
Multisystem Inflammatory Syndrome in Children at Early Age

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Abstract

Introduction: Multisystem inflammatory syndrome in children (MIS-C) is the dangerous complication in the pediatrics population associated with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). It leads to the injury of several organs and impairment of their function. Treatment protocols have been placed to avoid the long-term consequences of this syndrome which may be severe enough to cause death of the affected patient.

Case description: A 50 days old boy with no previous medical conditions presented to the hospital with respiratory distress and had a negative reverse transcription polymerase chain reaction (RT-PCR) test for novel coronavirus and his family denied contact with a COVID-19 infected individual. The patient clinical status deteriorated and was not responding to antibiotics and nebulizers. This raised our suspicion for MIS-C so a SARS-CoV-2 serology was performed and were found out to be positive. Treatment started but the patient deteriorated rapidly and ended up intubated on mechanical ventilation then passed away after a cardio-pulmonary arrest.

Discussion: During the COVID-19 pandemic, respiratory complaints must be considered to be associated with coronavirus infection and must not be ruled out by just performing a PCR test from a nasopharyngeal sample. Knowing that MIS-C usually do not appear during the acute phase of coronavirus infection but rather after the resolving of the infection.

Conclusion: This case raises the necessity of performing serology for SARS-CoV-2 for a patient presenting with respiratory complaints and with non-resolving multi-organ inflammatory injury. Also, no age group can be considered safe and protected from complications of coronavirus infection. This is why serious precautions must be applied when a suspected or infected individual is dealing with other people.

Keywords: MIS-C; SARS-CoV-2; Pediatrics; Serology

Introduction

An alarming rate of spreading of SARS-CoV-2 infection has been noticed since the novel virus was first reported on December 2019. At the beginning of the pandemic physicians noticed that children have a milder course of infection and even many pediatric cases went asymptomatic and subclinical. Later, reports from the United Kingdom described the emergence of a new entity in the pediatric population where children were severely affected with the novel coronavirus to the degree that they required supportive care through mechanical ventilation and multiple organs support due to pan-organ involvement and shock-like state.

In comparison to the acute phase of the COVID-19 where the respiratory symptoms are the major complaint, MIS-C is characterized by fever, vomiting, abdominal pain and diarrhea [1]. This fact leads to the misinterpretation of such complaints and misdiagnosis. Here we present the case of a very young, 50 days old, boy patient who presented to our hospital with respiratory symptoms but a negative RT-PCR test for COVID-19 and later was found to be suffering from complications of COVID-19 virus which is known as MIS-C.

Case Report

History and presentation

A 50 days old previously healthy baby boy with no prior hospitalization or post-natal complications presented to the emergency department (ED) of Rafik Hariri University Hospital with one day history of low-grade fever, cough and vomiting. History goes back to 2 days prior to presentation when the baby started having post-prandial vomiting with low grade fever associated with cough and tachypnea. Family mentioned no contact with a COVID-19 infected patient. Upon presentation, the baby was tachypneic and was moderately dehydrated. Vital signs showed mild tachycardia with low grade fever. Physical examination showed clear chest on auscultation and no other associated abnormalities were found.

Diagnostic focus and assessment

Immediately after presentation blood was drawn out for hematologic and biochemical tests and for blood culture. Results are shown in tables below. Also, a urine sample was taken for analysis and culture which came back negative. In addition, a chest X-ray (CXR) was done showing no infiltrates or consolidations (Figure 1).



PCR test for SARS-CoV-2 was taken at the ED and was negative indicating no presence of COVID-19 infection so the patient was admitted to the pediatric department.

Therapeutic focus and assessment

The patient was started on intravenous (IV) ceftriaxone and vancomycin for possible early pneumonia and on normal saline nebulizers for possible bronchiolitis. On the second day of hospitalization the patient's respiratory status deteriorated and he started having desaturation so he required oxygen by face mask. A repeated nasopharyngeal swab for SARS-CoV-2 RT-PCR was also negative. So CXR was done revealing bilateral patchy infiltrates (figure 2) that was not present on the previous day so a diagnosis of atypical pneumonia was established and clarithromycin was added.

Table 1: Hematology and Biochemistry test results on day 1 and 3 of hospitalization.

	Day 1	Day 3
Haemoglobin (g/L)	12.8	9.1
White blood cells (cu/mm ³)	11,100	11,600
Haematocrit (%)	37.7	27.3
Mean cell volume (fL)	97	94
Platelets (cu/mm ³)	238000	38000
Neutrophil (%)	36.6	53

Lymphocyte (%)	57.8	37.5
INR	1.2	3.3
Alkaline phosphatase (IU/L)	---	172
SGOT (IU/L)	---	961
SGPT(IU/L)	---	685
Gamma GT (IU/L)	---	85
Sodium (mEq/L)	139	138
Potassium (mEq/L)	4.8	3.7
HCO ₃ (mEq/L)	18	13.7
Creatinine (μmol/L)	0.5	0.55
CRP (mg/dL)	1.3	2.8
Cardiactroponin (ng/L)	---	0.23
CPK (IU/L)	---	639
IL-6 (pg/ml)	---	112
D-dimer (μg/mL)	---	5.72
Albumin (g/L)	---	30

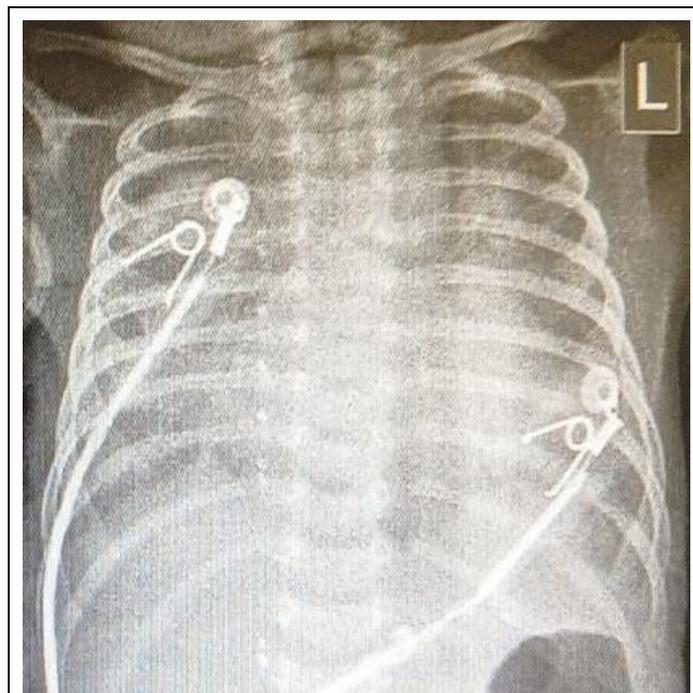


Figure 2: Chest X-ray on second day of hospitalization.

On the third day, tachypnea increased significantly and subcostal retractions developed which increased the work of breathing so he was intubated immediately. On physical examination, hepatomegaly was noticed and bilateral lower limb pitting edema developed. Blood drawn out for COVID-19 serology and other tests (Table 1, 2 and 3) showing positive serology for SARS-CoV-2 immunoglobulins indicating recent infection with COVID-19. Diagnosis of multisystem inflammatory syndrome in children (MIS-C) was established so Intravenous Immunoglobulins (IVIG) and steroids were started. Despite respiratory support and intensive care and management, cardiorespiratory arrest took place on the fourth day of hospitalization and the patient unfortunately passed away on the same day.

Table 2: Results of blood and urine culture after 48 hours of incubation.

	After 48 hours
Blood cultures	No growth
Urine culture	No growth

Table 3: Serology showing immunoglobulins for SARS-CoV-2 and indicates immunity. Negative for all the values < 0.9 COI (Cut Off Index); equivocal for all the values between 0.9 and 1.1 COI; positive for all the values >1.1 COI [2].

IgA SARS-CoV-2 immunoglobulins	9.24 COI
IgM SARS-CoV-2 immunoglobulins	8 COI
IgG SARS-CoV-2 immunoglobulins	2.3 COI

Discussion

MIS-C is a febrile inflammatory syndrome with multiple organ involvement. According to the Center of Disease Control and Prevention (CDC) for the diagnosis of MIS-C six main conditions must be present. The first and second conditions are fever $\geq 38^{\circ}\text{C}$ for more than 24 hours and laboratory evidence of inflammation which are both present in this case as persistent fever and elevated interleukin-6 (IL-6) marker. The third and fourth conditions are an illness requiring hospitalization and involvement of two or more systems which are also applicable to the case described above where the patients clinical condition necessitates a hospital admission and even the need for intensive care with involvement of the respiratory, cardiac and gastrointestinal systems. Additionally, evidence of recent SARS-CoV-2 infection was found through a positive serology for COVID-19 immunoglobulins. Lastly, the sixth applicable condition is that no alternative diagnosis is applicable where all possible differential diagnoses were ruled out before confidentially establishing the diagnosis of MIS-C.

It is noted that 52% of affected individuals have no underlying medical conditions [3] which is the case of the described patient who was previously healthy with no known chronic medical conditions prior to contracting COVID-19 infection.

Some clinical and laboratory markers make MIS-C a diagnosis of exclusion due to its diverse infectious and non-infectious differential diagnoses including atypical Kawasaki disease that have many common features with MIS-C. The second differential diagnosis is severe bacterial sepsis that also leads to cardiovascular decompensation and shares certain laboratory markers with MIS-C. For example, although viral infections are characterized by elevated lymphocyte percentage, reviews studying the features of MIS-C showed that it is characterized by neutrophilia and lymphocytopenia. Also, the ratio of neutrophils to lymphocytes appeared to increase and to be a predictive index for the severity of the disease [4]. Another marker, procalcitonin, which was considered a marker to differentiate bacterial and viral infections has shown to be elevated in MIS-C [3]. Additional differential diagnosis includes appendicitis and systemic lupus erythematosus whose first manifestations can be fever and abdominal pain.

COVID-19 can present during acute infection as mild upper respiratory tract illness which can go unnoticed and this may help in masking SARS-CoV-2 infection during parents' interview.

Moreover, in a study from the United States conducted on hospitalized patient suffering from MIS-C, 58% of patients who developed MIS-C have only serologic evidence of coronavirus infection without positive RT-PCR test. Additionally, it showed that about 4% of the affected patients aged less than one year [5]. This adds uniqueness to the case we presented above where the patient is a 50 days old infant.

Conclusion

During COVID-19 pandemic, it is necessary to keep the diagnosis of MIS-C in mind in front of a rapidly deteriorating child. A negative PCR test for COVID-19 does not exclude the diagnosis of MIS-C in children since more cases are being reported after the acute phase of the infection when the PCR has turned to be negative. Serology for SARS-CoV-2 must become a routine test for pediatric patients admitted for respiratory symptoms regardless of history of exposure to a COVID-19 infected individual especially when the parents are considered poor historians. Another reason is that children may have contacted other children who are asymptomatic but are infected and carrying the COVID-19 virus and are spreading it to the surrounding individuals. Here emerges the importance of further research to explain why certain children have a greater susceptibility for developing MIS-C although many of which are previously healthy and suffers no comorbid or chronic medical conditions.

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