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Case Report

Severe olfactory and gustatory dysfunctions in a Japanese pediatric patient with coronavirus disease (COVID-19)

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ABSTRACT

Coronavirus disease (COVID-19) is often characterized by abnormal olfactory and gustatory symptoms in adults; however, detailed studies on pediatric patients with COVID-19 are extremely limited. A 13-year-old Japanese girl presented with fever and cough, and after 2 days, her olfactory and taste sensations suddenly disappeared. A real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was performed using a nasopharyngeal swab. Because a positive result was seen, she was admitted on the 7th day of illness. On admission, the visual analogue scale (VAS) score for smell and taste was 0 of 100%. An intravenous olfaction test using prosultiamine (Alinamin test) was performed on the 15th day of illness to evaluate olfaction, and an increase in latency (33 seconds) and a decrease in duration (55 seconds) were observed. In the odor identification test using 12 different odor cards, only 7 odors were correctly identified. On the 18th day of illness, SARS-CoV-2 tested negative in the RT-PCR test; simultaneously, the VAS score for smell and taste fully improved to 100 of 100%. On the 77th day of illness, full recovery was confirmed in the Alinamin test (latency, 7 seconds; duration, 82 seconds). In this present case, an improvement in olfactory and gustatory dysfunctions was observed with negative results in RT-PCR test for SARS-CoV-2.

1. Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection is characterized by not only cold-like symptoms, such as fever and cough, but also pneumonia (coronavirus disease [COVID-19]) [1,2]. Olfactory and gustatory dysfunctions are also well-known symptoms of COVID-19 in adults [2–4]. In a European study, the incidence of olfactory and gustatory dysfunctions associated with COVID-19 in adults is reported to be >80% [2]. Although the severity varies from mild to severe, >80% of adult patients have the severe type of the disease [4]. Female sex and young age are risk factors associated with olfactory dysfunction in COVID-19 in adults [4]. Meanwhile, data of pediatric patients with COVID-19 with olfactory and gustatory dysfunctions are limited [5], and there are no reports on the detailed clinical course of pediatric COVID-19 patients exhibiting olfactory and gustatory dysfunctions.

Here, we present a case of a Japanese pediatric patient with COVID-19 exhibiting severe olfactory and gustatory dysfunctions. The virologic and olfactory/gustatory tests were conducted throughout the clinical course. The institutional review board of Nihon University Itabashi Hospital approved this case study with written informed consent from the patient and parents (approval number: RK-200714-4).

2. Case report

A previously healthy 13-year-old Japanese girl presented with fever and cough; after 2 days, her olfactory and taste sensations suddenly disappeared. A real-time reverse transcriptase-

Abbreviations: ACE-2, angiotensin-converting enzyme 2; COVID-19, coronavirus disease 2019; CT, computed tomography; Ig, immunoglobulin; RT-PCR, real-time reverse transcriptase-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VAS, visual analogue scales.

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polymerase chain reaction (RT-PCR) test for SARS-CoV-2 detection was performed using a nasopharyngeal swab. Because the RT-PCR result was positive, she was admitted to our hospital on the 7th day of her illness.

The patient did not have any underlying medical disease. There were no recent overseas travels or attending school for >1 month before admission. Regarding family history, her mother had fever and cough 4 days before the patient exhibited the symptoms. Subsequently, because respiratory distress developed 3 days before the patient hospitalized, her mother was diagnosed with COVID-19 pneumonia based on the multiple infiltrative shadows on chest computed tomography (CT) and a positive RT-PCR result for SARS-CoV-2. Her mother was treated with favipiravir and ciclesonide.

Upon admission, height and weight of the patient were 164.0 cm and 45.5 kg, respectively. Her vital signs were as follows: body temperature was 37.0 °C, heart rate was 78 beats per min, respiratory rate was 18 breaths per min, blood pressure was 118/65 mmHg, and transcutaneous oxygen saturation was 99% on room air. No fever or upper respiratory symptoms were noted at the time of admission and her consciousness was clear. No throat redness was observed. Chest and abdominal physical findings were normal. Visual analogue scale (VAS) score for smell and taste was 0 of 100%. The smell of curry was not distinguished by the patient; moreover, she could not distinguish among sweetness, bitterness, and sourness.

Laboratory and radiological findings on admission were as follows: No increase in inflammatory reactions and abnormality in liver function or electrolytes were found in the routine blood tests. Serum zinc and copper levels were 63 μg/dL and 95 μg/dL, respectively. Chest CT did not reveal infiltrative shadows in the lung fields (Table 1). In the serum SARS-CoV-2 antibody test (Innovate Biological Technology Co., Ltd., Hebei, China), both SARS-CoV-2 immunoglobulin (Ig) G and IgM were negative.

The clinical course is shown in Fig. 1. After admission, the patient was followed up without any medications. No exacerbations of fever or cough were observed during hospitalization. The olfactory and gustatory dysfunctions persisted, and the VAS score remained at 0 of 100%. A tendency toward improvement was noted from the 14th day of illness. An intravenous olfaction test using thiamine propyl disulfide (Takeda Pharmaceutical Co., Ltd., Osaka, Japan), known as Alinamin test, was performed to evaluate olfaction on the 15th day of illness. The results showed an increase in latency (33 seconds) and decrease in duration (55 seconds) (normal adult subjects: latency of 5–10 seconds and duration of 60–90 seconds) [6]. On the 15th day of illness, the odor identification test using 12 different odor cards (Open Essence, FUJIFILM Wako Pure Chemical Corp., Osaka, Japan) was performed to evaluate the severity of olfactory dysfunction when the patient felt the recovery. As a result, 7 of 12 odors were correctly identified (normal adult subjects: 10 for men and 11 for women) [7]. The repeated Alinamin test on the 21st day of illness showed a latency of 20 seconds and duration of 33 seconds, indicating a tendency toward improvement in latency, but no improvement in duration was observed with unknown reasons. RT-PCR results for SARS-CoV-2 detection were positive on the 9th, 10th, 13th, and 16th days of illness and negative on the 18th day of illness; simultaneously, the VAS score for smell and taste fully improved to 100 of 100%. Positive results in detecting serum SARS-CoV-2 IgG, but not IgM, were found on the 14th and 20th days of illness. After the negative RT-PCR result for SARS-CoV-2 was confirmed on the 20th day of illness, she was discharged on the 23rd day of illness.

After discharge, the Alinamin test was repeated on the 52nd day of illness and revealed latency of 20 seconds and duration of 87 seconds, showing marked improvement in duration. Finally, on the 77th day of illness, full recovery was confirmed in the Alinamin test (latency, 7 seconds; duration, 82 seconds).

Table 1
Laboratory and radiological findings on admission.

Hematological test		Biochemical test	
WBC	6500/μL	TP	6.9 g/dL
Net	57.0%	Alb	4.4 g/dL
Lymph	38.0%	AST	18 U/L
Eo	2.0%	ALT	12 U/L
Baso	0.0%	LDH	145 U/L
Mono	2.0%	CK	43 U/L
Aty lym	1.0%	UN	12.0 mg/dL
Hb	14.0 g/dL	Cr	0.54 mg/dL
Plt	26.1 × 10^4/μL	Sodium	142 mEq/L
		Potassium	4.1 mEq/L
Coagulation test		Chloride	105 mEq/L
PT%	86%	CRP	0.10 mg/dL
INR	1.08	Serum iron	87 μg/dL
APTT	33.8 sec	Serum zinc	62 μg/dL
Fibrinogen	283 mg/dL	Serum copper	95 μg/dL
D-D dimmer	1.0 μg/mL	IgG	924 mg/dL
		IgA	248 mg/dL
		IgM	68 mg/dL
Chest computed tomography		C3	90 mg/dL
No infiltrative shadows in the lung fields		C4	20 mg/dL
		CH50	50.5 U/mL
		Ferritin	40.8 ng/mL

Alb, albumin; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; CK, creatine kinase; Cr, creatinine; CRP, C-reactive protein; Hb, hemoglobin; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; INR, international normalized ratio; LDH, lactate dehydrogenase; Plt, platelet; PT%, prothrombin time%; RBC, red blood cell; TP, total protein; UN, urea nitrogen; WBC, white blood cell (Net, neutrophils; Eo, eosinophils; Mono, monocytes; Lymph, lymphocyte; Baso, basophils; Aty lym, atypical lymphocytes).

3. Discussion

SARS-CoV-2 invades the angiotensin-converting enzyme 2 (ACE-2) receptor, which is thought to be a therapeutic target for COVID-19 [8,9]. As a mechanism of olfactory and gustatory dysfunctions in COVID-19, SARS-CoV-2 may be directly or indirectly mediated via the ACE-2 receptor in nerve cells and may cause some neurological symptoms [9]. ACE-2 gene expression in the nasal mucosa has been reported to be age-dependent and lower in children than in adults [10]; therefore, it may contribute to the low incidence of olfactory and gustatory dysfunctions in pediatric patients with COVID-19 [5].

The VAS can be used to subjectively and easily evaluate taste and olfactory sensations. In this method, the normal or usual olfactory and gustatory statuses are shown as 100%, and the current status is self-reported. In this case, we mainly used VAS for the quantitative evaluation of olfactory and gustatory dysfunctions associated with COVID-19 over hospitalized duration to prevent nosocomial SARS-CoV-2 infection.

Other assessments of olfaction sensation such as the Alinamin test and Open Essence were also used. The Alinamin test is performed by intravenous administration of propyl disulfide [11]. Latency, which was defined as the time between the initiation of injection and recognition of the odor (garlic smell), and duration, which was defined as the time between the recognition and disappearance of the odor, are measured. Furukawa et al. showed that latency is influenced by olfactory acuity and duration depends on olfactory adaptation [11]. They have also reported that non-responders to the Alinamin test had poor recovery [11], indicating that the Alinamin test can estimate the prognosis of olfaction. In this case, although the Alinamin test was performed and showed abnormal results on the recovery phase (15th day of illness), a positive response to the Alinamin test was confirmed. Open

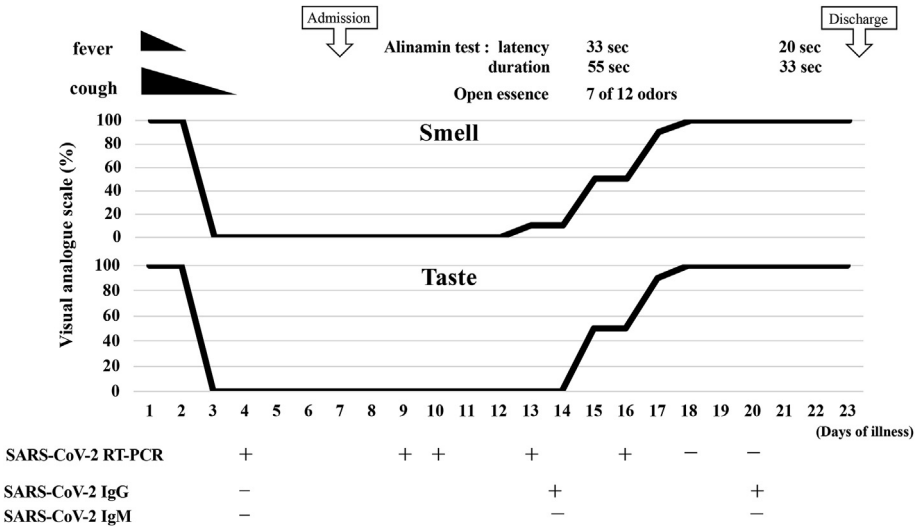

Fig. 1. Clinical course of the patient. Ig, immunoglobulin; RT-PCR, real-time reverse transcriptase-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; sec, seconds.

Essence, which is a Japanese odor identification test using 12 different odor cards, was also performed and it showed partially correct answers. Finally, full recovery of olfactory dysfunction in the patient confirmed.

RT-PCR tests for SARS-CoV-2 detection were performed intermittently during the hospitalized period. A negative result was confirmed on the 18th day of illness. Although no reports were found on pediatric patients with COVID-19 exhibiting olfactory and gustatory dysfunctions, Qiu et al. reported that the duration of RT-PCR positivity for SARS-CoV-2 in pediatric patients with COVID-19 was an average of 9 days for mild and 11 days for moderate type cases [12]. This suggests that the duration of RT-PCR positivity in the present case was long.

As a limitation, olfactory and gustatory dysfunctions were assessed using only VAS during the early phase of COVID-19 in the patient, because of the retrospective case report.

In conclusion, we reported the clinical course in a pediatric patient with COVID-19 with severe and transient olfactory and gustatory dysfunctions. In this present case, an improvement in olfactory and gustatory dysfunctions was observed with negative results in RT-PCR test for SARS-CoV-2.

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Authorship

All authors meet the following ICMJE authorship criteria:

All authors contributed to the intellectual content of this manuscript. YK and IM wrote the first draft of this manuscript. YK, KNi, and IM designed this study. YK, KNi, HG, KNa, SS, and KK were pediatricians who cared for the patient and collected the clinical data. MT and TO performed otolaryngological examinations and collected the data. All authors revised the work critically for important intellectual contents and approved the final version of this work.

Declaration of competing interest

None.

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