Case Report

A Case of COVID-19 Successfully Treated with Minocycline and Saiko-Keishi-To

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Abstract: Since the beginning of 2020, tetracycline (TC), such as minocycline (MINO), has been used to inhibit coronavirus disease 2019 (COVID-19). Traditional Japanese Kampo medicine, such as Saiko-keishi-to (SKT), has recently received a lot of attention for its anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) effects. We describe a COVID-19 patient treated with MINO and SKT in anticipation of their anti-SARS-CoV-2 properties. A 90-year-old male patient with Alzheimer's disease was referred to a medical clinic due to fever, appetite loss, and general malaise. Based on positive SARS-CoV-2 rapid antigen tests, he was diagnosed with COVID-19. He did not have COVID-19 pneumonia, but he had difficulty in eating on his own. As a result, he was referred to a hospital for admission. After admission, he was treated with molnupiravir to avoid aggravation. Seven days after his admission, he was discharged. After his discharge, he was referred to our hospital as an outpatient due to a prolonged mild fever and general malaise. As a precaution, a real-time reverse transcription-polymerase chain reaction (RT-PCR) test was performed, which yielded a positive result. Therefore, the aforementioned symptoms were thought to be caused by prolonged COVID-19. He was treated with MINO and SKT due to the anti-viral properties of these two drugs. The RT-PCR test became negative 7 days after receiving this treatment, and the fever and general malaise subsided.

Keywords: COVID-19; SARS-CoV-2; minocycline; Kampo; Saiko-keishi-to

Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in late 2019 and has since become a major global threat to human health. The recent, rapid development of COVID-19 vaccines is a huge accomplishment that offers hope of ending the global pandemic. However, the spread of the highly transmissible Omicron variant of COVID-19 has thrown the pandemic into doubt. Further, new drugs are being developed as non-vaccine treatments. However, they are insufficiently effective and expensive. Therefore, finding quickly effective and low-cost drugs against COVID-19 and conducting clinical trials on these drugs remains a worthwhile and beneficial endeavor. Drug repurposing is a well-known strategy for redeploying existing licensed drugs for newer indications, allowing for the shortest possible transition from bench to bedside for meeting therapeutic needs. Regarding existing licensed drugs, tetracycline (TC) (e.g., minocycline (MINO), and doxycycline (DOX)) has been used since the beginning of 2020 due to its efficacy in inhibiting COVID-19 [1, 2]. The anti-SARS-CoV-2 effects of traditional Japanese Kampo medicine, such as Saiko-keishi-to (SKT), have recently received a lot of attention [3]. We describe a COVID-19 patient treated with MINO and SKT in anticipation of their anti-SARS-CoV-2 properties.

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Case

A 90-year-old male patient with Alzheimer's disease was referred to a medical clinic due to fever, appetite loss, and general malaise. The results of the laboratory tests revealed a white blood cell (WBC) count of 5,000/μL and C-reactive protein (CRP) levels of 1.30 mg/dL. Based on positive SARS-CoV-2 rapid antigen tests, he was diagnosed with COVID-19. He did not have COVID-19 pneumonia, but he had difficulty in eating on his own. As a result, he was referred to a hospital for admission. To avoid aggravation, he was treated with molnupiravir [4]. He was discharged 7 days after his admission. After his discharge, he was referred to our hospital as an outpatient due to a prolonged mild fever and general malaise. During this visit, laboratory findings revealed a WBC count of 5,250/μL (basophils, 0.6%; eosinophils, 0.8%; neutrophils, 79.0%; lymphocytes, 13.3%; and monocytes, 6.3%) and CRP levels of <0.2 mg/dL. The systemic survey, which included a chest roentgenogram and urinalysis, revealed no abnormal findings suggestive of infection. As a precaution, a real-time reverse transcription-polymerase chain reaction (RT-PCR) test was performed, yielding a positive result with a cycle threshold (Ct) value of 33. Therefore, the aforementioned symptoms were thought to be caused by prolonged COVID-19.

He received treatment with MINO (100 mg, b.i.d.) for 7 days and SKT (2.5 g, t.i.d.) for 7 days due to the anti-viral properties of these two drugs. Four days after receiving this treatment, RT-PCR test was positive with a Ct value of 37. Seven days after receiving this treatment, RT-PCR test became negative with a Ct value of 41. Simultaneously, the fever and general malaise subsided.

Discussion

In clinical use, TCs such as MINO and DOX are well-known antibiotics. They are highly lipophilic and chelate zinc compounds on matrix metalloproteinases (MMPs). Several SARS-CoV-2 functions, including replication, are associated with the host MMP complex. Therefore, the zinc-chelating properties of TCs may aid in inhibiting COVID-19 in humans, limiting SARS-CoV-2 replication within the host [5, 6]. Moreover, the in silico assay demonstrated that TCs inhibited the binding of the SARS-CoV-2 spike protein to angiotensin-converting enzyme (ACE) II receptor [7].

Regarding TC treatment for mild and moderate COVID-19, Yates et al. reported successful treatment of four high-risk COVID-19 patients with comorbid pulmonary disease with DOX at 100–200 mg/day for 5–14 days [1]. Furthermore, Gironi et al. reported that DOX and MINO improved mild COVID-19-related symptoms within 10 days [2].

SKT is a traditional Japanese Kampo medicine with unique theories and therapeutic methods based on traditional Chinese medicine. Kampo medications are mostly made from organic plant-based ingredients. The components used to make SKT include JP Bupleurum Root, JP Pinellia Tuber, and JP Scutellaria Root [3]. Saikosaponin, a component of SKT and a Bupleurum extract, demonstrated in vitro anti-viral activity against human coronavirus 229E by inhibiting viral attachment to cells in a dose-dependent manner, blocking viral penetration into cells, and interfering with the early stages of viral replication [8]. The in silico assay revealed that saikosaponin has a high affinity for binding to a SARS-CoV-2 target receptor, the ACE II receptor [9]. Based on these findings, SKT is most likely effective on COVID-19 [10]. In fact, three cases of COVID-19 pneumonia were successfully treated with SKT in combination with other drugs [3]. Very recently, treatment with kakkon-to, and sho-saiko-to-ka-kikyo-sekko that contains saikosaponin as a component, was reported to be effective for fever relief with suppression of disease progression in COVID-19 patients [11]. Therefore, Kampo medicines other than SKT, that contain saikosaponin, could be efficacious against COVID-19.

Because the mechanisms of action of the drugs differ, multidrug therapy is more effective than single-drug therapy. Moreover, multidrug therapy may help to prevent the

spread of drug-resistant SARS-CoV-2 [12]. Therefore, MINO and SKT treatment could effectively treat COVID-19.

In any case, clinical trials are required to better assess the optimal doses and durations, as well as the efficacy and tolerability of this treatment before it can be widely used.

Conflict of Interest

The authors declared no conflicts of interest.

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