


**Case Report**

## Covid-19 Infection in Patients with Crohn's Disease on Intensified Adalimumab Treatment with Gastrointestinal Symptoms

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### Introduction

The main concern in inflammatory bowel disease (IBD) patients on anti-TNF $\alpha$  antibodies during SARS-CoV-2 pandemic is the potential consequence of immunosuppressive therapy. Despite the initial concern that such treatment could lead to a more severe disease course, recent evidence suggests that in a significant proportion of patients it is the activation of the immune system, and not the virus

itself, that causes severe lung damage. Thus, it was hypothesized that the use of anti TNF $\alpha$  antibodies could be beneficial in SARS-CoV-2 infection [1]. TNF $\alpha$  has various biological effects such as amplification of proinflammatory and chemotactic mediators, migration of neutrophils and up-regulation of adhesion molecules. Therefore, besides direct cytopathic effect of SARS-CoV-2, suppressing of host inflammatory response could serve as another treatment option [2].

Furthermore, a randomized controlled trial investigating efficacy and safety of adalimumab in the treatment of patients with severe Covid-19 pneumonia has recently been registered [3]. Since the evidence is scarce and there is a rising interest on the effect of anti TNF $\alpha$  antibodies in SARS-CoV-2 infection, we report, to our knowledge, the first case of SARS-CoV-2 infection in Crohn's disease (CD) patient on intensified adalimumab treatment with favorable clinical course.

### Case

A 47-year-old female patient was diagnosed with ileal CD five years ago and started on adalimumab due to azathioprine intolerance. For the last 13 months patient received 40 mg adalimumab every week and was in sustained endoscopic and clinical remission. Two days after her last administration of adalimumab she experienced symptoms of cough, fever (38.0°C), chest pain, headache and general weakness. Oral and nasal swabs were analyzed using polymerized chain reaction (PCR) and resulted positive for SARS CoV-2 virus, so the patient was admitted to the hospital. At the time of the admission she was treated with symptomatic therapy without any need for oxygen replacement therapy. Laboratory values were in the reference ranges (CRP 4.1 mg/L, ref. range <5 mg/L), and chest X-ray did not show any signs of pneumonia. On the second day of hospital admission she developed gastrointestinal symptoms; up to three soft stools per day and intermittent abdominal pain, accompanied with anosmia and altered sense of taste (metallic taste). Since this was early stage of epidemic in Croatia, treatment with lopinavir-ritonavir was initiated, but was suspended after three days due to drug intolerance (nausea, vomiting). Nausea and vomiting subsided quickly, but soft stools and abdominal pain persisted during entire course of Covid-19. Fever was present until the fourth

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day of disease, and the rest of the symptoms of Covid-19 disease were present in mild form during approximately two and a half weeks. During that time therapy with adalimumab was stopped and was continued again after two consecutive negative nasal and oral swabs (approximately three and a half weeks after Covid-19 diagnosis). Interestingly, patient's husband was also infected with SARS-CoV-2 but had a more serious disease course with development of pneumonia and fever that lasted for over 14 days.

## Conclusion

We find our case interesting for several reasons. Firstly, our case report describes another CD patient on adalimumab with favorable clinical course. Namely, mild clinical course of SARS-CoV-2 infection was recently reported in a 30-year-old male with CD on standard regimen of 40 mg of adalimumab every other week [4]. Secondly, despite the fact that our patient received higher immunosuppression (weekly administration of adalimumab) he also had a favorable disease course. High level of immunosuppression was one of our main concerns. Namely, immunosuppression could have its negative consequences such as enhanced viral replication and increased risk of secondary bacterial infections. However, analysis of patients from Nancy and Milan cohorts found that IBD patients develop less severe forms of SARS-CoV-2 infection [5]. This is in line with a recent case of a SARS-CoV-2 infection that was described in patient in his late 60s with ulcerative colitis treated with infliximab (5 mg/kg/8-weekly) together with azathioprine and high-dose of oral Mesalazine. Despite symptoms of cough and fever he also had no radiological signs of pneumonia and needed no specific treatment. This was not the case with his wife who developed Covid-19 driven pneumonia [6]. Mild disease course of SARS-CoV-2 infection in our patient might be attributed to her age, female gender and general good health prior to the infection, but what is interesting and similar to the case from Kuniaki et al., her husband also experienced a more serious disease course [6]. Although men are at risk for a more serious disease course [7], it is unexpected that a patient with high immunosuppression on weekly adalimumab treatment had a significantly milder disease compared to a healthy male of the same age group. Therefore, since there are already some preliminary results of benefit and safety of anti TNF $\alpha$  therapy in SARS-CoV-2, clinical trials are of interest and potentially beneficial [8]. Thirdly, our patient experienced gastrointestinal symptoms, including diarrhea, a symptom which could be underestimated due to heterogeneous prevalence among studies [9]. Since the stool consistency normalized and abdominal pain alleviated before adalimumab was continued, we concluded that gastrointestinal symptoms were caused by SARS-CoV-2 infection, rather than CD activity, even though stool analysis on SARS-CoV-2 virus was not performed. According to the recent meta-analysis on

gastrointestinal manifestations of SARS-CoV-2 of 60 studies and 4243 patients, pooled prevalence of all gastrointestinal symptoms was 17.6% and pooled prevalence of diarrhea and abdominal pain/discomfort was 12.5% and 9.2%, respectively [10]. Since there could come to an overlap in clinical picture of SARS-CoV-2 infection and IBD, special attention should be paid when monitoring disease activity during active infection.

In conclusion, despite the fact that current data on effects of anti - TNF- $\alpha$  therapy on clinical course of SARS-CoV-2 infection are scarce, there are several case reports that report mild clinical course in IBD patients on relatively high immunosuppression.

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