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ORIGINAL ARTICLE

Cutaneous manifestations in a patient with temporarily associated pediatric multisystemic inflammatory syndrome with COVID-19: case report

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Abstract

Objectives: To describe the cutaneous manifestations presented by a patient with pediatric multisystemic inflammatory syndrome (MIS-C) temporarily associated with SARS-CoV-2. **Methods:** Female patient, 10 years old, presenting arthralgia in the wrists and ankles, edema in hands and feet, persistent fever, appearance of diffuse, and itchy maculopapular rash associated withodynophagia and productive cough. Evolution of the rash to violaceous lesions on the face, trunk and limbs (upper and lower), in addition to the appearance of vesicles on the face, within 48 hours. CBC suggestive of an infectious condition, with CRP 307mg/L (insert reference value) and ESR 61mm. RT-PCR for SARS-CoV-2 positive. **Results:** Diagnosis of pediatric multisystemic inflammatory syndrome temporarily associated with SARS-CoV2. Transferred to ICU for monitoring and intravenous human immunoglobulin initiated. Good evolution, with the disappearance of injuries and discharge with outpatient follow-up. **Conclusion:** MIS-C has several dermatological manifestations and pediatricians must be attentive to the diagnosis, not limited to a specific presentation. In this case report, the importance of referral to tertiary referral centers for better case management and timely recognition of the syndrome in these patients is emphasized.

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INTRODUCTION

We still know very little about the pathophysiology of multisystem inflammatory diseases, possibly associated with SARS-CoV2. There are reports of cases of previously healthy patients who, after acquiring the infection, manifested papulovesicular, urticarial, morbilliform, pernio-like erythema, among other unspecified viral exanthemas, some similar to Kawasaki syndrome^{1,2}.

Numerous publications have reported that most respiratory symptoms in SARS-CoV2 infection are mild and scarce, being preceded or followed by exanthema and other integumentary lesions, such as livedo reticularis and ischemic lesions³. Most cases are self-limited, without reports of major complications, but patients with pediatric multisystem inflammatory syndrome temporarily associated with SARS-CoV2 (P-MIS), have a greater potential for severity^{4,5}.

Due to the scarcity of data on cutaneous manifestations present in SARS-CoV-2 infection, the authors aim to contribute with evidence on these manifestations in P-MIS.

CASE REPORT

A 10-year-old female patient came to the pediatric clinic complaining of arthralgia in the wrists and ankles, edema of the hands and feet and persistent fever for 2 days (prior to hospital admission). It evolved with the appearance of diffuse hyperemic macules and papules throughout the body, with intense itching associated withodynophagia and wet cough. (Figures 1 and 2). Upon physical examination, she presented with bilateral palpebral edema, diffuse urticarial macules and plaques throughout the body, but with improvement in her arthralgia and pruritus after administration of dexchlorpheniramine and dipyrone. Blood pressure was 110x90 mmHg. She was discharged with regular analgesia and antihistamines. He returned 24 hours later, with evolution of the urticarial macules and papules to purplish vesicles (on the face, trunk and upper and lower limbs) (Figures 3 and 4), fever of 39.3°C, arthralgia in the wrists and ankles, in addition to two vomiting episodes. We treated her for anaphylaxis and collected samples for RT-PCR for SARS-CoV-2. Her lab workup showed the following changes: Blood count (15500 leukocytes: 94.5% neutrophils, 21% rods, 1.7% monocytes, 3.4% lymphocytes; PCR: 307.71 mg/L (reference value: 0 to 5mg/l), ESR 61mm (reference value: 0 to 10mm/hour), TAP: 65.7% (reference value: 70 to 100%), APTT: 41.6 seconds (reference value: 24.5 to 37.5 seconds). We prescribed her Ceftriaxone 4g/day for 48 hours until her blood culture result was negative.

She developed anaphylaxis (worsening of the urticarial lesions and dyspnea), we then administered 0.01mg/kg of intramuscular adrenaline, with good response. The



Figure 1. Maculopapular exanthema, itchy edema of the hands and ankles (admission).

result of the rapid test for SARS-CoV-2 (IgM and IgG) was non-reactive, and the patient was on the 5th day of her illness. The RT-PCR result for SARS-COV-2, collected on the 3rd day of illness, was positive. Her chest radiography was unchanged.

She was diagnosed with P-MIS (Table 1) for presenting the criteria according to a document published by the World Health Organization (WHO)⁶.

The patient was transferred to the ICU for monitoring and treatment with intravenous human immunoglobulin (2g/kg/single dose), infused within 24 hours. The medical team in charge chose not to prescribe acetylsalicylic acid (ASA), as the patient did not meet all the criteria for complete Kawasaki disease. Her Doppler echocardiogram was normal. After the end of the immunoglobulin infusion, the patient was transferred to the pediatric ward, without complications, and had complete improvement of her skin lesions. She was discharged from the hospital after 09 days. He is still being followed up in an outpatient pediatric rheumatology clinic.

Table 2 depicts the laboratory tests performed by the patient, the dates and their respective reference values.



Figure 2. Itchy maculopapular exanthema on the limbs (admission).



Figure 3. Purplish maculopapular and vesicular exanthema on the face (4th day of evolution).

DISCUSSION

In a recent document published by the World Health Organization⁶, they suggest a preliminary definition for pediatric multisystem inflammatory syndrome temporarily associated with SARS-CoV2:

- Children and adolescents aged 0-19 years with fever = 3 days.
- And two of the following: 1. Bilateral non-purulent conjunctivitis, rash, or signs of mucocutaneous inflammation (oral, hands or feet). 2. Hypotension or shock. 3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiogram findings or troponin/proBNP elevations). 4. Evidence of coagulopathy (PT, APTT, and elevated D-dimer). 5. Acute gastrointestinal problems (diarrhea, vomiting or abdominal pain).
- And Elevated markers of inflammation such as ESR, CRP or procalcitonin. And no other cause of microbial infection.
- And evidence of COVID-19⁶.

In the first published case series of multisystem inflammatory syndrome, we had eight patients with ages

ranging from 4 to 17 years. They had high and persistent fever (38-40°C), rashes of varied presentations, non-purulent conjunctivitis, edema of the hands and feet, abdominal pain, vomiting and diarrhea. All had severe and multisystem disease, and progressed to shock. They were treated with intravenous gamma globulin (2 g/kg/single dose, in the first 24 hours), antibiotic therapy (clindamycin and ceftriaxone) and anti-inflammatory acetylsalicylic acid (80-100 mg/kg/day). The patients had detectable antibodies, reinforcing the concept that it was a post-infectious syndrome².

In the United States of America, more than 100 children and adolescents (between 1 and 21 years of age, with more than 50% of them between 5 and 14 years old) were described with clinical and laboratory characteristics of complete Kawasaki syndrome, incomplete Kawasaki, and/or shock. All of them had fever, more than half had rash of varied presentations, abdominal pain and diarrhea. In 90% of cases we found SARS-CoV-2 RNA or antibodies against the virus. The cases occurred days or weeks after the disease, suggesting that this inflammatory syndrome may be a late complication, characterized by a disproportionate immune response to the infection^{3,4}.

In France, 21 children and adolescents, aged 3 to 16 years, presented with a characteristic picture of Kawasaki



Figure 4. Purplish maculopapular exanthema (4th day of evolution).

Disease for a period of 15 days, with 12 (57%) of African descent; 12 (57%) had shock and 16 (76%) myocarditis. All the patients had gastrointestinal symptoms during the first days of illness and rash with varied presentations. Of

the total, 19 (90%) had evidence of recent SARS-CoV-2 infection. All received intravenous immunoglobulin 2g/kg/single dose and 10 (48%) received corticosteroids. All were discharged⁷.

In a case series with 58 children from 08 hospitals in England, from March to May of 2020 with characteristics of multisystem inflammatory syndrome (P-MIS-TS) associated with SARS-CoV-2, it showed a wide spectrum of signs and symptoms and disease severity, where 30 (52%) children had polymorphic rash⁸.

Spain reported two cases of children aged 2 months and 6 years with a positive result for SARS-CoV-2, presenting isolated skin manifestation or associated with mild symptoms. The 2-month-old female child had mild fever together with pruritic acute urticaria on the face and upper extremities, with dissemination to the trunk and lower extremities, lasting for 4 days. The 6-year-old male child presented a low-grade fever and, within 2 weeks, an erythematous, confluent and non-pruritic maculopapular eruption on the trunk and neck, with dissemination to the cheeks, upper and lower extremities, lasting for 5 days⁹.

An English study described, a series of vesicular exanthemas in 22 patients with SARS-CoV-2, evidenced by nasopharyngeal swab. The mean latency time from systemic symptoms to rash was 3 days, with a mean duration of cutaneous manifestations of 8 days. Of these 22 patients, only one was a child - 8 years old, female, whose lesion was papulovesicular on the trunk, dispersed, without pruritus, lasting for 7 days; the onset time was 3 days, associated with fever and cough¹⁰.

Pediatricians should be aware of the skin manifestations associated with the Pediatric multisystem inflammatory syndrome temporarily associated with SARS-CoV2 for timely recognition in diagnosis and adequate follow-up in a tertiary referral center.

Table 1. WHO criteria for P-MIS, used for case confirmation.

WHO criteria	Patient's Results
Age: 0-19 years	Age: 10 years
Fever > or = 3 days	Fever: 03 days
Inflammation laboratory (Erythrocyte Sedimentation rate, C-reactive protein or procalcitonin)	CRP = 307.71 mg/L ESR = 61.0 mm/h
At least 2 of the following changes: Rash or non-purulent bilateral conjunctivitis or mucocutaneous inflammatory signs (oral cavity, on hands and feet) . Hypotension or shock . Findings of myocardial dysfunction, pericarditis, valvulitis or coronary changes (echocardiographic or elevated troponin or NT-pro -BNP)	Skin rash: itchy and reddish maculae and papules diffused around the body, which evolved to become purplish and facial vesicles.
Evidence of coagulopathy (TAP, PTT and D-dimer)	TAP = 65.7 % TTPA = 41.6 seconds
Acute gastrointestinal symptoms (diarrhea, vomits or abdominal pain)	Vomit and abdominal pain
Without another evident microbiological cause of inflammation, including bacterial sepsis, streptococci and staphylococci toxic shock syndrome	Negative blood culture
Evidence of COVID-19 (RT-PCR, antigen or serology) OR	Detectable RT-PCR for SARS COV-2
Probable contact with COVID patients.	Unconfirmed.

Table 2. Laboratorial workup, day of evolution and respective reference values.

	Unit	Reference value	Day 2	Day 3	Day 5
Red blood cells	X10+6/uL	4.00-5.20	5.32	4.34	4.65
MCV	fl	82.0- 92.0	81.2	81.8	81.7
Hemoglobin	g/dL	11.5-15.5	13.4	11.0	11.7
MCH	pg	28.0-30.0	25.2	25.3	25.2
Hematocrit	%	40.0-50.0	43.2	35.5	38.0
CHCM	g/dL	32.0-36.0	31.0	31.0	30.8
RDW	%	12.0-17.0	12.9	13.2	13.3
Leucocytes	X10+3/uL	4.0-14.0	10.0	15.5	11.0
Neutrophils	%	1.2-7.2	8.1	14.6	9.7
Rods	%	0.0-4.0	6.0	21.0	4.0
Segmented	%	30.0-60.0	--	--	--
Eosinophils	%	1.0-5.0	0.7	0.1	0.8
Basophils	%	0.0-3.0	0.3	0.4	0.2
Monocytes	%	2.0-10.0	2.6	1.7	1.2
Lymphocytes	%	30.0-70.0	15.5	3.4	10.0
Platelets	X10+3/uL	150-450	259	223	297
Prothrombin time	Sec	9.1-12.1	---	14.5	13.5
TTPA	Sec	24.5-37.5	---	41.5	35.7
CRP	mg/L	0.0-5.0	90.52	307.71	314.79
ESR	mm/h	0.0-10.0	16.0	61.0	69.0
Blood culture			negative		
RT-PCR for SARS COV-2				Detectable	
SARS COV-2 fast test					IgG – IgM –

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