

**A family case of COVID-19 pneumonia with different chest CT features and duration of SARS-CoV-2 shedding: a case report from Japan**

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## Summary

Coronavirus disease 2019 (COVID-19) pneumonia in children characteristically has a milder clinical presentation, with milder inflammatory biomarkers and radiological findings. Accumulating evidence indicates a difference in chest computed tomography (CT) features and duration of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) shedding between children and adults. Here, we report a family case of COVID-19 pneumonia in which two brothers (age 14 years and 2 years) had different findings. On admission, the 2-year-old had few symptoms with no sign of pneumonia, whereas the older brother had presented with pneumonia on admission. Both were positive for SARS-CoV-2 infection on polymerase chain reaction. They both had obvious characteristic signs of COVID-19 pneumonia on chest CT. However, CT findings in the younger brother were non-specific and similar to other pneumonias. The older brother required longer treatment because of a longer shedding period of SARS-CoV-2 detected in nasopharyngeal samples. Both boys were discharged without complications. This family case suggests that the clinical features of COVID-19 pneumonia might differ between younger and older children.

## Text

A previous report suggested that not only the clinical symptoms but also the chest computed tomography (CT) features of children with coronavirus disease 2019 (COVID-19) are different from those of adults (1). In addition, the duration of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) shedding in children is currently not well documented. Informed consent was obtained from the parents of patients and assent was obtained from children considered old enough (> 9 years old).

In this family case, the father and mother (both aged mid-forties) and their two sons (aged 14 years and 2 years) presented with clinical symptoms. The 2-year-old and then subsequently his mother and older brother were treated at our hospital.

A week before the 2-year-old's admission, his father was admitted to the intensive care unit at another hospital and placed on mechanical ventilation with a diagnosis of severe COVID-19 pneumonia. His mother and brother were diagnosed with mild pneumonia at another hospital. Three days before his admission to us, the 2-year-old's body temperature was elevated (37.6°C). Coughing and nasal discharge started the day before admission. Based on his history of close contact with a family member with COVID-19 pneumonia, he was regarded as highly likely to have COVID-19 pneumonia and was transferred to our hospital.

On presentation, the 2-year-old had mild symptoms including coughing and nasal discharge. Laboratory tests showed white blood cell count (WBC) of 7,300/ $\mu$ L (hemogram not examined), lactate dehydrogenase (LDH) of 289 U/L, and C-reactive protein (CRP) of 0.06 mg/dL. Chest radiography showed no evidence of pneumonia (Figure 1A). However, chest CT showed multiple ground-glass opacities (GGO) distributed bilaterally (Figure 2A). Similarly, his older brother had GGO on chest CT (Figure 2B), although chest radiography revealed no signs of pneumonia (Figure 1B). We started the patient and his brother on intravenous ceftriaxone (80 mg/kg/day) and oral azithromycin (10 mg/kg/day) for bacterial

pneumonia. On the night of admission, the patient had oxygen saturation around 94% with an elevated temperature (38.0°C), so we started oxygen at 1 L/min of via a nasal canula. On hospital day 2, oxygen administration was stopped and his temperature dropped naturally. Because the results of real-time polymerase chain reaction (PCR) on admission was positive for all 3 family members, we stopped the intravenous ceftriaxone and oral azithromycin for both boys. On hospital days 7 and 10, the 2-year-old had consecutive negative real-time PCR results for SARS-CoV-2.

For his brother, however, real-time PCR results took longer to come back negative. His symptoms were coughing, nasal discharge, and fatigue on admission. On the night of hospital day 2, oxygen saturation was around 93% and he was administered 0.5 L/min oxygen via a nasal canula. He became symptom-free around hospital day 8. Laboratory data showed WBC 9,100/ $\mu$ L (hemogram not examined), LDH 171 U/L, and CRP 3.80 mg/dL. He had consecutive negative real-time PCR results for SARS-CoV-2 on hospital days 23 and 24.

Their mother had presented with coughing. Laboratory data showed WBC 6,300/ $\mu$ L (neutrophils 60.7%, lymphocytes 29.2%, monocytes 5.0%, eosinophils 4.8%, and basophils 0.3%), LDH 183 U/L, and CRP 0.52 mg/dL. Chest radiography showed GGO in the left lower lobe, and chest CT revealed GGO in the left upper and middle lobes and bilaterally in the lower lobes (Figures 1 and 2C). She had consecutive negative real-time PCR results for SARS-CoV-2 on hospital days 10 and 12. The three family members were discharged together without any complications.

In our case, the brothers' chest CT findings showed signs of pneumonia that were consistent with COVID-19 pneumonia. A recent study by pediatric radiologists reported that chest CT in 24 pediatric patients with COVID-19 revealed abnormalities including GGO (88%), consolidation (58%), linear opacities (33%), and nodules (25%) and mainly involved the lower lobes (2). The same study also described the CT findings of children as being more

centrilobular or peribronchovascular (tree-in-bud pattern) compared with those of adults (2). Other studies of COVID-19 patients have shown more localized GGO and more common peribronchial opacities in children than in adults (3, 4). Of particular interest in our family case series is the difference in chest CT findings between the younger and older brothers—the younger brother had a centrilobular pattern and the older brother had a peripheral pattern of opacities similar to that seen in adults. A possible explanation for this difference between the boys might be that the greater upper airway resistance in younger children may result in greater deposition of aerosol particles in the tracheobronchial tree than in the alveoli (5). Given that chest CT findings in children with COVID-19 are often non-specific and similar to those of other lower respiratory infections such as mycoplasma, adenovirus, influenzae type A, and human metapneumovirus (6, 7), it is difficult to distinguish CT findings of COVID-19 pneumonia from those of other pneumonias (2).

We also found differences durations of SARS-CoV-2 shedding in nasal discharge between the very young and adolescent brothers. Lu et al. reported that prolonged duration of viral shedding in 110 children with COVID-19 was associated with fever, pneumonia, and lymphocyte counts  $<2,000/\mu\text{L}$  (8). Xu et al. reported the mean SARS-CoV-2 shedding times in children of  $11.1\pm 5.8$  days in symptomatic cases from symptom onset and  $9.4\pm 5.1$  days in asymptomatic cases (9). Also, older age was found to be associated with delayed clearance of SARS-CoV-2 in nasopharyngeal samples (10, 11). This may be due to the age-dependent expression of angiotensin-converting enzyme 2 (ACE-2), which is a proven cell receptor for SARS-CoV-2 (12), in the nasal epithelium. Bunyavanich et al. demonstrated that angiotensin-converting enzyme 2 gene expression in nasal epithelium was significantly greater in older children (age 10 to 17 years) than in younger children (age  $<10$  years) (13).

The proposed hypothesis to explain the difference in severity of COVID-19 between children and adults included putting adults at higher risk and protecting children; as such,

age-related increase in endothelial damage and changes in clotting function, higher density, increased affinity and different distribution of ACE-2 receptors, and differences in innate and adaptive immunity (14). Differences in immune responses among children and adults to SARS-CoV-2 may be due to higher levels of cross-neutralizing antibodies, immature B and T cells and higher regulatory T cell response, and lower IL-6 and TNF- $\alpha$  production, limiting inflammatory response (15).

The features of COVID-19 pneumonia in children are different from those in adults and may also differ between younger and older children. To the best of our knowledge, this is the first report to show potential age differences in the clinical features of COVID-19 pneumonia in children. Further study is required to elucidate the pathogenesis of pediatric COVID-19 pneumonia.

#### **Conflict of interest**

None to declare.

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## **Figure legends**

### **Figure 1**

Posteroanterior chest radiographs on admission for the same-family cases of COVID-19 pneumonia. Bilateral peribronchial thickening in (A) the 2-year-old boy and (B) the 14-year-old brother. (C) Ground glass opacities in the left lower lobe of the 46-year-old mother.

### **Figure 2**

Chest CT images of the 3 cases. (A) GGO and consolidation in the left lower lobe showing a centrilobular pattern in the 2-year-old boy. (B) GGO in the right lower lobe only in the 14-year-old brother. (C) GGO in the left upper and middle lobes and in both lower lobes in the 46-year-old mother.

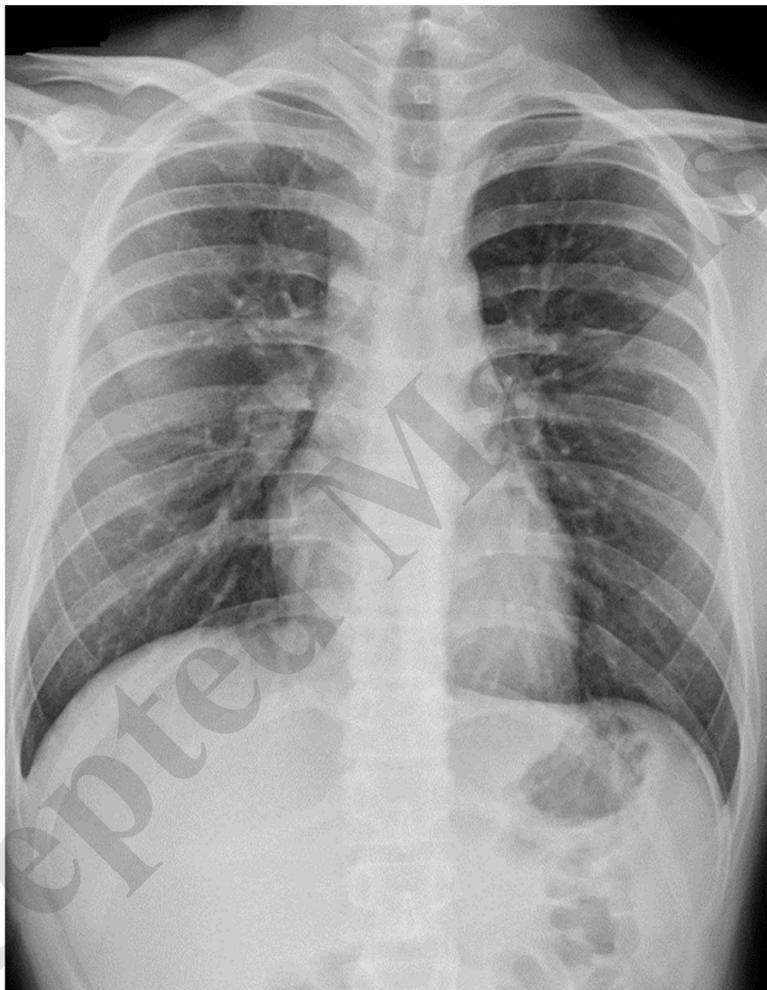
### **Figure 3**

Clinical course, viral load of the same-family cases.

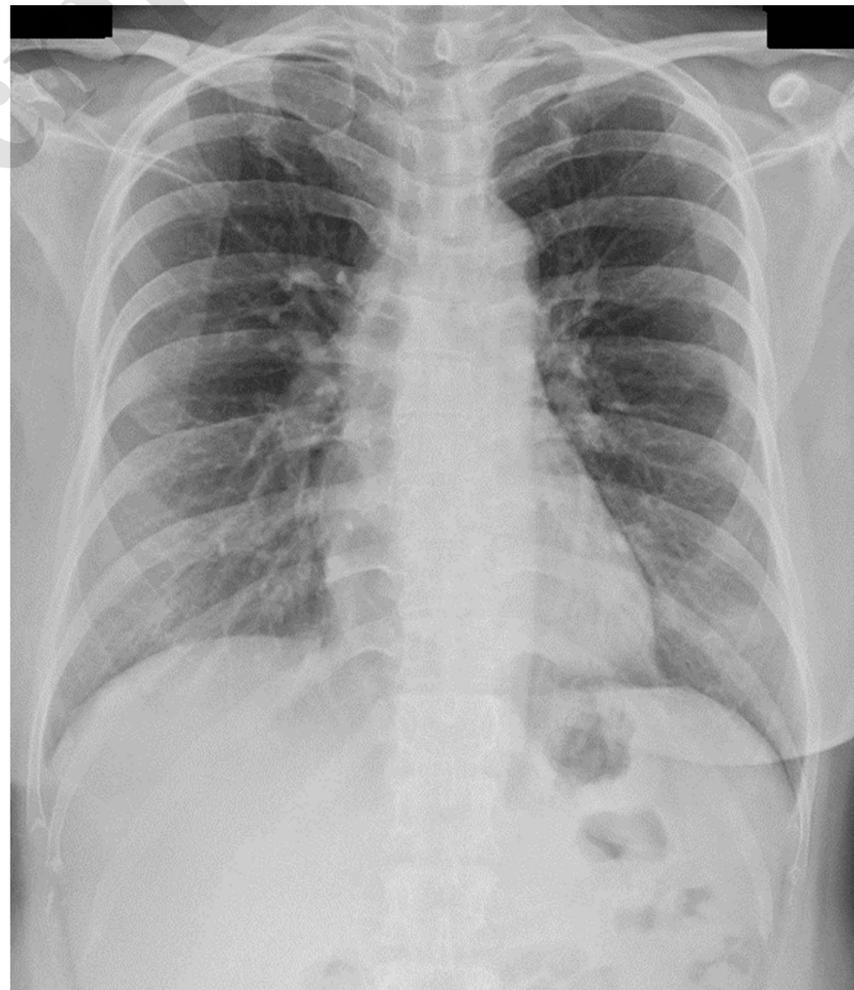
A



B



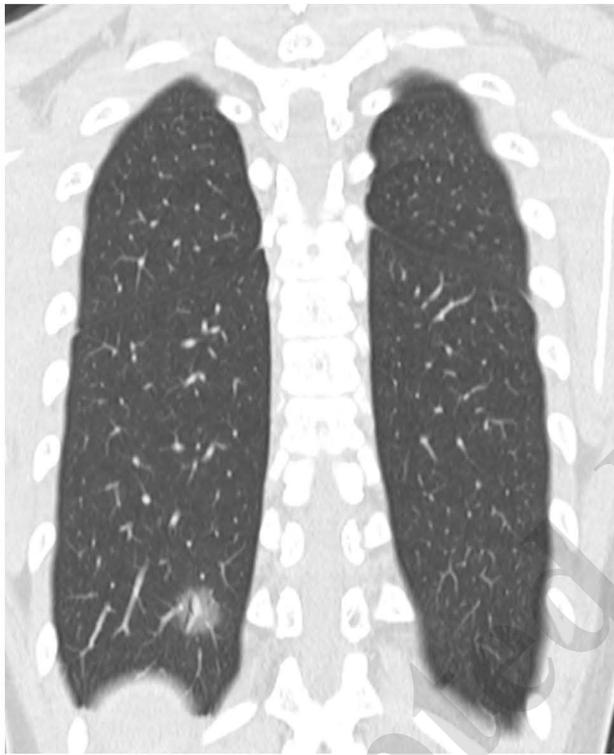
C



A



B



C

