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Intensive Care

Multisystemic Inflammatory Syndrome in Children (Disease with Several Faces): About 2 Cases in the Pediatric Intensive Care Unit in Rabat Children Hospital

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Abstract **Case Report**

Since the advent of the COVID 19 pandemic, very few severe cases have been described in the pediatric population and very few have required admission in intensive care unit (ICU). However, a new entity has emerged worldwide including multi-systemic inflammatory disease in children related to COVID infection called PIMS or MIS-C for multisystemic inflammatory syndrome in children. We report the case of two children admitted to the Pediatric Intensive Care Unit of the Rabat Children's Hospital for a severe multisystemic inflammatory syndrome related to an undetected COVID-19 infection; the first case presented a Status epilepticus while the second case was in shock due to myocarditis. The diagnosis of MIS-C was made with reference to WHO criteria and treatment was based on corticosteroid bolus only, due to lack of IV Ig. The evolution was favorable for both patients.

Keywords: SARS-COV2, COVID19, PIMS, MIS-C.

INTRODUCTION

Multisystemic inflammatory syndrome in children (MIS-C) is a new pediatric systemic inflammatory entity that has emerged in the epidemic context of SARS-COV2. It is a rare and severe disease characterized by multisystemic inflammation, persistent fever and multiple organ dysfunction. Its pathophysiological mechanisms remain poorly elucidated with several hypotheses without any definitive approval. The objective of this article is to remind the importance of thinking of the diagnosis of MIS-C in front of any evocative syndrome even in the absence of confirmed exposure in children. We describe the case of two patients who were diagnosed with MIS-C and who required hospitalization in the pediatric intensive care unit of the Rabat Children's Hospital.

CASE REPORT

Case 1

The patient A.G was a 15-years-old adolescent, who had not been vaccinated against COVID19 and had no recent COVID infection or positive case in his family. He went to the pediatric emergency department with respiratory discomfort, abdominal pain, vomiting and fever that had been evolving for 3 days. He was hospitalized and put on antibiotics, but the onset of a status epilepticus required, 6 days later, his admission to the pediatric intensive care unit.

Clinically, the child was febrile at 38.5°c, polypneic with a SpO2 of 95% at ambiant air, a GCS of 10/15, a stiff neck, and generalized tonic-clonic convulsions of unclear duration. Cardiovascularly, there were no murmurs or added noises, with an EKG showing regular sinus rhythm with heart rate (HR) at 120 bpm, and a heart axis in place without any repolarization disorders.

The patient received a loading dose of Phenobarbital, and an initial blood test was performed showing: Elevated CRP with hyperleukocytosis at 14140 with PNN predominance, thrombocytopenia, hepatic cytolysis with increased LDH and ferritinemia. DDimer levels were elevated to 9060 ng/mL with a positive Troponin level of 0.146. Lumbar puncture was performed on 2 occasions and came back negative with negative multiplex panel meningoencephalitis PCR and negative CSF BK test. Brain CT (Figure 1) showed meningeal enhancement.

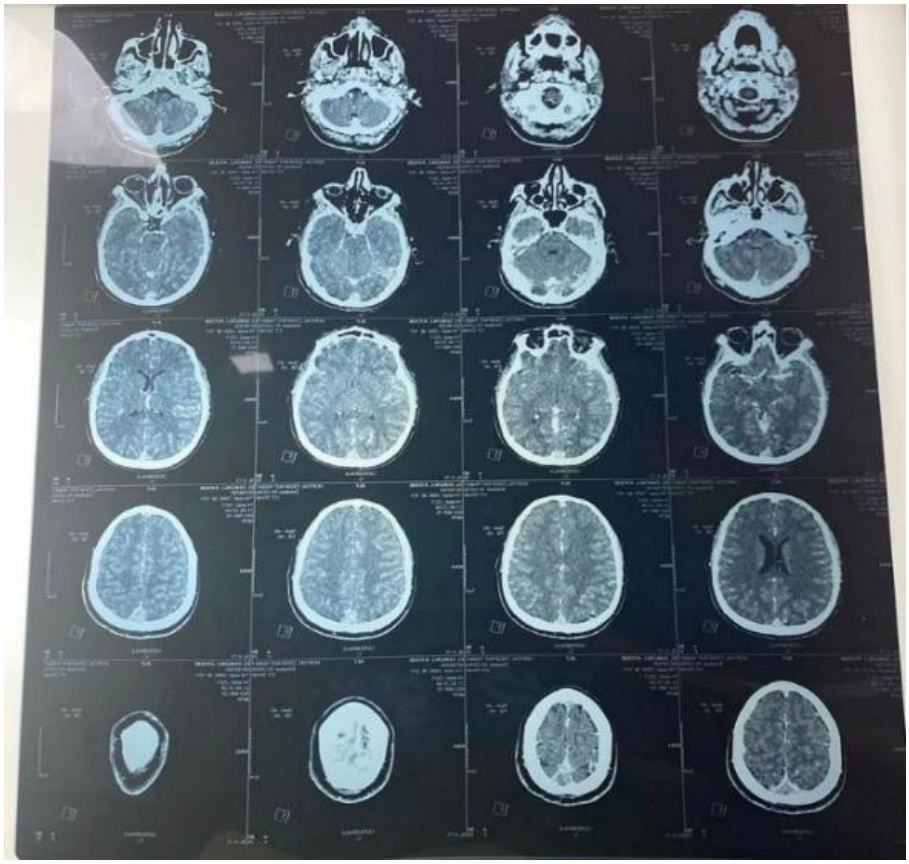

Figure 1: Brain CT showing meningeal enhancement.

Two covid rapid tests and a covid PCR came back negative with a viral serology showing positive IgG anti SARS COV-2 antibodies at 14.73 U/mL. Chest X-ray showed bilateral basal opacities with a chest CT scan (Figure 2) finding condensations of the 2 pulmonary hemi fields in relation to pneumonitis.

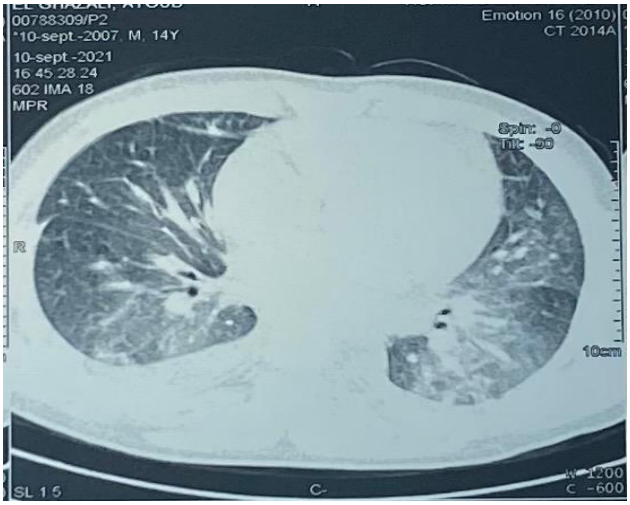

Figure 2: Section of a chest CT showing pneumonitis.

A transthoracic utrasound was performed showing a hypokinetic left ventricle with an ejection fraction (EF) of 54% in favor of myocarditis.

As a result, the diagnosis of a post-COVID inflammatory syndrome was retained and the patient was put on a bolus of 10mg/kg of Solumedrol for 3 days, followed by 2mg/kg/d of Solumedrol with regression of the inflammatory balance, and normalization of the transthoracic ultrasound. The patient, however did not improve his GCS (GCS 12), a brain MRI was performed (Figure 3) which showed cerebral venous thrombosis complicated by right fronto-parieto-temporal venous infarction with intra-parenchymal hematomas.

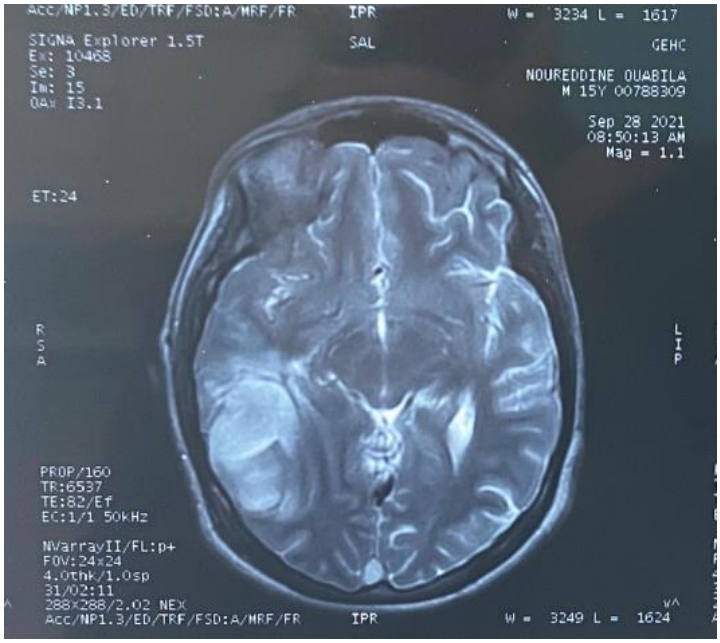

Figure 3: Brain MRI showing cerebral vein thrombosis

The patient was put on 100 IU/Kg of low molecular weight heparin (twice a day) resulting in a marked improvement in his state of consciousness (GCS 15).

Case 2

The patient K.Y was a 14-years-old adolescent, who had also not been vaccinated against COVID19, with no history of recent covid infection but with a covid contact 2 weeks earlier. The patient had a fever for 7 days treated with amoxicillin-clavulanic acid without improvement. The evolution was marked by the persistence of the fever and the appearance of vomiting, headaches and non-pruritic skin lesions motivating his consultation at a local hospital where a treatment made of Ceftriaxon, Gentamycin and Betamethasone was administered, then transferred to the pediatric intensive care unit, due to the development of a state of shock.

Clinically, the patient was febrile at 40°C with a stiff neck, polypnea at 50 c/min, and a SpO2 at 94% at AA. He was tachycardic at 140 bpm, hypotensive at 80/40 mmHg with an elongated skin recoloration time (5 sec) and coldness of the extremities. On cardiovascular auscultation: a mitral murmur rated at 5/6 was perceived, with an EKG showing regular sinus rhythm, and a diffuse repolarization disorder without mirror image with incomplete right branch block. On mucocutaneous examination, there were papular lesions in the shape of a cockade that faded on in vitro pressure, especially on the lower limbs and abdomen (Figure 4), with palpebral erythema (Figure 5) and non-purulent bilateral conjunctivitis.

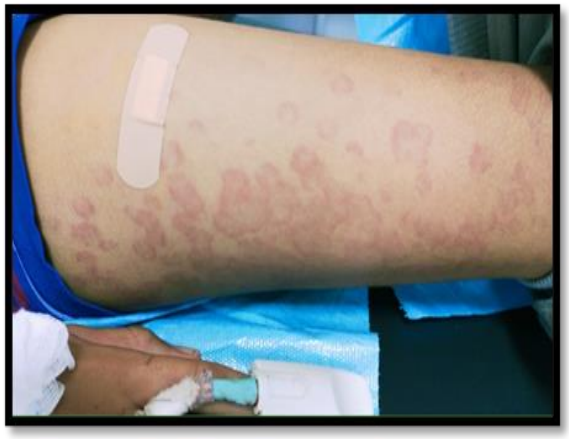

Figure 4: Papular lesions in the shape of a cockade on the right thigh

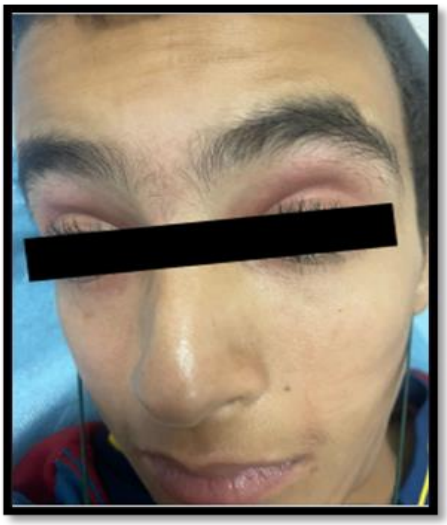

Figure 5: Palpebral erythema

The abdomen was tender with epigastric and right hypochondrial tenderness.

The patient was given a vascular filling, and a central veinous line was put for the introduction of Noradrenaline at the speed of 0.35µg/kg/min. The blood test showed: A hyperleukocytosis to 25000, lymphopenia to 556 mm³, D-Dimer level elevated to 5,771.02 ng/ml, positive troponin to 0.993. A lumbar puncture came back negative. A cerebral and thoraco-abdominal CT scan was performed revealing few condensations and ground glass of peripheral distribution in the dorsal segment of the right upper lobe, a hepatomegaly of 14.6cm and a splenomegaly of 11.6cm. A COVID PCR came back negative with COVID serology showing positive IgG at 2.65 COI. A transthoracic ultrasound was performed showing a hypokinetic left ventricle with an EF of 53%, minimal mitral insuffisency, in favor of myocarditis.

The diagnosis was a cardiogenic shock due to myocarditis in the context of a MIS-C. The patient was given a bolus of 10mg/kg of Solumedrol for 3 days, followed by 2mg/kg/d of Solumedrol and a Noradrenaline withdrawal, with a good clinical evolution, regression of skin lesions and inflammatory balance, and normalization of the transthoracic ultrasound.

DISCUSSION

Since the beginning of the COVID19 pandemic, most cases of MIS-C were described in Europe and North America. The first patient reported in Africa dates from August 2020 [1], while the first one in Morocco dates from January 2021 [2] and since then, the number of cases has been rising; that is why the WHO has set up criteria [3] to identify and confirm the diagnosis of MIS-C (Figure 6).

Preliminary case definition[a]

Children and adolescents 0–19 years of age with fever ≥ 3 days

AND two of the following:

1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
2. Hypotension or shock.
3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

AND

Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.

AND

No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

AND

Evidence of COVID-19 **(**RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

Figure 6: MIS-C diagnostic criteria according to the WHO

Although the exact cause is still unknown, a number of theories have been proposed, including the presence of high levels of Zonulin, a protein that increases the permeability of the gut allowing the escape of SARS-COV2 antigens into the bloodstream [4], or the discovery of a superantigen-like motif in the SARS-COV2 spike protein that interacts with T-cells triggering the cytokine [5] storm responsible for MIS-C.

Our patients presented with two different pictures; the first one was mainly neurological; with a status epilepticus and a meningeal syndrome with subsequent discovery of a cerebral venous thrombosis, in addition to respiratory and digestive symptoms with myocarditis. The second one was in a state of shock due to myocarditis with meningeal stiffness, as well as a cutaneous, respiratory and digestive involvement. Among the elements that led us to evoke the diagnosis of MIS-C, there are the background (older child with 14-15 years old, and a previous COVID contact for the second patient), the presence of a long-lasting fever with clinical signs of multisystemic involvement in the absence of other causes that could explain the symptomatology (negative infection workup), elevated inflammatory markers with coagulopathy (elevated D'Dimers), evidence of a previous COVID infection (positive IgGs) that went unnoticed for the two patients, as well as the presence of signs of myocarditis on the transthoracic ultrasound in relation to post-viral myocarditis. Post-vaccination myocarditis was ruled out as both our patients were not vaccinated against COVID19. Our two patients received corticosteroids alone with significant clinical and biological improvement, however, a study showed that combination therapy (IV Ig and methylprednisolone) would result in better recovery, less risk of treatment failure and a shorter length of stay in the pediatric intensive care unit [7]. Due to lack of resources, we were not able to introduce IV Ig to them.

In Morocco, although we see more and more cases in our practice, the Children's Hospital of Rabat has admitted 23 cases of MIS-C since the beginning of COVID19 pandemic; the only severe cases are these two patients; hence the interest of our article.

CONCLUSION

The multi systemic inflammatory syndrome in children is a new entity that any practitioner in contact with the pediatric population has to evoke in front children with fever and at least two criteria as described by WHO in the actual pandemic situation.

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