF Therapy and Infections

Tumor necrosis factor alpha (TNF-α) is part of the innate immune system's response against infections. It is a potent proinflammatory molecule which plays a role in the production of cytokines, recruitment of inflammatory cells, and target cell apoptosis [12].

Anti-TNF-α therapies were the first class of biologics to be used to treat moderate to severe IBD. These therapies are known to increase the risk of serious and opportunistic infections, and up to one-third of IBD patients develop non-serious infections within 1 year of beginning therapy. Other risks related to anti-TNF therapy include infusion reaction, risk of antibody formation, lupus-like syndrome, and malignancies such as lymphoma and melanoma [13].

A metanalysis done in rheumatoid arthritis (RA) patients showed increased risk of serious infection in patients on biologics compared to patients on disease-modifying antirheumatic drugs (DMARDs). Factors found to affect the risk of

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

developing infections include previous treatments used, the dose of anti-TNF administered, and use of combined biologic therapy [14]. Another metanalysis that included 49 randomized controlled trials investigated risk of infection in IBD patients who received biologics, concluding that there is an increase in risk of infections but no significant difference in serious infections. They defined serious infections as those that are life-threatening, need intravenous antibiotics, or require inpatient hospital admission [15].

Various factors have been proposed to increase the risk of infection while on biologic agent therapy. One of these factors is concomitant use of corticosteroids in patients who are on anti-TNF treatment. This was found in another metanalysis of patients with Crohn's disease treated with adalimumab recruited from 8 clinical trials. They found that the use of corticosteroids while on adalimumab significantly increased the infection risk, especially in the first period of biologic therapy. Also, they found that combining immunomodulators (such as methotrexate) with biologics was associated with a lower risk of serious infection at 1 year. A linear correlation between the incidence of serious infection and the Crohn's Disease Activity Index (CDAI) measured at follow-up visits was also observed [16]. Another systematic review showed no difference in increased risk of serious infection between biologic monotherapy and combined treatment with biologics and immunomodulators [17]. A metanalysis and systematic review by Singh et al found that monotherapy with an immunosuppressive agent (methotrexate or thiopurines) is associated with a lower risk of infection compared to anti-TNF monotherapy [18].

Another factor is duration of biologics therapy. After-market registries showed that risk of serious infection is the highest during the first year of anti-TNF therapy, then it decreases with time. The Swedish biologics register ARTIS found that risk of infection is higher with biologics than with DMARDs in the first year of use, but not thereafter. This finding could be influenced by better disease control leading to less use of corticosteroids [19].

In a metanalysis done for several IBD trials of various biologics, including anti-TNF, the most common infection found was upper respiratory tract infection. Other infections were lower respiratory tract infection, urinary tract infection, and gastroenteritis [20].

Dixon et al found that the most common site of serious infection in anti-TNF-treated RA patients was the lower respiratory tract, followed by skin and soft tissue, bone, and urinary tract [21]. The incidence of sinusitis with anti-TNF-α was reported in 2 studies as being 7-15% [22,23]. Yoshihara et al suggested that the incidence of refractory sinusitis requiring otolaryngology evaluation and treatment for patients who are on anti-TNF therapy was approximately 2% [24].

Methotrexate is also known to increase the risk of serious infection [25]. Long-term use of methotrexate might be another factor in our patient that could have contributed to developing this serious infection. However, a systematic review showed that methotrexate was associated with increased risk of infection in patients with rheumatoid arthritis but not in other non-rheumatoid arthritis inflammatory disorders, including inflammatory bowel disease [26].

Our literature review found no reports of cases of PPT in patients receiving biologics. Although our patient's history of recurrent sinusitis put him at risk of developing PTT, the immunosuppression effect of infliximab could be contributory. However, the potential for TNF-α inhibitor therapy to help achieve better control of IBD may outweigh the risk of infections related to TNF-α inhibitors.

Conclusions

PPT is a serious complication of untreated sinusitis. IBD patients on biologics who have sinusitis tend to have higher risk of developing such complications because of their decreased ability to fight infection. Although the risk of serious infections declines significantly after the first year of using biologics, physicians should keep a low threshold for investigating symptomatic patients for serious infections, as they require prompt intervention. Despite the potential complications from using biologics, the benefits of this therapy in IBD patients outweigh the risks.

Conflicts of Interest

None.

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

References:

1. Adegbola SO, Sahnan K, Warusavitarne J, et al. Anti-TNF therapy in Crohn's disease. Int J Mol Sci. 2018;19(8):2244
2. Andersen NN, Jess T. Risk of infections associated with biological treatment in inflammatory bowel disease. World J Gastroenterol. 2014;20(43):16014-19
3. Flamm ES. Percivall Pott: An 18th century neurosurgeon. J Neurosurg. 1992;76(2):319-26
4. Bambakidis NC, Cohen AR. Intracranial complications of frontal sinusitis in children: Pott's puffy tumor revisited. Pediatr Neurosurg. 2001;35(2):82-89
5. Heale L, Zahanova S, Bismilla Z. Pott puffy tumor in a five-year-old girl. CMAJ 2015;187:433-35
6. Kombogiorgas D, Solanki GA. The Pott puffy tumor revisited: Neurosurgical implications of this unforgotten entity. Case report and review of the literature. J Neurosurg. 2006;105(2 Suppl.):143-49
7. Salomão JF, Cervante TP, Bellas AR, et al. Neurosurgical implications of Pott's puffy tumor in children and adolescents. Childs Nerv Syst. 2014;30(9):1527-34
8. Gülhadiye A, Nursen B, Senem CK, Arzu K, Gülnar S. Pott's puffy tumor in a12-year-old boy. Pediatr Int. 2015;57(1):163-65
9. Koltsidopoulos P, Papageorgiou E, Skoulakis C. Pott's puffy tumor in children: A review of the literature. Laryngoscope. 2020;130(1):225-31
10. Verbon A, Husni RN, Gordon SM, et al. Pott's puffy tumor due to Haemophilus influenzae: Case report and review. Clin Infect Dis. 1996;23(6):1305-7
11. Palabiyik FB, Yazici Z, Cetin B, et al. Pott puffy tumor in children: A rare emergency clinical entity. J Craniofac Surg. 2016;27(3): e313-e316.
12. Olsen NJ, Stein CM. New drugs for rheumatoid arthritis. N Engl J Med. 2004;350(21):2167-79
13. Quezada SM, McLean LP, Cross RK. Adverse events in IBD therapy: The 2018 update. Expert Rev Gastroenterol Hepatol. 2018;12(12):1183-91
14. Singh JA, Cameron C, Noorbaloochi S, et al. Risk of serious infection in biological treatment of patients with rheumatoid arthritis: A systematic review and meta-analysis. Lancet. 2015;386(9990):258-65
15. Bonovas S, Fiorino G, Allocca M, et al. Biologic therapies and risk of infection and malignancy in patients with inflammatory bowel disease: A systematic review and network meta-analysis. Clin Gastroenterol Hepatol. 2016;14(10):1385-97
16. Osterman MT, Sandborn WJ, Colombel JF, et al. Crohn's disease activity and concomitant immunosuppressants affect the risk of serious and opportunistic infections in patients treated with adalimumab. Am J Gastroenterol. 2016;111(12):1806-15
17. Wheat CL, Ko CW, Clark-Snustad K, et al. Inflammatory bowel disease (IBD) pharmacotherapy and the risk of serious infection: A systematic review and network meta-analysis. BMC Gastroenterol. 2017;17(1):52
18. Singh S, Facciorusso A, Dulai PS, et al. Comparative risk of serious infections with biologic and/or immunosuppressive therapy in patients with inflammatory bowel diseases: A systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2020;18(1):69-81
19. Askling J, Fored CM, Brandt L, et al. Time-dependent increase in risk of hospitalisation with infection among Swedish RA patients treated with TNF antagonists. Ann Rheum Dis. 2007;66(10):1339-44
20. Shah ED, Farida JP, Siegel CA, et al. Risk for overall infection with anti-TNF and anti-integrin agents used in IBD: A systematic review and meta-analysis. Inflamm Bowel Dis. 2017;23(4):570-77
21. Dixon WG, Watson K, Lunt M, et al. Rates of serious infection, including site-specific and bacterial intracellular infection, in rheumatoid arthritis patients receiving anti-tumor necrosis factor therapy: Results from the British Society for Rheumatology Biologics Register. Arthritis Rheum. 2006;54(8):2368-76
22. Tynjälä P, Kotaniemi K, Lindahl P, et al. Adalimumab in juvenile idiopathic arthritis-associated chronic anterior uveitis. Rheumatology (Oxford). 2008;47(3):339-44
23. Maini R, St Clair EW, Breedveld F, et al. Infliximab (chimeric anti-tumour necrosis factor alpha monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomised phase III trial. ATTRACT Study Group. Lancet. 1999;354(9194):1932-39
24. Yoshihara S, Kondo K, Kanaya K, et al. Tumour necrosis factor inhibitor-associated sinusitis. Rhinology. 2014;52(3):246-51
25. Caporali R, Caprioli M, Bobbio-Pallavicini F, Montecucco C. DMARDS and infections in rheumatoid arthritis. Autoimmun Rev. 2008;8(2):139-43
26. Ibrahim A, Ahmed M, Conway R, Carey JJ. Risk of infection with methotrexate therapy in inflammatory diseases: A systematic review and meta-analysis. J Clin Med. 2018;8(1):15

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]