Childhood Immunoglobulin A Vasculitis Associated with COVID-19: A Case Report

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Abstract
Primary immunoglobulin A vasculitis (IgAV) is one the most common childhood vasculitis. A 5-year and 10-month-old girl child patient presented with confluent palpable purple red rash, mainly over both ankles. This was associated with edematous, tender ankles, limited range of movement, and inability to walk. A concomitant coronavirus disease 2019 (COVID-19) was documented by nasopharyngeal swab. This case suggested that COVID-19 can trigger IgAV in children. Hence, awareness of COVID-19 infection in IgAV should be present, and it may be useful to investigate COVID-19 as one of the causes of IgAV, especially in the presence of an epidemic.

Keywords
► immunoglobulin A vasculitis
► children
► COVID-19

Introduction
Immunoglobulin A vasculitis (IgAV) is one the most common childhood vasculitis. It is a nonthrombocytopenic immunoglobulin A vascular reaction that affects mainly the skin, gastrointestinal and musculoskeletal systems, in addition to the kidney. This disorder commonly presents with purpuric rash that spreads over the lower limbs and buttocks, and it may extend upwards to involve the trunk and upper extremities. This rash could be also bullous and hemorrhagic, and is characterized by being palpable, erythematous, and of variable sizes. Gastrointestinal bleeding, abdominal pain, glomerulonephritis, arthritis, and arthralgia are other manifestations that may accompany the rash. Histopathologically, leukocytoclastic vasculitis with immunoglobulin A deposition in the vessel wall is a pathognomonic finding.

IgAV often occurs in childhood. It is a rare condition among adults, with more preponderance among males. The exact etiology of IgAV is not well known, but it may be related to various infectious triggers. In many cases of IgAV, a preceding bacterial streptococcal infection, Epstein–Barr, or varicella viruses’ infections were documented. Other immunological triggers involve several drugs, insect bites, and vaccines, such as the measles vaccine.

Herein, we presented a case of a girl child patient who developed a confluent palpable purple red rash over both ankles, associated with bilateral ankle edema, tenderness, and a limited range of movement. During hospitalization, she was confirmed to have coronavirus disease 2019 (COVID-19) nasal swab. This case suggested that COVID-19 can trigger IgAV in children. Hence, awareness of COVID-19 infection in IgAV should be present, and it may be useful to investigate COVID-19 as one of the causes of IgAV, especially in the presence of an epidemic.

Case Report
We reported a case of 5-year and 10-month-old girl, from Yemen, who completed her vaccinations according to the national vaccination program and had normal motor and mental development. The patient had past history of atopic dermatitis with recurrent exacerbations for which she received courses of local steroids, followed by local emollients. The atopic dermatitis was completely healed at the time of the patient presentation. There are no known data regarding previous upper respiratory tract or gastrointestinal infections, or possible contact with SARS-CoV-2-positive individuals.

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She was referred from an outpatient clinic to the Emergency Department of Andalusia Hai Al Jamea Hospital on July 5, 2020. Her main complaints started 2 days ago with fever, generalized muscular pain, and skin rash. She received paracetamol alternating with ibuprofen for these symptoms with no improvement. There were no associated hematuria, oliguria, or gastrointestinal manifestations. In addition, no manifestations suggestive of cardiac or respiratory affection were identified. The patient had no family history of similar conditions or chronic diseases.

The girl’s weight and height were on the 50th and 60th percentiles, respectively. Her vital signs were reported (blood pressure, 100/60 mm Hg; heart rate, 120 beats/min; respiratory rate, 25 cycles/min; temperature, 38 °C). The patient was admitted in a generally good state, fully conscious, spontaneously breathing, with no abnormal findings on examination (head and neck, neurologic, cardiac, chest, abdominal, and upper limbs). The lower limbs showed bilateral ankle edema with limited range of movement, tenderness, and inability to walk. Skin over both ankles were edematous and tender, with palpable purple red vasculitic rash, mainly over both ankles, abdominal, and upper limbs. The described palpable purple red skin rash and arthritic manifestations in this case favored the diagnosis of IgAV and large joint arthritis in ankle joints suggested the diagnosis of IgAV.

The laboratory evaluation of immunoglobulin A, D-dimer, and platelet count can be applied separately for distinguishing IgAV from other conditions like sepsis and muscular pain, besides the epidemiologic situation of COVID-19 pandemic. Nasopharyngeal swab was obtained for polymerase chain reaction for SARS-CoV-2 infection and the result was positive. On the 6th day, the elevated white blood cells and C-reactive protein returned to normal (8.7 x 10^3/L and 6.3 mg/L, respectively).

Blood, urine, and stool cultures were all negative, daily assessment of occult blood in stool and urine analysis showed no abnormality, and serial assessments of kidney and liver functions as well as coagulation profile were normal. The patient was discharged with completely resolved arthritis on the 6th day, while skin manifestations resolved on follow-up at the outpatient clinic (on day 14) as illustrated in – Fig. 2.

Discussion

We presented an interesting case that showed confluent palpable purple red vasculitic rash, mainly over both ankles, associated with clinical manifestations of acute arthritis. Typically, both ankles were edematous and tender, with limited range of movement and inability to walk. In addition, a concomitant COVID-19 infection was documented.

The described palpable purple red skin rash and arthritic manifestations in this case favored the diagnosis of IgAV according to the EULAR/PRINTO/PRES criteria for Henoch–Schönlein purpura. The laboratory evaluation of immunoglobulin A, D-dimer, and platelet count can be applied separately for distinguishing IgAV from other conditions like sepsis patients with rash, urticaria, and simple hematuria.

Some case reports of IgAV in association with COVID-19 in adults have been published. However, no previous cases with this association have been described in children.

Although the precise cause of IgAV is still unknown, several types of infectious triggers cause the disease. Viral infections have been proved to play a role in its pathogenesis. In our patient, COVID-19 viral infection was confirmed by a positive nasopharyngeal swab. This raises the possibility that SARS-CoV-2 infection might be a stimulant factor for autoimmune reactions and might cause IgAV. Some reports support our hypothesis; they highlighted that COVID-19 can give vasculitis-like purple skin rash, which in some cases represents the initial presentation without any respiratory compromise. It has been reported that autopsy and surgical tissues of COVID-19 cases showed diffuse lymphocytic
vascular endotheliitis and apoptotic bodies. Additionally, accumulation of viral elements as well as inflammatory cells within endothelial cells has been demonstrated by Varga et al. Furthermore, arthralgia and myalgia are common manifestations of COVID-19. However, clinical arthritis was not typically caused by it.

**Conclusion**

This case suggests that COVID-19 can trigger IgAV. It may be useful to investigate COVID-19 as among the etiological factors of IgAV, especially in the presence of an epidemic.

**Funding**

None.

**Conflict of Interest**

None declared.

**References**


**Table 1** Laboratory investigations of the studied patient

<table>
<thead>
<tr>
<th>Days</th>
<th>WBCs/L</th>
<th>Platelets/L</th>
<th>Plateletcrit, %</th>
<th>Hb, mg/dL</th>
<th>Serum IgA, mg/dL</th>
<th>Serum CRP, mg/L</th>
<th>ESR, 1st h mm</th>
<th>Serum ferritin, ng/mL</th>
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<tbody>
<tr>
<td>On admission</td>
<td>$1.7 \times 10^3$</td>
<td>$5.43 \times 10^9$</td>
<td>0.1</td>
<td>11</td>
<td>6,748</td>
<td>170</td>
<td>6</td>
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<td>Fourth day</td>
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<td>260</td>
<td>450</td>
<td>Positive</td>
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Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; IgA, immunoglobulin A; PCR, polymerase chain reaction; WBCs, white blood cells.

Note: Reference ranges: serum IgA (70–400 mg/dL); serum ferritin (7–140 ng/mL for 6 months to 15 years age group); D-dimer (<250 ng/mL); CRP (below 3.0 mg/L).

**Fig. 2** Therapy data of the studied patient.

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