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Commentary

A Case of Severe Pulmonary Aspergillosis Successfully Treated by Isavuconazole

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Abstract: Isavuconazole (ISCZ) is a novel antifungal agent that is expected to be effective against severe fungal diseases. A case of chronic pulmonary aspergillosis that was refractory to existing agents, such as micafungin, but was successfully treated by ISCZ, is presented.

Keywords: Aspergillosis, Cytochrome P450, Fungus, Isavuconazole, Therapeutic Drug Monitoring

1. Commentary

There are several types of antifungal agents, such as amphotericin B, echinocandins, and azoles for the treatment of aspergillosis and/or mucormycosis [1, 2]. Of the azoles, most are related to cytochrome P450 (CYP), and interactions with other agents, including immunosuppressive agents such as tacrolimus and cyclophosphamide, must be considered [1, 3]. In addition, careful therapeutic drug monitoring (TDM) is needed to maintain the appropriate concentrations of the drugs and to inhibit liver/kidney injury when voriconazole (VCRZ) is used [1, 4].

Recently, isavuconazole (ISCZ) has been developed and recommended as the preferred agent for chronic pulmonary aspergillosis and severe mucormycosis [1, 2]. ISCZ showed not only significant clinical effectiveness, but could also be used easily without TDM [5]. Side effects, such as liver and renal dysfunction, are rare after the use of ISCZ compared with VCRZ and itraconazole (ITCZ) [5, 6].

A case of fungal infection that was refractory to existing agents, but successfully treated by ISCZ, is presented.

This case was approved by the Institutional Review Board of Saitama Medical University International Medical Center (#2022-073) on September 07, 2022 and registered as UMIN000047995. The patient provided written, informed consent as part of the comprehensive consent obtained at admission to have any accompanying images and case details published. The patient was provided the means to opt out of this clinical study in particular. This study adhered to the Declaration of Helsinki.

A 70-year-old man was diagnosed with chronic pulmonary aspergillosis (CPA). He had been admitted for brain infarction, with old tuberculosis found as an underlying disease. After admission, he developed pneumonia (Figure 1A), and *Enterobacter aerogenensis* (*E. aerogenensis*) was isolated from his sputum. Therefore, antibiotic therapy with tazobactam/piperacillin (TZP) was started, because the isolated *E. aerogenensis* was susceptible to TZP. However, the infiltration shadow on his chest X-ray did not improve, aspergillus antigen was positive, and β-d-glucan (BDG) was increased to 309.1 pg/ml in his blood. CPA was then diagnosed, and micafungin (MCFG), 150 mg drip infusion once daily, was started. Two weeks later, his chest X-ray became worse (Figure 1B), and BDG did not change (374.1 pg/ml). MCFG was changed to ISCZ 200 mg three times/daily for

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two days followed by 200 mg daily. Two weeks later, his chest X-ray improved (Figure 1C), and BDG decreased to 77.4 pg/ml.

This case suggested that ISCZ is effective for severe fungal infections including CPA that are refractory to existing antifungal agents, such as MCFG, which was easy to use because TDM was not needed, but it might not be effective against severe CPA. VCRZ was usually used as the first-line drug for CPA treatment because of its strong effectiveness, but TDM was needed to maintain the appropriate blood concentration. Furthermore, liposomal amphotericin B was sometimes used to treat CPA, but there were several side effects, including hypokalemia.

In conclusion, ISCZ is an antifungal agent that was effective and was used easily to treat a severe fungal disease, refractory CPA. More experience using ISCZ and detailed analysis are needed.

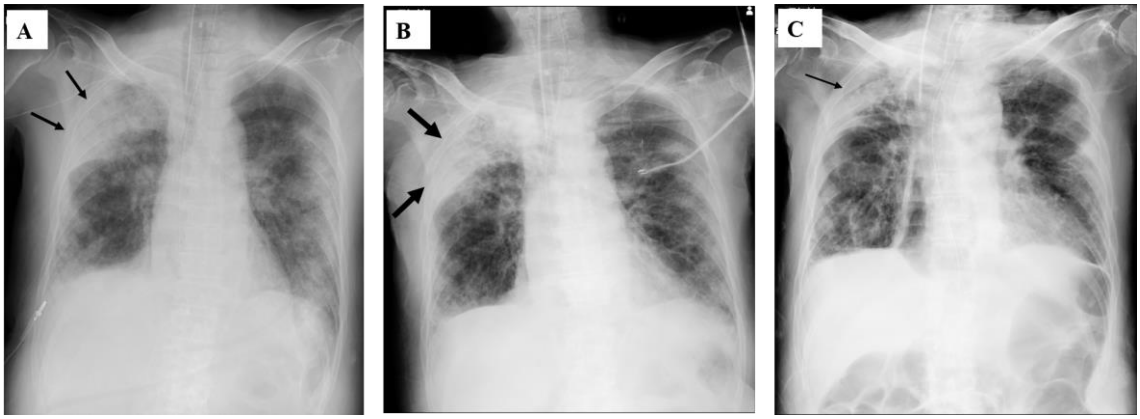

Figure 1. The patient's chest X-ray findings. (A) An infiltration shadow is seen in his right upper lung field, (B) his infiltration shadow worsens despite tazobactam/piperacillin followed by micafungin, but (C) his infiltration shadow improves after isavuconazole treatment. Arrows indicate the infiltration shadows.

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