

Temporal Improvement of a COVID-19-Positive Crohn's Disease Patient Treated With Bismuth Subsalicylate

Douglas C. Wolf, MD¹, Christine H. Wolf, MD¹ and David T. Rubin, MD²

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An 85-year-old man with known Crohn's disease (CD) was scheduled to be seen on an urgent basis on March 23, 2020, because of a 10-day history of diarrhea. A previsit call was made because of the coronavirus disease-19 (COVID-19) pandemic. Normally a vigorous man, he complained of 4 liquid stools a day, anorexia, fatigue, and a 13-pound weight loss from 184 to 171 pounds over the preceding 10 days. He also described a nonproductive "hacking and debilitating cough" for the past 10 days that had not improved despite a 5-day course of azithromycin prescribed by his primary care physician.

Crohn's disease had been diagnosed incidentally during a screening colonoscopy and biopsy during the previous decade. His

last colonoscopy in 2017 for the evaluation of intermittent diarrhea revealed an ileocecal valve stricture and no colon or rectal involvement. He was on no anti-inflammatory therapy for his CD and only took loperamide as needed every few weeks.

Given the pandemic, management was performed by telehealth. While waiting for laboratory results, he was prescribed bismuth subsalicylate (BSS) 525mg orally 2–4 times a day. Within 6 h of the first dose, his diarrhea was improved.

Laboratory results of interest included oropharyngeal swab reverse transcription polymerase chain reaction for SARS-CoV-2 positive, anemia 11.3 g/dL (13.0–17.7), lymphopenia $0.6 \times 10^9/L$ (0.7–3.1), elevated erythrocyte sedimentation rate 69 mm/hr (<30), and elevated C-reactive protein 99mg/L (<10). Stool for *Clostridioides difficile* and other pathogens was negative.

Over the next 6 days, with BSS as his only additional medication, he had steady improvement of his diarrhea, cough, appetite, energy, and well-being; both diarrhea and cough were 80% improved after 6 days of BSS. By day 10, his cough was gone and stooling nearly normal, off BSS.

Both cough and diarrhea have been reported as prominent symptoms of COVID-19. Lymphopenia, as seen in this case, was identified in the China experience as associated with poor outcomes (1,2). Although it is possible that the patient's symptoms were due to a concomitant community-acquired pneumonia and improved suddenly on day 5 of azithromycin, we believe that both his diarrhea and cough improved because of BSS. The mechanism of action of BSS has not been determined, but BSS improves acute diarrhea (3) and also has multiple antimicrobial effects (4). *In vitro* studies have reported the efficacy of several bismuth-based complexes which work as

potential inhibitors of the severe acute respiratory syndrome coronavirus helicase adenosine triphosphatase and seem to exert antiviral activity (5,6). In addition, acetylsalicylic acid has been shown to block influenza virus propagation via inhibition of nuclear factor kappa beta (7).

We suggest that BSS may have contributed to this man's improvement and survival despite his risk factors for poor outcomes from COVID-19. BSS has limited and well-known side effects, is generally well-tolerated, widely available, and deserves consideration during the COVID-19 pandemic.

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¹Center for Crohn's and Colitis, Atlanta Gastroenterology Associates, Atlanta, Georgia, USA; ²University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, Illinois, USA. **Correspondence:** Douglas C. Wolf, MD. E-mail: doug.wolf@atlantagastro.com.