Temporal loss of efficacy of monoclonal CGRP-antibody treatment following an infection with SARS-CoV-2: A case report

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Increase of migraine frequency or pain intensity triggered by viral infections is common, in some patients a migraine status may be a consequence (1). In most patients migraine decreases after complete resolution of the infection and the course of disease reaches previous state. Due to the pandemic situation of SARS-CoV-2 patients switching from episodic to chronic migraine frequency are reported in close temporal relation to a COVID-19 disease (2).

Until now there is one case published reporting decrease of efficacy of treatment with the monoclonal CGRP (calcitonin gene-related peptide)-receptor antibody erenumab in a migraine patient previously suffering from episodic migraine. Improvement in this patient was reported due to increasing the monthly erenumab dose from 70 to 140 mg (3).

Herein we report on a migraine patient who had significantly responded to a monoclonal antibody acting on the CGRP pathway with complete loss of efficacy following a COVID-19 disease.

The male patient (age 35 years) was diagnosed with migraine with typical aura since adolescence. He reported previous treatment with topiramate which had been stopped because he developed a depression. He received treatment with metoprolol and amitriptyline without efficacy. Flunarizine caused dizziness and tiredness. He was diagnosed with chronic migraine with corresponding 25 headache days per month and additional medication overuse in march 2020 and underwent withdrawal treatment of acute medication with significant improvement. Afterwards he suffered from 13 headache days per month and treatment with fremanezumab 225 mg per month was initiated in August 2020. After first three months of treatment the headache frequency decreased to 8 days per month and mean pain intensity decreased from 9 to 6 on the numeric pain rating scale (NRS from 0-10). Further a nearly complete resolution of attack accompanying symptoms (nausea, vomiting, photophobia) was reported after initiating the antibody treatment. He still needed attack aborting medication (zolmitriptan 5mg) on every headache day.

Within the next months a stable course of disease with mean 7 migraine days per month was reported, the patient only needed attack aborting medication on 5 of the 7 migraine days. The stable course could be documented from February 2021 until November 2021. In November 2021 the patient reported infection with SARS-CoV-2. He developed fever, cough and fatigue symptoms which lasted for about 7 days. The infection was PCRconfirmed on November 11, 2021. The patient was previously vaccinated with the mRNA-vaccine Comirnaty (Pfizer/BioNTech) in April and had his second vaccination in May 2021. He was already scheduled for a booster vaccination in November which had to be cancelled due to the acute infection. With the beginning of the infection the patient suffered from daily recurring migraine-like unilateral pulsating headache attacks with nausea, vomiting, photophobia...
and phonophobia. The patient himself recognized these attacks as typical well known migraine attacks, this time the attack aborting medication with zolmitriptan could only slightly decrease the headache intensity but could not entirely abort the attacks. A prednisolone pulse therapy with 100 mg per day was initiated in January 2022 under the suspicion of a migraine status triggered by the viral infection. Unfortunately, the patient did not respond to the treatment. The CGRP-antibody treatment was continued, in February 2022 the patient received a second prednisolone pulse therapy with the same dosage as before which could not abort the headache either. Overall, the patient suffered from an exacerbation of almost daily recurring migraine attacks of high intensity and loss of efficacy of the prophylactic therapy with the CGRP-antibody fremanezumab. In December 2021 he experienced 19 and in January 17 migraine days of severely high intensity, an additional headache due to medication overuse could be ruled out. In February 2022 the patient reported a spontaneous reduction of high intensity migraine attacks, 9 days were documented for this month, attack aborting medication showed a better effect again. The last CGRP-antibody injection was documented on January 26. Although the patient experienced a reduction of migraine days, we decided to stop the prophylactic treatment with fremanezumab and observed the spontaneous course of disease.

In March 2022 the patient experienced an increase of migraine days again, on March 17 he already had 7 severe migraine attacks. As a consequence, the CGRP-antibody therapy was started again, which resulted in a soon reduction of severe migraine attacks. Since April 2022 until present the patient’s course of disease is stable again with an average of 7 migraine days per month under treatment with fremanezumab.

A worsening of the migraine was in close temporal relationship to a COVID-19 infection, which is frequently reported (2). Remarkable in this case is that the previous treatment with the monoclonal CGRP-antibody showed a clear loss of efficacy. Due to the temporal correlation of increase of migraine frequency and pain intensity and a PCR-confirmed infection with SARS-CoV-2, a loss of efficacy of CGRP-antibody treatment is plausible. The differential diagnosis of headache attributed to a viral infection could apply for the duration of the acute infection but does not explain the further observed course. The patient referred to the headache as well known in migraine-like quality which equaled the status before responding to treatment with the CGRP-antibody fremanezumab. The patient showed no signs of post-COVID symptoms like depression or neurocognitive impairment which are also known to worsen migraine. There were no clinical signs of a cerebral venous thrombosis or meningoencephalitis as a possible explanation.

A further differential diagnosis is the migraine status caused by an acute viral infection. This diagnosis is also questionable due to the long period of ongoing symptoms for several months, neither did the patient respond to prednisolone pulse therapy.

The Patient did not receive a third mRNA-vaccination after the recommended 6 months. Based on these findings migraine patients should be informed about the risk of exacerbation of migraine caused by a SARS-CoV-2 infection which could possibly result in higher migraine frequency and higher pain intensity even when treated with a CGRP-antibody. Physicians treating migraine patients should encourage their patients to get vaccinated against SARS-CoV-2 in order to prevent above mentioned migraine complications.

CONFLICT OF INTEREST

Klaus Koschatzky received honoraria for consulting and lectures from Novartis, Lundbeck and Eli Lilly.

Charly Gaul has received honoraria for consulting and lectures within the past three years from Allergan Pharma, Lilly, Novartis Pharma, Hormosan Pharma, Grünenthal, Sanofi-Aventis, Weber & Weber, Lundbeck, Perfood, and TEVA. His research is supported by a grant of the German Research Foundation (DFG). He does not hold any stocks of pharmaceutical companies. He is honorary secretary of the German Migraine and Headache Society.

PATIENT CONSENT

The patient gave written consent to have his case published.

References

