JORDANIAN AMERICAN PHYSICIANS ACADEMY JOURNAL

RESEARCH **CASE REPORT**

Anaphylaxis as the Only Presenting Symptom of COVID 19

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INTRODUCTION

Most children with SARS-CoV-2 infection are asymptomatic or exhibit only mild symptoms. (1) A varied incidence of cutaneous rashes has been described in different studies.(2) A recent review of the cutaneous manifestations in patients with COVID-19 highlighted that urticarial rash is common at the onset of the disease but one case was found of a child to have associated anaphylaxis. (3)(Table 1). This report describes a 10-year-old child who presented to a tertiary care hospital in Jordan with anaphylaxis as the only presenting symptom of COVID-19.

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CASE PRESENTATION

This is a case of a 10-year-old previously healthy male, who has been in his usual state of health until he developed a severe urticarial rash over his neck, which progressively increased to involve his body. The rash was associated with angioedema that included facial and eyelid swelling. The patient did not have any fever, cough, emesis, abdominal pain, or diarrhea.

The family denied any history of new food ingestion or drug administration. There was no history of contact with strange substances, pets, or environmental allergens leading up to this event.

At the emergency department, the patient was hypotensive with a blood pressure reading of 85/50. His temperature was 37 C, O2 saturation was 98% on room air, and heart rate was around 100 beats per minute. There was no tachypnea or signs of respiratory distress, and no wheezes were appreciated on auscultation. The remainder of the physical examination was unremarkable, apart from the diffuse urticaria. Epinephrine IM 0.01mg/kg, chlorpheniramine 2 mg, and an IV bolus of normal saline 20cc/kg over 20 min were immediately administered. The patient was stabilized and his blood pressure came back to normal.

The patient was admitted to the Pediatric Intensive Care Unit (PICU) and maintained on the following medications: famotidine 20 mg once daily, chlorpheniramine 2 mg every 6 hours, and hydrocortisone 5 mg/kg divided every 6 hours. A polymerase chain reaction (PCR) test using a nasopharyngeal swab (NS) for SARS-CoV-2 was positive.

The family denied contact with any confirmed COVID-19 case. Complete blood count was unremarkable with normal white cell count and differential and no lymphopenia or eosinophilia. Other labs did not reveal any significant findings. Testing for the tryptase level was not available.

The patient remained clinically stable until 6 hours into admission when he had another episode of diffuse urticaria, facial swelling, and hypotension with a blood pressure of (79/47) compatible with a rebound anaphylactic reaction that required epinephrine. The remainder of his hospital course was uneventful with steady improvement in his clinical status.

OUTCOME AND FOLLOW UP

The patient was discharged home. His medication regimen included chlorpheniramine, famotidine, hydrocortisone, and EpiPen with the same doses. One day after being discharged the patient experienced another anaphylactic relapse that required epinephrine.

Revision of the patient's family history revealed that his father had a single episode of angioedema with no identifiable trigger. The patient's levels and function of C4 and C1 esterase were normal, making the diagnosis of Hereditary Angioedema unlikely.

DISCUSSION

To the best of our knowledge, our case represents the first report of anaphylaxis as the sole presenting symptom of COVID-19 in a pediatric patient. We performed a review of published studies describing hypersensitivity manifestations such as urticaria, angioedema, or anaphylaxis as presenting features of COVID-19 (Table 1). Although most anaphylactic episodes are immunoglobulin E–mediated, viral-induced anaphylaxis may occur secondary to mast cell activation by nonallergic triggers. (4) Mast cells can release pro-inflammatory mediators including IL-1 and IL-6 through various stimuli selectively without degranulation induced by an allergen. (5)It is well documented that cytokine release syndrome (CRS) is a systemic inflammatory response that can be caused by infection among other factors. (5) CRS is characterized by a sharp increase in the levels of pro-inflammatory cytokines including interleukin-6 (IL-6). (5)

Anaphylaxis due to viral infections has been rarely described in the literature. (6) COVID-19-associated anaphylaxis has been described in one previous pediatric case, but this case was associated with rhabdomyolysis as well. (7)

Of interest, the viral-induced anaphylaxis in our case was multiphasic. Multiphasic anaphylaxis is defined as a recurrence of symptoms that develop following the apparent resolution of the initial anaphylactic episode. (7, 8) In most cases of viral-induced urticaria and the rare cases of viral-induced anaphylaxis, other than COVID, patients were known to have risk factors for allergic reactions including multiphasic anaphylaxis, atopy, food allergy, or family history of angioedema as in our case. (7, 9)

CONCLUSION

We would strongly recommend that Pediatric providers should keep in mind the possibility of COVID-19, along with other viral illnesses, as possible causes of unprovoked anaphylaxis. Diagnostic evaluation for COVID-19 or other infectious diseases and safety considerations should be undertaken in the correct clinical context.

Table 1. Review of published studies describing urticaria, angioedema, or anaphylaxis as presenting features of COVID-19.

Number	Year	Citation	Age	Presentation	Systemic involvement	Anaphylaxis
1	2019	Khalili [10]	2mo,6 yrs	Acute urticaria	None	No
2	2020	Locky [11]	36yr	Angioedema and urticaria	Acute bronchospasm	No
3	2020	Rotulo [12]	6yr	pruritic skin eruptions	None	No
4	2020	Cohen [13]	62yr	Angioedema	None	No
5	2020	Alhaq [14]	40yr	Angioedema and urticaria	None	No
6	2020	Hassan [15]	46yr	Urticaria and angioedema	Fever ,RS symptoms	No
7	2020	Lavery [16]	11-17yr	Urticaria	None	No
8	2021	Zipursky [17]	27yr	Urticaria and angioedema	GI symptoms and fever	No
9	2021	Royer [18]	34yr	Urticaria and angioedema	RS symptoms	No
10	2021	Watashi [19]	39yr	Urticaria	headache,, GI symptoms, myalgia, arthralgia	No
11	2021	Lopez [20]	30,47 yr	Urticaria	RS symptoms	No
12	2021	Bach [7]	Child	Anaphylaxis and rhabdomyolysis	Headache ,myalgia	Yes
13	2021	Ozdemir [21]	1yr	Urticaria and angioedema	None	No
14	2021	Brooks [22]	5yrs	Acute urticaria	None	No
15	2021	Houshmand [23]	10yrs	Acute urticaria	None	No
16	2022	Park [24]	51yr	Angioedema	GI and RS symptoms	No
17	2022	Manzano [25]	28-65yr	Angioedema and urticarial rash	RS symptoms	No
18	2023	Chen [26]	6mo	Acute urticaria	RS and GI	No

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