

## CASE STUDY

## HYDROXYCHLOROQUINE IS NO MIRACLE CURE FOR COVID-19 INFECTION –IMAGING AND CLINICAL COURSE IN AN ELDERLY FEMALE

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**IGOR ALEXANDER HARSCH<sup>1</sup>, MARCIN SKIBA<sup>1</sup>, ERIC LOPATTA<sup>2</sup>, PETER CHRISTOPHER KONTUREK<sup>1</sup>**<sup>1</sup>DEPARTMENT OF INTERNAL MEDICINE II, THURINGIA CLINIC “GEORGIUS AGRICOLA”, SAALFELD/SAALE, GERMANY<sup>2</sup>DEPARTMENT OF RADIOLOGY, THURINGIA CLINIC “GEORGIUS AGRICOLA”, SAALFELD/SAALE, GERMANY

### ABSTRACT

The risk for an unfavourable course of SARS-CoV-2 pneumonia rises with age and comorbidities. We report the case of an elderly female where the sum of such factors – together with massive findings in the computed tomography of the lung – led us to a therapy with hydroxychloroquine as a compassionate use. The unfavourable outcome demonstrates that – despite the enthusiasm of some authors – hydroxychloroquine is no miracle drug. The worldwide SOLIDARITY trial will help clinicians to assess the potential of the repurposed antimalarial drugs better.

**KEY WORDS:** chest CT, Chloroquine, compassionate use, COVID-19, Hydroxychloroquine, repurposed agent, SARS-CoV-2

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### INTRODUCTION AND THE AIM

Ai et al. [1] recently published an imaging study in 1014 patients who had chest computed tomographies (CT) performed and reported a sensitivity of 97% for the SARS-CoV-2 virus pneumonia. That said, computed tomography of the thorax has become an important tool not only in the detection of SARS-CoV-2 pneumonia, but also for an evaluation of the severity of the pulmonary involvement [2]. Advantages of an early CT imaging (if available) are a higher sensitivity to detecting lung opacities compared to chest radiographs where the lack of visible early abnormalities may cause a higher number of false-negative patients. The chest CT reveals typical radiological features such as ground-glass opacities, multifocal patchy consolidations and interstitial changes with a peripheral distribution. Furthermore, COVID-19 testing may take about a day and can be problematic due to limited laboratory capacities and lack of nucleic acid kits [2].

If a massive finding in the chest CT is noted, the clinician is faced with the problem of not having a specific antiviral therapy available. This is a problem that is exacerbated if the patient's prospects for the further course of the disease are already poor, usually due to age and comorbidities. Although multiple drugs with potential against COVID-19 are still in the experimental stages in development, according to the current status only the “repurposed agents” hydroxychloroquine (HCQ)/chloroquine and remdesivir, as well as lopinavir/ritonavir can be considered as options. Remdesivir was originally developed in therapy against the Ebola virus, but showed no significant advantages here [3], with regard to its use against the COVID-19, there are yet only published data from a compassionate use study available [4]. Robust and significant results from randomized clinical trials are

still pending. This also applies to hydroxychloroquine/chloroquine, which are actually used as medication for malaria. Compared to remdesivir, these preparations have the advantage of immediate availability and low costs. They are also recommended for use in China, for example by the multicenter collaboration group of the Department of Science and Technology of Guangdong Province and Health Commission of the Guangdong Province [5]

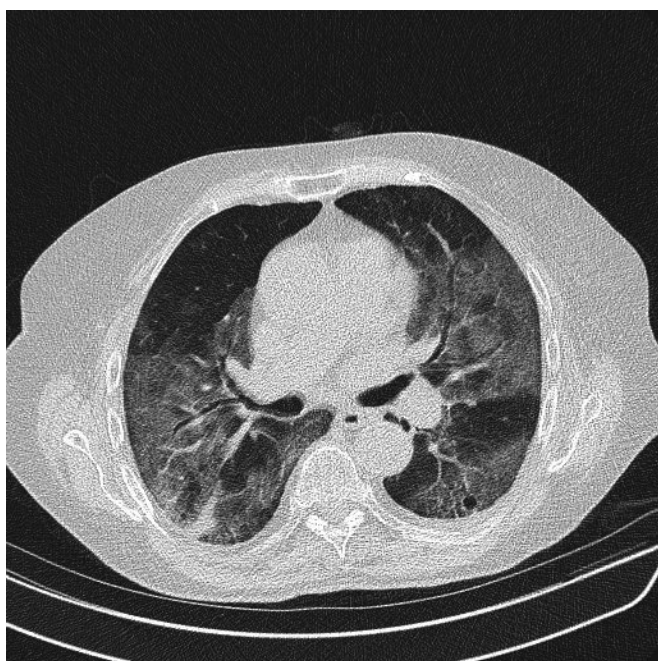
### CASE DESCRIPTION

In April 6th, a 88-year-old female was admitted to our clinic due to increasing dyspnea. She lived in a nursing home for the elderly where some residents including her had already been tested positive for COVID-19 infection. Her comorbidities were hypertension, atrial fibrillation and she suffered from hemiparesis of the right body half after a hemorrhagic stroke in 2009. Upon hospitalization, the patient was fully alert and vigilant, serum procalcitonin was negative and serum C-reactive protein was 109 mg/l (<5).

Further laboratory values at admission:

Pathological: ASAT 1.44  $\mu$ kat / l (0.17-0.85); d-dimer 4166 (<230  $\mu$ g/l); creatinine 156 (44-80  $\mu$ mol/l). In the small blood count with an otherwise normal status and normal leukocyte count, the lymphocytes were found to be slightly reduced in absolute terms at 0.4 Gpt / l (1.1-3). The following values were within normal range: sodium, potassium, ASAT, gamma -GT, troponin-T, coagulation, TSH, fT3, fT4.

The CT of the chest showed extensive bipulmonary ground glass opacities with a major preponderance in the lower lobes of the lung, typical for a COVID-19 infection (Fig. 1-3). Since the extent of the infiltrations made an unfavourable course



**Fig. 1.** Axial reconstruction with slice thickness and interval of 1.5 mm. This slice shows multiple ground-glass opacities with involvement of the upper and lower lobes as well as a subpleural dominant reticular pattern and an early consolidation in the right lower lobe.



**Fig. 2.** Sagittal reconstruction with slice thickness and interval of 3.0 mm. This view demonstrates the dorsally predominant distribution of the ground-glass opacities and the involvement of the posterior part of the right middle lobe. In particular the small interlobar effusion, which is uncommon for Covid-19-pneumonia and probably caused by the comorbidities, is to be noted.

likely and after obtaining the patient's as well as her daughter's informed consent, a therapy with hydroxychloroquine (400 mg bid.) was immediately started as compassionate use. The dose was reduced to 200 mg bid. after two days and



**Fig. 3.** Coronal reconstruction with slice thickness and interval of 3.0 mm. This image demonstrates the extension of the ground-glass opacities and the grazing-paving pattern in the posterior segments of the right and left upper and lower lobes.

maintained. The daily electrocardiogram (ECG) monitoring revealed no ECG changes suggestive for cardiotoxicity and the patient had no gastrointestinal side effects. However, especially in terms of respiratory problems, the clinical course was unstable with highs and lows in the patient's condition. Finally, her clinical condition deteriorated and she died on April 11<sup>th</sup> due to cardiopulmonary failure.

## DISCUSSION

Chloroquine, and its related derivative HCQ, are drugs that are commonly used for treating malaria. They have gained attention within the medical community as a potential therapy for the SARS-Cov-2 pneumonia as repurposed agents. Several studies worldwide (at least 15 in China) are still investigating the efficacy and safety profile of these drugs and in preliminary results, chloroquine was reported to be superior to control therapy by improving lung image findings, promoting the virus-negative conversion and shortening the disease course [6]. Some of these effects may be based on an interference with ACE-2-receptor mediated endocytosis [7].

Despite the enthusiasm of some authors [6], the WHO states that currently, there is still an insufficient database to assess the efficacy of chloroquine and HCQ in treating patients with COVID-19, or in preventing them from contracting the coronavirus [8]. As for the more commonly used HCQ, it needs to be considered, that it can lead to QT interval prolongation and torsades de pointes arrhythmia in susceptible individuals. Furthermore, co-prescription of other drugs such as azithromycin (which is also sometimes used for the treatment of COVID-19) could amplify this risk. HCQ also interacts with other cardiac drugs such as beta blockers and digoxin and increases the blood levels of these drugs [9].

In the case described here, the considerable amount of pulmonary infiltrations, together with the age and the comorbidities of the patient made a fatal course of the disease very likely. This is also underlined by the elevated levels of d-dimer since elevated levels of d-dimer are discussed as a marker for an unfavorable outcome in SARS-CoV-2 infections. Zhang et al. [10] reported significantly higher levels of d-dimer as associated with a more severe course of the disease in an analysis of the records of 140 hospitalized COVID-19 patients. This sum of factors is why we had decided for an immediate compassionate use of HCQ. However, the case exemplifies that a therapy with HCQ is far from a miracle cure. To date, a number of clinical trials are in progress to test the safety and effectiveness of other candidate drugs such as Interferon- $\alpha$ , lopinavir/ritonavir, ribavirin or arbidol [11]. However, the high number of studies (at least 300 currently) [12] on such drugs could unfortunately also lead to positive effects being observed in various (small) subgroups, with the situation becoming increasingly confusing. Fortunately, the World Health Organization (WHO) has organized a multinational randomized trial (SOLIDARITY trial) to study the effect of drugs that have been identified as promising based on in-vitro data and clinical experience with SARS-CoV-2 infections: These are remdesivir, lopinavir and ritonavir; furthermore the combinations lopinavir and ritonavir + interferon; and chloroquine or hydroxychloroquine [13].

## CONCLUSION

In the age of the COVID-19 pandemic, the compassionate use of some drugs – especially in severe cases with poor prognosis – can be justifiable. Since the use should then naturally take place quickly, chloroquine or HCQ are suitable in most countries due to the rapid availability. This therapy is already recommended by some specialist societies – especially in Asia. But it is by no means a miracle medication, as the case described here shows. The current discussion is also increasingly focusing on the cardiotoxic potential of antimalarials. Hopefully, the WHO SOLIDARITY study will soon provide clinicians with reliable and robust information about the true value of these drugs.

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## ORCID and contributorship

Igor Alexander Harsch – 0000-0003-2716-0066: <sup>A,B,C,D,E,F</sup>  
 Marcin Skiba <sup>A,B</sup>  
 Eric Lopatta <sup>B,D,E,F</sup>  
 Peter Christopher Konturek <sup>A,D,E,F</sup>

## Declarations

*Consent for publication: The patient and her daughter gave written permission to publish her case.*  
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## Conflict of interest

*Authors declare no conflict of interest.*

## CORRESPONDING AUTHORS

### Igor Alexander Harsch

Thuringia Clinic Saalfeld “Georgius Agricola”, SAALFELD/SAALE, GERMANY  
 tel: +49[0]3671/541569; Fax: +49[0]3671/541403  
 e-mail: iharsch@thueringen-kliniken.de

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