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Case Report

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Multisystem Inflammatory Syndrome (MIS-C Or PIMS) or Kawasaki Like: Serious Complications in Two Children Post-Infection With SARS-Cov-2

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Abstract

Multisystem inflammatory syndrome in children (MIS-C) is a potentially severe condition that presents in children with recent SARS-CoV-2 infection.
Patients with this syndrome meet the criteria for Kawasaki disease shock syndrome defined by Kanegaye et al.
The therapeutic management is still debated but the combination of immunoglobulins and intravenous corticosteroids has shown superiority to immunoglobulins alone.
We present two cases of this Multisystem Inflammatory Syndrome in Children (MIS-C) associated with SARS-CoV-2 infection diagnosed as per the criteria defined by World Health Organization and Center for Disease Control and Prevention.
Patients with MIS-C should ideally be managed in a pediatric intensive care environment since rapid clinical deterioration may occur.

Introduction

Multisystem inflammatory syndrome or toxic shock syndrome or "Kawasaki like disease" is a disease similar to Kawasaki disease which appears to emerge with an unusually high incidence with the waning of the SARS-Cov-2 pandemic [1].

Patients with this syndrome meet the criteria for toxic shock of kawasaki disease defined by Kanegaye et al. by the presence of systolic hypotension, clinical signs of hypoperfusion, a patent inflammatory syndrome, bicytopenia involving the erythrocyte and platelet lines, coagulopathy, reduction in myocarditis function [2].

Therapeutic management is still debated but the combination of immunoglobulins and intravenous corticosteroids has shown superiority to immunoglobulins alone. Adjuvant therapy, such as the use of vasopressor / inotropic drugs or ventilation should be initiated promptly if the patient has acute circulatory failure [3].

More than half of the children (59%) required admission to the PICU [4]. We report two cases of kawasaki-like following infection with SARS-Cov-2 with serious complications.

Clinical Cases

Clinical case 1:

Our first case was a 9-year-old child admitted for feverish consciousness disorder. She had no pathological history without the notion of taking a toxicant. The patient had presented 5 days before her admission a fever at 39 ° C associated with food vomiting and diarrhea treated with paracetamol 15mg / kg / 8h with metronidazol 10mg / kg / 8h, without improvement with appearance of maculopapular skin lesions. 'erasing in vitro pressure (figure 1) with bilateral conjunctivitis (figure 2).

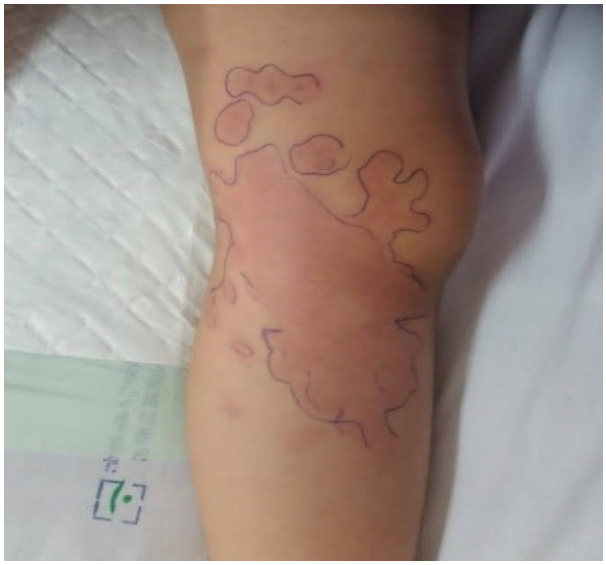

Figure 1: Skin rash

Figure 2: Conjunctivitis

On the day of admission, the patient had presented abdominal tenderness with neurological disturbances, the Glascow score (GCS) was 12/15 (EOR = 4, VR = 3, MR = 5). The pupils were symmetrical and responsive. The patient did not present a deficit in the nociceptive stimulation. Hemodynamic and respiratory states were stable. The capillary blood sugar was normal. Skin lesions were present on all four limbs. From a diagnostic point of view, a brain scan was performed eliminating a hemorrhagic, thromboembolic or tumor cause. A lumbar puncture (LP) followed by an injection of ceftriaxone (at a dose of 100 mg / kg / day) and injectable 2cyclovir (at a dose of 10 mg / kg / 8 hours) were then performed. The fundus of eye revealed: Grade 2 papilledema. The PL showed 5 white blood cell cellularity, normal glycorachia and normal proteinorachia. The lipasemia was normal. Nasopharyngeal PCR test for SARS-Cov-2 RNA was negative.

One day after his admission our patient had presented a clinical worsening with the deterioration of the neurological state GCS was at 9/15 (EOR = 2, VR = 2, MR = 5), a brain MRI was performed, not showing anomalies (figure 3). Hemodynamic instability was installed, a level of troponins and BNP (Brain Natriuretic Peptide) were high, BNP: 2592pg/mL, D dimers: 2400ng/mL feritin: 1200ng/mL .an echocardiography showed no abnormalities.

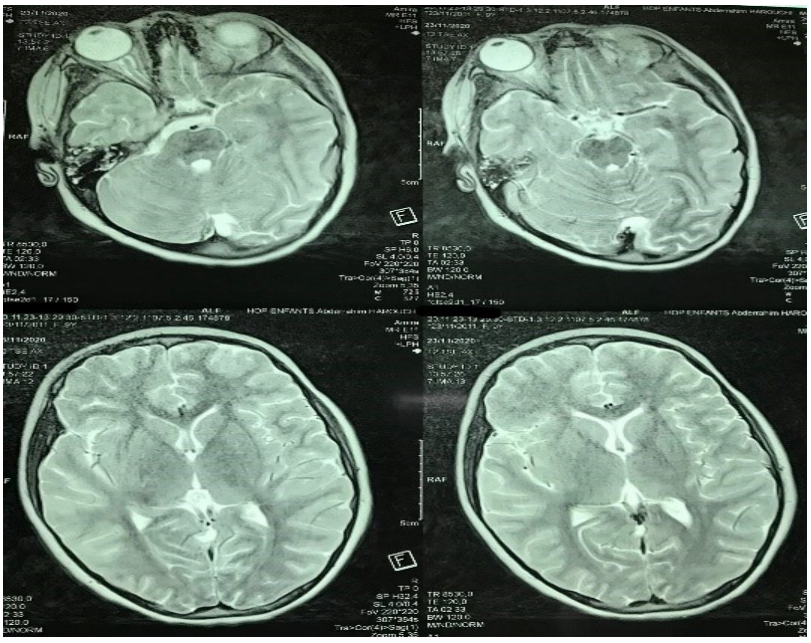

Figure 3: Normal MRI

Our patient had multiorgan failure with inflammatory syndrome, high CRP level, renal failure and hepatic cytolysis with haematological involvement made up of thrombocytopenia and lymphopenia.

Our patient was intubated ventilated his hemodynamic state was optimized by vasoactive drugs. Faced with abdominal defense and peritoneal effusion on abdominal ultrasound, septic shock on peritonitis was suggested and then a surgical exploration was made white.

The test for anti-SARS-CoV-2 type IgM + IgG antibodies was positive.

In order to complete the extension workup, a thoracic CT was performed to look for pulmonary involvement which was found to be normal. The work-up carried out for immunosuppression was negative: hepatitis, HIV and Syphilitic serologies, glycated hemoglobin (HbA1C) normal, there were no signs in favor of a malignant hemopathy or a tumor. The patient was put on corticosteroid therapy 2mg / kg / day with immunoglobulins 2g / kg / 48h.

The patient was extubated after 2 days of treatment, with a favorable outcome and recovery ad integrum clinical and biological.

Clinical case 2:

Our second case was a 6-year-old child admitted for acute myocarditis. He did not present any pathological history. The patient had presented 6 days before his admission a fever at 38.9 ° C associated with a dry cough treated with paracetamol 15mg / kg / 8h with Azithromycin 10mg / kg / day, without improvement with the appearance of maculopapular skin lesions. Erasing pressure in vitro with bilateral conjunctivitis and cheilitis (figure 4).
Nasopharyngeal PCR test for SARS-Cov-2 RNA was negative.

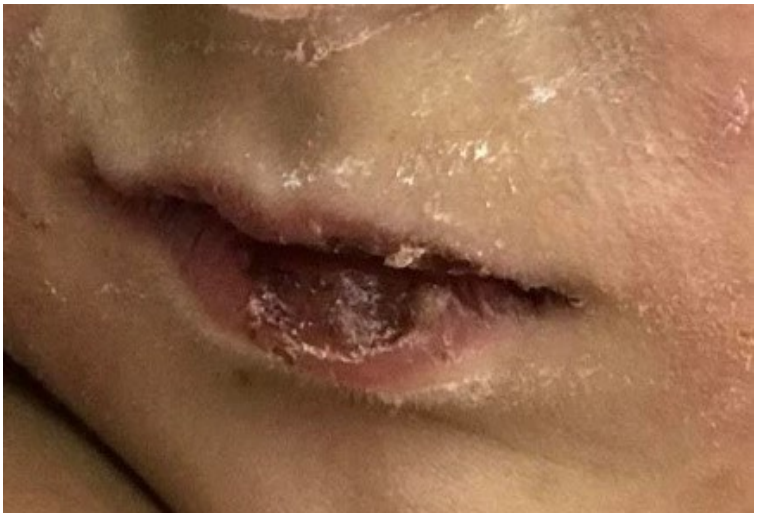

Figure 4: Cheilitis

On the day of admission, the patient presented with hemodynamic instability, with elevated D-dimer, troponin and BNP levels. Our patient was conscious GCS = 15/15, stable on the respiratory plan, an echocardiography was carried out had shown: Right coronary dilated without image of aneurysm, appearance in favor of a myocarditis with an undilated LV, site of a dysfunction systolic: LVEF at 28%, RV systolic dysfunction associated with mild PAH: PAPS at 40 mmhg (Figure 5). CRP : 247mg/L, D dimer : 6328ng/mL, ferritin : 5770ng/mL, troponine-T HS : 100.3 ng/L.

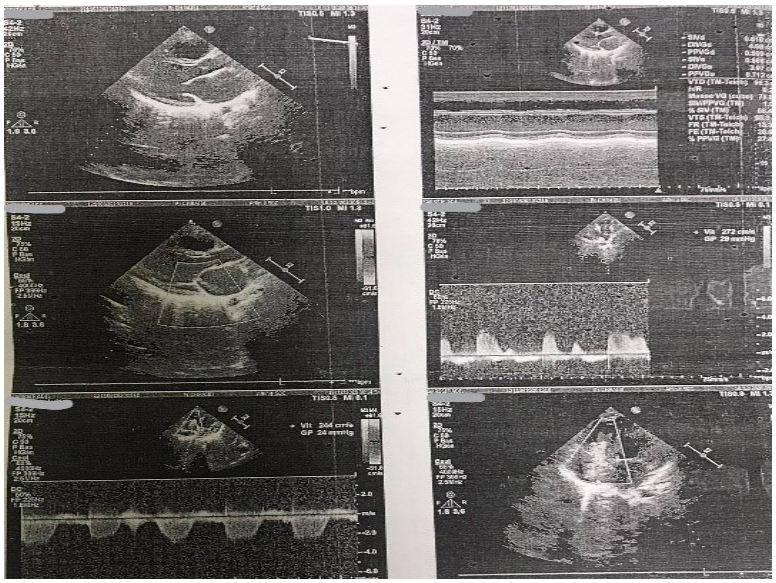

Figure 5: Echocardiographic appearance of myocarditis

The patient had received Immunoglobulin 2g / kg / 48h, Acetyl salicylated acid, Converting enzyme inhibitor, diuretics, a bisoprolol-type beta blocker.

The test for anti-SARS-CoV-2 type IgM + IgG antibodies was positive.

The evolution was marked by the impairment of renal function which required the use of peritoneal dialysis, the converting enzyme inhibitor was stopped and a three-day bolus of methylprednisone at 30 mg / kg was added. / jr. On day 3 of dialysis improvement of renal function and disconnection of dialysis and recovery of myocardial contractility *left ventricular ejection fraction* of 56%.

Discussion

Two similar cases have been reported in Italy in children with repeated nasal swabs for SARS-CoV-2 negative with high titers of IgG and IgM against SARS-CoV-2 virus, suggesting that the inflammatory response developed following viral infection when the virus was no longer detectable [5]. In New York, 15 children with severe inflammatory conditions have been reported with or without evidence of associated COVID-19 [6]. Two other American anecdotal cases, the first from Mississippi and the second from Detroit, with COVID-19 confirmed by PCR, were also the subject of a detailed description that met the criteria for MK shock syndrome [07, 08]. All were admitted for a strong suspicion of MK with specificities such as gastrointestinal symptoms, hemodynamic instability and myocarditis for the most part [9].

Following these publications, the World Health Organization (WHO) has developed a preliminary definition of these cases in order to report them on a platform for better pathogenetic understanding and better targeted therapeutic management. The definition of the cases is as follows [10]:

Children aged 0 to 19 years having been febrile for at least 3 days and presenting 2 of the following parameters:

- A rash or bilateral non-purulent conjunctivitis or cheilitis or extremity involvement,
- Hypotension or hypovolemic shock,
- Signs of myocardial dysfunction, pericarditis, valvulitis or coronary artery abnormalities (including echocardiography abnormalities or elevated troponin / proBNP levels),
- Evidence of coagulopathy (by PT, TCA, high D-dimers),
- Acute gastrointestinal symptoms (abdominal pain, diarrhea, vomiting). And an increase in markers of inflammation (sedimentation rate, C reactive protein and procalcitonin). And no other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes. And evidence of COVID-19, either probable contact or PCR or positive serology or antigenemia.

Recently, the Center for Disease Control and Prevention (CDC) has adapted and supplemented certain criteria proposed by the WHO [11].

- An age of up to 21 years
- A fever> 38.0 8C, of 24 hours minimum
- A severe picture requiring hospitalization
- Two or more organ damages (gastrointestinal, dermatological, cardiological, neurological, renal or hematological)
- Biological inflammation, with one or more abnormalities: Reactive C protein (RCP), procalcitonin (PCT), sedimentation rate (SR), fibrinogen, D-Dimers, ferritin, lactate dehydrogenase (LDH) or interleukin (IL-6) high; neutrophilic polynucleosis or lymphopenia; low albumin; a biologically proven SARS-CoV-2 infection (PCR, serology or antigen) or,
- Contact with a person infected with SARSCoV-2 within 4 weeks; no differential diagnosis.

The majority of children are treated with intravenous immunoglobulins (IGIV) 2 g / kg IV in one dose over 12 hours, or in two doses over 48 hours and high-dose corticosteroids: intravenous methylprednisone at 1 mg / kg twice daily for 5 days or until normalization of CRP, followed by oral prednisone / prednisolone at 2 mg / kg / day with decrease over 2 to 3 weeks. Or Intravenous methylprednisolone at 10 to 30 mg / kg once a day (maximum 1 g / day) for 3 days followed by oral prednisone / prednisolone at 2 mg / kg / day until the 7th day or until normalization of the RCP, then decrease over 2 to 3 weeks [03]. A recent article shows better efficacy, with faster recovery of cardiac function, in children treated with this combination versus IGIV alone [12]. The doses of corticosteroids are identical to those recommended in severe Kawasaki disease [13]. It is recommended to combine antibiotic therapy with 3rd generation cephalosporins (C3G) intravenously, during the first 48 hours, while waiting to have eliminated a bacteriological cause for the fever.

Conclusion

We note that in period of COVID-19 epidemic, a picture of multisystemic inflammatory disease in a febrile child, exposed directly to SARS-CoV-2 (or contagion), in the 4 preceding weeks, should raise suspicion the diagnosis of MIS-C, especially when there is clinical digestive, mucocutaneous and / or cardiac involvement, as well as a significant biological inflammatory syndrome. The similarities of clinical and biological picture with other pediatric inflammatory diseases mean that the diagnosis of MIS-C should not be made in excess, especially since this disease is rare. Indeed, the rapid management of a severe bacterial infection, by appropriate antibiotic therapy, should not be delayed.

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