Case Report

Mycoplasma Respiratory Infection Mimicking COVID-19

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Keywords

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Abstract

In the current pandemic with SARS-CoV-2, children can present with severe acute respiratory infection, qualifying as COVID-19 according to published guidelines. However other etiologies should not be overlooked. We present a case of a 10-year old boy with Down syndrome, who presented with fever and respiratory failure. A CT scan of the lungs showed lesions very suggestive of COVID-19. He was admitted to an intensive care unit because of deep hypoxemia requiring high flow nasal oxygen. Polymerase chain reaction on nasopharyngeal swabs was repeatedly negative for SARS-CoV-2 but positive for *Mycoplasma pneumoniae*.
This case report illustrates possible diagnostic pitfalls when treating children in this pandemic.

Introduction

Since December 2019 there has been a rapid spread of the new coronavirus SARS-CoV-2, first within China, but then quickly to the rest of the world. The first epidemiological studies in the Chinese population show that children represent only 2.2% of the total number of infections and that infection is generally less severe with a negligible mortality (1,2-4). Subsequent reports from Europe confirm the low burden of SARS-CoV-2 in children, with very few admissions to intensive care, even in children with immunosuppression (5-8). Whether this is from shielding by school closures or by a reduced susceptibility to infection remains unclear (9).

The gold standard diagnostic test for SARS-CoV-2 infection is a polymerase chain reaction (PCR) on a respiratory sample, in most cases a nasopharyngeal swab. CT scan of the lungs has been put forward as an alternative way of diagnosing COVID-19 because of bronchoalveolar lavage (BAL) proven SARS-CoV-2 infection in swab negative adults (10,11). An acute respiratory infection with compatible chest CT and negative PCR is accepted as case definition of SARS-CoV-2 infection in several guidelines and many adult cases of were diagnosed based on CT findings (12).

We report a case of a child with Down syndrome presenting with a severe respiratory infection. According to adult guidelines, he was diagnosed with COVID-19 based on the highly suggestive findings on chest CT scan. SARS-CoV-2 PCR tests on nasopharyngeal swabs were repeatedly negative, and *Mycoplasma pneumoniae* was eventually shown to be the cause of the respiratory infection.

Case Presentation

On March 30th 2020, a 10-year old boy with trisomy 21 presented at the emergency department of our regional hospital with a two weeks' history of gradually worsening dyspnea and cough, despite treatment with oral amoxicillin and inhaled bronchodilators. The child had been treated in an intensive care setting for a respiratory infection at the age of 6 weeks and had a history of viral induced wheezing and immunodeficiency (lymphocytopenia and hypogammaglobulinemia) for which he received intravenous immunoglobulins from 2010 till 2017 through an implantable venous access device (Port-a-Cath), discontinued after recovery of peripheral blood lymphocytosis and serum immunoglobulin levels. No frequent or severe infections were reported during the last 3 years. The boy had no cardiac malformation. He suffered from psychomotor retardation and hypotonia, compatible with trisomy 21.

At presentation the patient was afebrile and somewhat apathic. Heart rate was 110 bpm, blood pressure 124/88 mm Hg, pulse oxygen saturation in ambient air was 78%. He was dyspneic with a respiratory rate of 64/min, chest retractions and use of accessory respiratory muscles. Poor air entry, diffuse fine crackles and wheezing were noted on chest auscultation. Heart sounds were normal. Liver was palpated at 6 cm below the right costal margin.

Arterial blood gases showed mild hypercapnia and mild hypoxemia. Oxygen by face mask and inhaled bronchodilators resulted in slight temporary improvement in oxygen saturation. Prednisolone IV 1 mg/kg was administered given the history of hyperreactive airways and wheezing. A third-generation cephalosporin was started.

Laboratory testing (Table 1) showed increased inflammatory markers, normal levels of immunoglobulins, raised aminotransferases, troponins and D-dimers. *M. pneumoniae* IgM was positive. A nasopharyngeal swab to test for COVID-19 was collected.

A bedside chest X-ray showed a limited confluent density in the right lung base. Given the discrepancy between severe hypoxemia and mild X-ray changes, a CT scan of the lungs was made before transfer to a tertiary care center with pediatric intensive care facilities, according to the current local 'COVID-guidelines'. The chest CT showed ground glass opacities in all lobes and was scored as very suggestive of an infection with the SARS-CoV-2 according to a standardized local protocol designed for the COVID epidemic based on recent literature (Figure 1) (13).

On arrival at the tertiary center, a cardiac ultrasound confirmed mild right ventricular dysfunction, pulmonary hypertension and a small pericardial effusion. Diuretics were started in combination with low molecular weight heparin (LWMH) at prophylactic dose. High flow nasal oxygen (HFNO) was delivered with a maximal FiO_2 of 1.0. Azithromycin was added to cefotaxime. Given the high oxygen requirements and increase in pCO_2 to 75 mmHg on venous blood gases, the child was transferred to the intensive care COVID unit. Supportive care was continued, with resolution of the hypercapnia and right heart failure after 48 hours and weaning of HFNO after 72 hours upon which the patient could be transferred to a pediatric infectious disease ward.

Four SARS-CoV-2 PCR tests on nasopharyngeal swabs over 48 hours were negative. The semi-quantitative PCR for *M. pneumoniae* obtained from the nasopharyngeal swab was strongly positive, in line with the positive serum

Table 1 Laboratory data on admission*

Variable	Value	*Reference Range*
Hemoglobin (g/dl)	12.2	*(11.5-15.5)*
White cells (per mm^2)	18,610	*(4,500-13,500)*
Absolute neutrophil count (per mm^2)	12,700	*(2.00-7.50)*
Absolute ymphocyte count (per mm^2)	3,160	*(1.50-4.00)*
Platelet count (per mm^2)	133,000	*(150,000-400,000)*
C-Reactive Protein (mg/liter)	105.1	*(<5.0)*
Prothrombin time (sec)	20.6	*(10-14.1)*
Activated partial thromboplastin time (sec)	27.2	*(24.6-38.4)*
Prothrombin time international normalized ratio	1.76	*(1.00-1.20)*
Fibrinogen (mg/dl)	328	*(276-471)*
D-dimers (ng/ml)	85 612	*(69-580)*
Blood urea nitrogen (mg/dl)	41.5	*(10.8-38.4)*
Creatitine (mg/dl)	0.54	*(0.26-0.77)*
Troponine I (ng/ml)	26.9	*(<17.5)*
Brain natriuretic peptide (pg/ml)	1180	*(0-99)*
Aspartate aminotransferase (U/liter)	998	*(<50)*
Alanine aminotransferase (U/liter)	1613	*(<50)*
Lactate dehydrogenase (U/liter)	1174	*(110-295)*
Mycoplasma pneumoniae IgM	positive	

* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values of creatinine to micromoles per liter, multiply by 88.4.

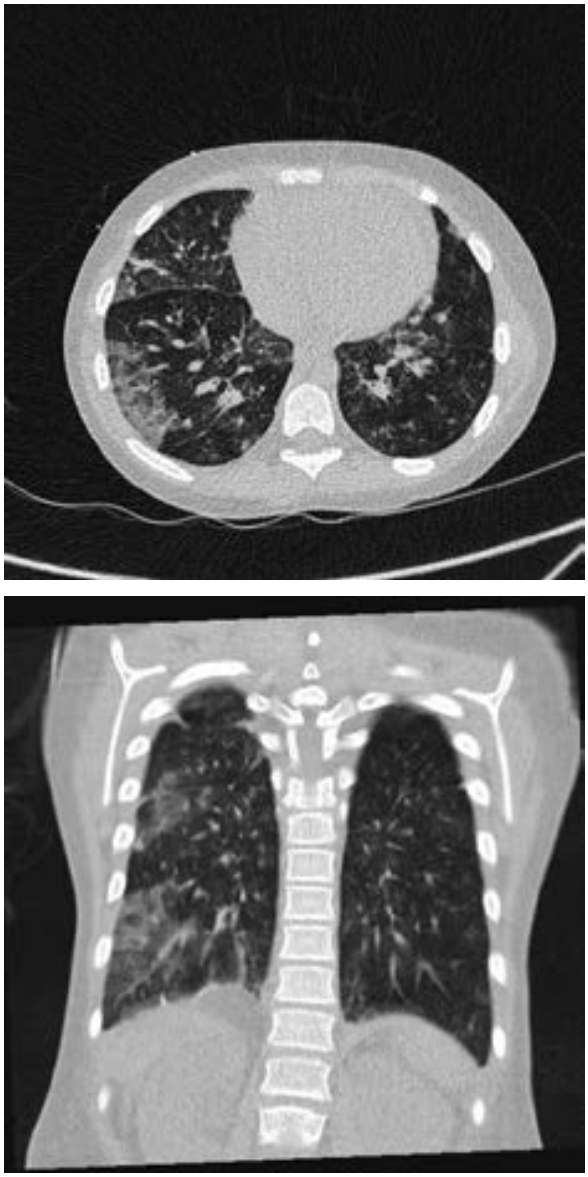
IgM for *M. pneumoniae*. A respiratory panel (containing 29 pathogens) confirmed a positive PCR for M. *pneumoniae* as well as herpes-simplex virus 1. Serology (Abbott semi-quantitative antibody test, IgG) for SARS-CoV-2 was negative 2 weeks after the onset of symptoms.

At day 11, low grade fever and need for supplemental oxygen persisted. A CT pulmonary angiography confirmed pulmonary embolism that was suspected because of the presence of an implantable IV access, pulmonary hypertension, and elevated D-dimers. LMWH was started at therapeutic doses. A repeat SARS-CoV-2 PCR was strongly positive (Cycle threshold (Ct) value 16,8). At that point serology for SARS-CoV-2 remained negative, demonstrating a probable nosocomial infection. Oxygen therapy could be stopped on day 16 and laboratory tests returned to normal. One week after the positive PCR, the serology also became positive. The patient was discharged from the hospital on day 18. On a follow-up visit 6 weeks later SARS-Cov-2 IgG were still positive. The immunological screening completed with a pneumococcal antibody response was normal.

Discussion

This patient with Down syndrome and a past medical history of ill-defined immunodeficiency presented with a severe respiratory infection leading tot respiratory failure requiring transfer to intensive care. The disease was characterized by fever, bronchial obstruction, profound hypoxemia and multifocal interstitial pneumonia on CT scan. The patient fulfilled the case definition for COVID-19, despite the negative PCR for SARS-CoV-2, and was cohorted accordingly. The impaired coagulation and elevated D-dimers contributed to the initial diagnosis. Research in adult population shows that severe COVID-19 is associated with a higher incidence of thromboembolic events (14). Other possible pathogens were also considered and treated, such as bacterial pneumonia with cefotaxime and atypical pneumonia with azithromycin. *Pneumocystis carinii* was considered unlikely given the normal lymphocytosis. Definitive results with a positive *M. pneumoniae* PCR and IgM, repeatedly negative SARS-CoV-2 PCR and negative serology 2 weeks into the respiratory symptoms make *M. pneumoniae* the most likely etiologic agent of the respiratory infection in this child. SARS-CoV-2 PCR on a nasopharyngeal swab can produce a false negative result, especially in the later stages of the disease where the virus still can be found in the lungs (15). However, we

Figure 1. Chest CT images (A,B) showing peripheral ground glass opacities



found evidence of an acute infection with *M. pneumoniae*: PCR and IgM were both positive. Moreover, the patient did not have lymphocytopenia which is less likely for a severe COVID-19 and he had bronchial obstruction, which is not frequently reported in COVID-19 (3,4). Improvement was dramatic after the initiation of macrolide antibiotic therapy. No bronchoalveolar lavage was performed in the acute setting because of the risk of the procedure, nor later in the light of the diagnosis of *M. pneumoniae* infection with improvement with macrolides. SARS-CoV-2 serology turned out to be negative.

Interstitial pneumonia with severe hypoxemia is a rare but known presentation of atypical pneumonia caused by *M. pneumoniae*. Trisomy 21 is associated with frequent and more severe infections, with some degree of immunodeficiency, as well as with pulmonary hypertension during lung infections (16-18). Our patient has had a previous episode of severe respiratory infection and a documented, albeit transient period of lymphocytopenia and hypogammaglobulinemia. Acute or chronic pulmonary embolism likely contributed to the severity of the initial presentation.

This case illustrates two pitfalls that can arise during this COVID-19 pandemic. First, the continuous flow of information and profound changes in the organization of care, both highly focused on COVID-19, create a so-called 'availability heuristics' causing clinicians to think first about COVID-19, rather

than about other diseases. The epidemiology of COVID-19 is dramatically different in children and adults, with discordances in disease sensitivity, contagiousness, clinical picture and prognosis. Severe pulmonary disease in children does hardly occur. In the largest pediatric cohort with COVID-19 reported so far, the disease was more severe in children whose diagnosis of SARS-CoV-2 infection was not PCR confirmed, pointing out to the role of other (co) infections in severe cases and at least in some confirmed cases (2). One small case series reports coinfections with influenza, Mycoplasma, RSV or CMV in 8/20 children (19). Nevertheless, individuals with Down syndrome may have a higher risk for more severe COVID-19 due to the anatomic, immunologic and metabolic comorbidities associated with trisomy 21 (20-22). They have an increased occurrence of autoimmunity and certain antibodies (e.g. anti-type 1 interferon) have already been shown to be a significant risk factor for severe COVID-19 in adults (22). In observational studies hospitalized patients with Down syndrome and COVID-19 are younger and have a more severe disease than matched non-Down syndrome controls; so caution is still advised in this patient population (23).

Secondly, this case highlights an important specificity of the diagnostic pathway for COVID-19 in children. In several reports and guidelines, chest CT is proposed as a screening tool for the diagnosis of COVID-19 infection, arguing a better sensitivity than the SARS-Cov-2 PCR. It also provides quicker results. Preliminary evaluations estimate its sensitivity at 97% using the RT-PCR as reference, but with a specificity of only 25% (24). In children, ground glass opacities are reported as the most common abnormality on chest CT with an incidence between 33 and 60% in hospitalized children (3,4,25). Chest CT expose children to ionizing radiations, and little information is available about what to expect in children with COVID-19. In this patient, the suggestive imaging results led to the diagnosis of COVID-19 even before the PCR results were known. The patient was therefore admitted to a COVID intensive care unit, which eventually led to a probable nosocomial infection. However, given the very low probability of severe COVID-19 in children, confirmation with a very nonspecific diagnostic test such as chest CT is in general not warranted, as its positive predictive value will be very low in a disease with a low prevalence. Even with a highly suggestive CT scan, alternative diagnoses remain more likely than COVID-19 in children with severe pulmonary infections. Of course, caution is necessary in children with a higher risk for a more serious disease course. On the contrary, a negative PCR, which is a very sensitive test, has a good negative predictive value if well obtained.

Overlooking an alternative diagnosis in COVID-19 times, based on current guidelines (lung CT-scan) is a real pitfall in some pediatric patients, especially if the alternative is treatable. This is even more so when difficult ethical decisions have to be taken as to whom further intensive therapy can be offered.

Conflict of Interest:

The authors have no conflicts of interest to disclose.

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