

Autoimmune Hemolytic Anemia in a Pediatric Patient With Severe Acute Respiratory Syndrome Coronavirus 2 Infection

To the Editors:

Multiple clinical manifestations have been described in relation with coronavirus disease 2019 (COVID-19). However, no previously reported cases of autoimmune hemolytic anemia (AIHA) associated to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been described in children so far. We report a case of severe AIHA in a 13-year-old female with SARS CoV-2 infection.

The patient was admitted to our hospital because of a 7-day period of fever (37.5°C), asthenia, headache, and a syncope episode without loss of consciousness. She denied respiratory or gastrointestinal symptoms. At admission, she had tachycardia with hemodynamic stability and mucocutaneous pallor. No other abnormalities were found in physical examination. Personal history revealed a previous diagnosis of Psoriasis.

Results of blood tests showed decreased hemoglobin (6.3 g/dL), hematocrit (17.8%), mean corpuscular volume (90.4 fL), mean corpuscular hemoglobin (32 pg), and haptoglobin (<7.38 µmol/L) associating reticulocytosis (301,600 mm³). Increased lactate dehydrogenase (458 U/L) and hyperbilirubinemia (1.9 mg/dL) with indirect predominance (1.25 mg/dL) were found. Platelets and leukocytes count, serum ions, and transaminases were normal.

Coagulation and D-dimer did not alter; C-reactive protein (2 mg/L) and ferritin (148.6 ng/mL) were normal. Direct Coombs test was performed with a positive result (positive immunoglobulin G4 [IgG4] and negative C3d). Normal level of glucose-6-phosphate dehydrogenase was found.^{#8232};

Due to the pandemic situation, the reverse transcription-polymerase chain reaction test was performed with a positive result, with negative virus-specific immunoglobulin M and negative virus-specific IgG. Six days later, a new reverse transcription-polymerase chain reaction test was performed, with the

negative result but positive virus-specific IgG. Other viral infections were ruled out. Antinuclear, antiextractable nuclear antigens, and anticardiolipin antibodies were negative. Chest radiograph showed no alterations.

AIHA was diagnosed and treatment with methylprednisolone pulses (250 mg/daily) was given for the first 72 hours. Afterward, the maintenance dose with prednisolone 1 mg/kg daily was administered. Hemolysis reduced and 14 days later, the hemoglobin value increased to 10.6 g/dL and without the need for blood transfusions.

Recently, 2 studies reported some cases of AIHA associated with COVID-19 in adults.^{1,2} The median age of adult cases reported by Lazarian et al² was 62 years and all of them presented risk factors for developing a severe form of COVID-19. All cases started after the beginning of symptoms of SARS CoV-2 infection. In contrast, our patient did not have any known risk factor for severe SARS CoV-2 infection, did not suffer any respiratory symptoms and anemia was the only clinical manifestation associated with SARS CoV-2 infection.

The etiology of AIHA in pediatric population is mostly associated with viral and bacterial infections.³ However, in teenagers and young adults, there is an increased association with underlying systemic illness, most commonly immunodeficiencies and autoimmune disorders.

Our results, after ruling out immunodeficiency, autoimmune disorder, or other viral infection, suggest that SARS CoV-2 could have triggered AIHA, being the first pediatric case reported so far.

In conclusion, this case suggests that SARS CoV-2 can trigger AIHA in predisposed children. In the current epidemiologic situation, upon the finding of severe hemolytic anemia without any apparent cause in a previously healthy child, SARS CoV-2 infection should be ruled out.

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Is Nasopharyngeal Swab Comparable With Nasopharyngeal Aspirate to Detect SARS-CoV-2 in Children?

To the Editors:

In December 2019 appeared in China a novel coronavirus, designated as SARS-CoV-2, responsible for a pandemic respiratory disease, known as coronavirus disease, with the Italian outbreak from February 2020. Children appear to have milder symptoms and less severe disease.¹ The tests currently used for the direct identification of SARS-CoV-2 include specimens taken from the upper and the lower respiratory tract.^{2,3} Since the use of nasopharyngeal aspirate (NPA) seemed to be better than nasopharyngeal swab (NS) to identify respiratory virus in pediatrics, we decided to compare these methods in detecting SARS-CoV-2 in children.⁴

Children hospitalized in our pediatric department underwent NS (Copan-503CS01 nasopharyngeal flocked swab) and NPA (Medicoplast mucus extractor 440-ch08), performed from both nostrils, on admission and after 24 hours. SARS-CoV-2 RNA was extracted from the paired samples through nucleic acid amplification, using the RT-PCR.

From March 13 to May 22, 2020, 300 paired specimens (NS/NPA) collected from 136 patients (134 hospitalized and 2 outpatients) were tested for SARS-CoV-2.

For clinical aims, we considered positive, to SARS-CoV-2 every patient whose NPA or NS or NPA/NS resulted positive or weak positive.

Out of the 134 patients hospitalized, 18 children tested positive [prevalence 13.4%, 95% confidence interval (CI)

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TABLE 1. NS and NPA Results

	NPA negative	95% CI	NPA positive	95% CI	Total
All children's specimens					
NS negative	251 (97.7%)	94.9%–98.9%	18 (41.9%)	28.2%–56.9%	269 (89.7%)
NS positive	6 (2.3%)	1.1%–5.1%	25 (58.1%)	43.1%–71.8%	31 (10.3%)
Total	257 (100.0%)		43 (100.0%)		300 (100.0%)
Children < 6 years of age					
NS negative	134 (97.8%)	93.4%–99.3%	4 (33.3%)	12.5%–63.6%	138 (92.6%)
NS positive	3 (2.2%)	0.7%–6.6%	8 (66.7%)	36.4%–87.5%	11 (7.4%)
Total	137 (100.0%)		12 (100.0%)		149 (100.0%)
Children ≥ 6 years of age					
NS negative	117 (97.5%)	92.5%–99.2%	14 (45.2%)	28.9%–62.6%	131 (86.8%)
NS positive	3 (2.5%)	0.8%–7.5%	17 (54.8%)	37.4%–71.1%	20 (13.2%)
Total	120 (100.0%)		31 (100.0%)		151 (100.0%)

8.2%–20.4%]; among the latter, 13 of them and 2 outpatient children were followed collecting their paired specimens until both resulted negative 24 hours apart.

Of the 300 paired specimens evaluated: 276 were concordant, 24 were discordant, so the naïve concordance was 92.0% (95% CI 88.3%–94.6%) with Cohen's kappa (K) 0.63. Among the paired specimens whose NPA resulted positive, 41.9% (95% CI 28.2%–56.9%) had NS negative; while among the paired specimens whose NPA resulted negative, 2.3% (95% CI 1.1%–5.1%) had NS positive.

Considering NPA as the gold standard for detection of SARS-CoV-2, we calculated sensitivities and specificities of NS. The overall sensitivity of NS was 58.1% (95% CI 43.1%–71.8%) and the specificity was 97.7% (95% CI 94.9%–98.9%). Since the different practice in specimen collection, we divided our cohort according to the children's age (<6 or ≥6 years, Table 1). Among children under 6 years, the concordance was K = 0.67. Regarding children of 6 years or older, the concordance was K = 0.60.

The NS has, in any case, a low sensitivity in detecting SARS-CoV-2 in children when referred to NPA. Our results, the first we know are available, suggest to prefer the collection of NPA whenever possible for the detection of SARS-CoV-2 in children.

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Clinical Severity of Gastroenteritis in Children Hospitalized With Rotavirus Infection Before and Post Introduction of a National Rotavirus Vaccination Program in Australia

There have been dramatic reductions in emergency department visits and hospital admissions for gastroenteritis in young children following the introduction of rotavirus vaccination, into the National Immunisation (NIP) program in Australia since May 1, 2007.^{1,2} However, the diversity of rotavirus strains causing disease in Australia

has increased following introduction of the rotavirus vaccine program, with postvaccination era predominant strains varying between states implementing RV1 (Rotarix; GlaxoSmithKline Biologicals, Belgium) versus RV5 (*Rotatq*; Merck & Co. Inc., Whitehouse Station, New Jersey 08889, USA) vaccine, illustrating the need for continued surveillance and monitoring of rotavirus disease and severity.³

To explore the impact of vaccination on clinical severity of rotavirus disease, we reviewed all laboratory confirmed rotavirus admissions to the Women's and Children's Hospital, a tertiary pediatrics hospital in South Australia, for children under 5 years of age during 2 time periods (prevaccine introduction: May 1, 2005–April 3, 2007 and postvaccine introduction May 1, 2009–April 30, 2013). Medical records were reviewed to determine the severity of rotavirus infections assessed using the Vesikari Clinical Severity Scale, VCSS⁴ and vaccination history was ascertained from the Australian Immunisation Register (AIR). Nosocomial infections were excluded, and readmissions to hospital within 72 hours were considered 1 event. Research ethics approval was obtained from the Women's and Children's Health Network Human Research Ethics Committee (REC322A).

A total of 233 pre- and 79 postvaccination period rotavirus admissions were identified and assessed. The proportion of children

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