Case Report
A case of administration of hydroxychloroquine in a hemodialysis patient with COVID-19

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Introduction

We report a case of a novel 2019 coronavirus infection (COVID-19). This patient was a hemodialysis patient, and was emergently transferred to our hospital which was a designated infectious disease medical institution possible for dialysis. The pneumonia progressed until he was transferred to our hospital. However, after he received hydroxychloroquine sulfate (trade name: Plakenil), his condition improved significantly. At present (as of March 6, 2020), the number of cases treated with hydroxychloroquine is small, and there are no case reports of dialysis patients with COVID-19.

Case Report

[Case] 69-year-old male, Japanese
[Chief complaint] Fever, cough, dyspnea
[History] Hemodialysis for diabetic nephropathy (2017-), secondary hyperparathyroidism, hyperphosphatemia, hypertension
[Medication history] evocalcet, lanthanum carbonate hydrate, amlodipine besylate, carvedilol, linagliptin, mitiglinide calcium hydrate/voglibose
[Drinking history/smoking history] None/ 40 cigarettes/day (49 years, from 20 y.o.)
[Allergy] None
[Overseas travel history] None
[Present illness]

He was a taxi driver and sometimes encountered foreigners, but he didn't remember carrying passengers having colds. He developed fever and cough on February 14, 2020, and was prescribed oseltamivir phosphate at the dialysis clinic A for diagnosis of influenza A. Although cough remained, the fever dropped on February 19 with a negative rapid influenza test. On February 24, a fever of 38°C was observed, and cough and dyspnea increased on February 25.

He was admitted to the dialysis clinic A. A chest X-ray showed a pneumonia in the right lower lung field, and meropenem (MEPM) 0.5g/day was started as bacterial pneumonia, but high fever sustained and improvement of clinical findings was poor. Pneumonia progressed and respiratory status was poor. He got worse (oxygen administration 3L/min) and was transferred to Hospital B on February 29. He was given ceftriaxone (CTRX) 1g/day, but his respiratory condition was getting worse (oxygen administration 7L/min). He was transferred to our hospital on March 1 due to bilateral pneumonia and a positive result of SARS-CoV-2 PCR test.

[At the time of admission]
Height 169cm, Weight 66kg, Clear consciousness, Temperature 37.3°C, Blood pressure 183/73mmHg, Heart rate 70/min, Respiration rate 36/min, SpO_2 98% (Reservoir mask 8L/min), abnormal breath sounds in both lung fields, no heart murmur, left forearm shunt, no lower leg edema.
[Inspection]
Shown in Table 1.
Other findings: Urinary pneumococcal/Legionella antigen test: negative/negative, Influenza rapid test: negative, Sputum culture: γ-streptococcus 1+, yeast-like fungus 1+,

WBC	9,400	/μl	TP	6.5	g/dl
Neut	75.8	%	Alb	2.4	g/dl
Lym	11.7	%	T-Bil	0.16	mg/dl
Mo	9.8	%	AST	24	U/l
Eo	2.5	%	ALT	6	U/l
Baso	0.2	%	ALP	354	U/l
RBC	353	$\times 10^4$ /μl	γ-GTP	13	U/l
Hb	10.8	g/dl	LDH	626	U/l
Hct	32.4	%	BUN	53	mg/dl
Plt	31.6	$\times 10^4$ /μl	Cre	9.07	mg/dl
			Na	138.2	mmol/l
PT-INR	1.10		Cl	102.4	mmol/l
APTT	42.9	sec	K	4.7	mmol/l
FDP	8.8	μg/ml	Ca	7.9	mg/dl
D-dimer	3.9	μg/ml	P	4.4	mg/dl
			CRP	15.2	mg/dl

Table 1

[Image]
Chest X ray (Fig. 1): infiltration shadows in right upper and lower lung fields
Chest CT (Fig. 2. February 29, 2020): multiple infiltrates and ground-glass opacities in both lung fields.

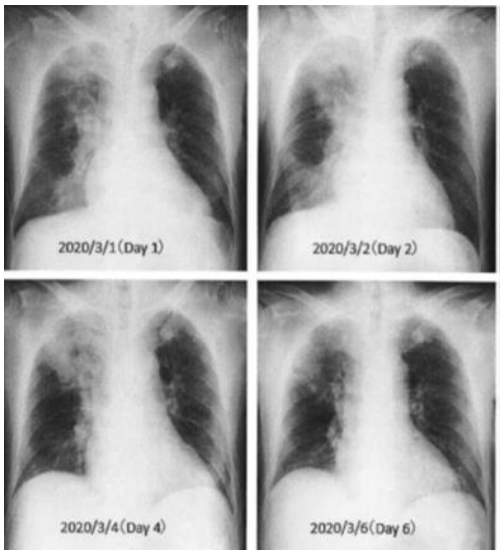

Fig. 1

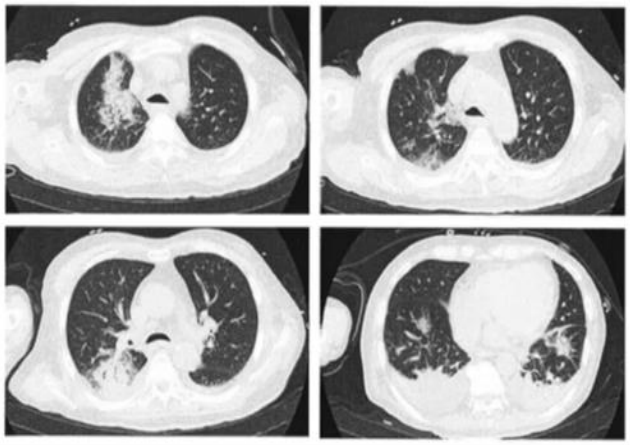

Fig. 2

[Progress after hospitalization]
On the day of hospitalisation, he required 5-8L/min of oxygen. Considering coexistence of other pathogens, meropenem (MEPM) and levofloxacin (LVFX) were started for bacterial and atypical pneumonia. Peramivir was given intravenously for 2 days considering the persistence of influenza virus. Hemodialysis was started on the second day of hospitalization. On the same day, a chest X-ray (Fig. 1) showed a worsened pneumonia in the right upper lung field. To prevent further deterioration of the condition, oral administration of hydroxychloroquine sulfate (product name: Plakenil) was started for the treatment of COVID-19. Because of malaise and anorexia since the admission, he was started tube feeding on the third day. On Day 3-4, oxygen administration decreased to 3-4L/min, and chest radiographs (Fig. 1) on day 4 showed an improvement of pneumonia in the right lower lung field. On Day 5, he didn't need oxygen no more and his cough improved significantly. Fever of 38°C or higher was observed until Day 4, but fever was resolved after Day 5. The chest X-ray on Day 6 (Fig. 1) showed significant improvement of pneumonia in the right upper lung field, and laboratory findings showed improvement of inflammation. Antibacterial drugs, hydroxychloroquine, and tube feeding were stopped until Day 11. He was discharged from our hospital on Day 19 after the SARS-CoV-2 PCR test becomes negative twice.

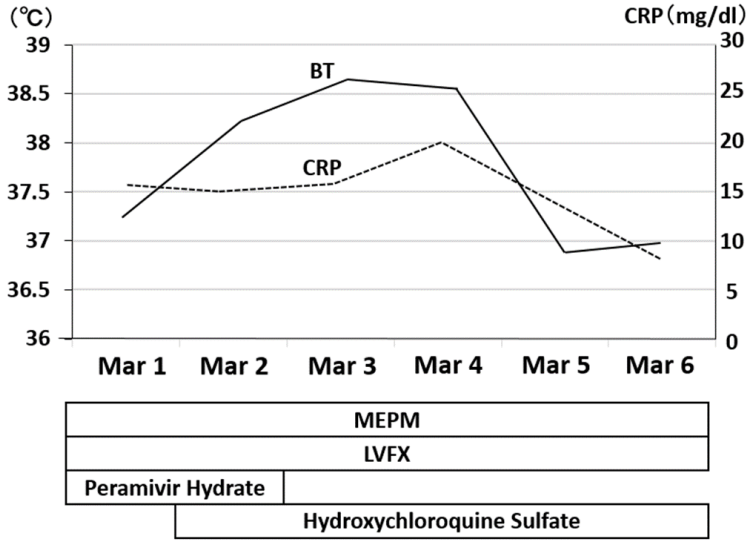

Table 2

Discussion

We report a case of hemodialysis patient suffering from COVID-19. Despite of a detailed interview, the route of transmission was undetermined. After admission, the pneumonia progressed, and his condition became worse considering for rescue breathing by endotracheal intubation. However, his condition improved on Day 2-3. Although antibiotic, peramivir, didlysis may have been effective, hydroxychloroquine was considered to be the most effective. Chloroquine has been used for many years as a treatment and prevention for malaria. And in recent years, chloroquine has been used as hydroxychloroquine for collagen diseases such as cutaneous and systemic lupus erythematosus. Chloroquine phosphate was used for Severe Acute Respiratory Syndrome (SARS) that spread from 2002 to 2003. Chloroquine phosphate was used for COVID-19 in China with clinical efficacy [1)]. Chloroquine has been reported to have antiviral activity against SARS-CoV-2 in vitro [2)] and considered to enhance therapeutic effect synergistically in vivo due to its immunomodulatory effect. This time, the administration dosage was based on the same dosage used for cutaneous and systemic lupus erythematosus. The dosage for dialysis patients has not been fixed, and we should administer this drug carefully when they have renal or hepatic dysfunction. The unchanged urinary excretion rate of hydroxychloroquine is 23-25% [3)], and it mainly

involves hepatic metabolism. We decided to administer the drug without reducing, because he urinated despite dialysis and the duration of treatment is short. The consent of the patient and family was obtained, and the in-house ethics committee approved the usage of this drug. It is considered that the distribution volume (Vd) of hydroxychloroquine is large and almost not removed by dialysis [4]. Hydroxychloroquine is known as a relatively safe drug under proper use, but its main side effects include nausea, diarrhea, retinopathy, rash, myelosuppression, cardiomyopathy, muscle weakness, hypoglycemia, headache, pigmentation and so on. The incidence of side effects can increase with higher doses and long-term administration. When cumulative dose reach 200g or more, side effects can occur easily in elderly patients or hepatic and renal dysfunction patients. Safety for pregnant women and children under 6 has not been established.

Although there remains the possibility that his condition improved as a natural course, we concluded that hydroxychloroquine worked effectively in this case. There is no established treatment for COVID-19, and it is necessary to empirically search for new treatments. There have been few cases reported in Japan receiving hydroxychloroquine for COVID-19, and further case accumulation is important.

Conflict of interest self-assessment: nothing to declare

Reference

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