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Multi-System Inflammatory Syndrome in Children Presented with Persistent Respiratory Alkalosis: A Case Report

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***Abstract*:- Multi-System Inflammatory Syndrome in Children (MIS-C) was identified by the US Centers for Disease Control and Prevention (CDC) as a person <21 presenting with fever ≥24 hour with at least two multisystemic-organ involvement, including predominantly gastrointestinal and cardiovascular symptoms associated with high inflammatory markers. Frequently, these manifestations may correspond to severe acute respiratory syndrome due to coronavirus-2 (SARS-CoV-2), which represent a challenge for any pediatrician or clinicians. In this report, we presented a five-year-old boy with persistent respiratory alkalosis. Moreover, we demonstrated the management protocol for such cases, which will aid in reducing the burden of such challenges.**

Keywords: Case report, SARS-CoV-2, COVID-19, Saudi Arabia

INTRODUCTION

In March 2020, the World Health Organization (WHO) was declared the coronavirus disease of 2019 (COVID-19) as a pandemic, which is the responsible cause of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Fortunately, children represent only 2% of the whole case since the onset of the coronavirus (COVID-19) pandemic with milder symptoms compared to adults [2]. Later, in mid-April, Riphagen S. et al. reported eight children sharing Kawasaki shock syndrome-related features similar to SARS-CoV-2, such as delayed reaction [3]. These symptoms were subsequently reported worldwide; thus, Multi-System Inflammatory Syndrome in Children (MIS-C) was identified by the US Centers for Disease Control and Prevention (CDC) as a person <21 presenting with fever ≥24 hr with at least two multisystemic-organ involvement, including predominantly gastrointestinal and cardiovascular symptoms associated with high inflammatory markers, in addition to a history of contact to COVID-19 cases or history of recent infection [4]. In contrast, these variant manifestations corresponded to (SARS-CoV-2) [5], which represent a challenge for any pediatrician or clinicians. In this report, we present a five-year-old boy with persistent respiratory alkalosis.

CASE PRESENTATION

A 5-year-old boy, who was previously healthy, came to the emergency department with a history of persistent fever for six days associated with headache, fatigue, abdominal pain, maculopapular inguinal rash, and decreased oral intake and activity. SARS-COV-2 infection was detected approximately two days ago. **Table 1** shows the clinical and laboratory characteristics of the child. The patient was lethargic and had appeared sick. Vital signs were febrile (38.9°C), borderline normal blood pressure (88/55 mmHg), with normal respiratory rate, SPO2 and heart rate. Initial laboratory findings showed normal WBCs, mild increase in neutrophil count, anemia, mild thrombocytopenia, hyponatremia, hypokalemia, mild hypochloremia, hypoalbuminemia, and elevated LDH. Coagulation profile was within the reference range. However, the D-dimer was elevated, the inflammatory markers revealed ESR (77 mm/hour), CRP (>27 mg/dL), ferritin (438.4 ng/mL), and the CKMB was (33.4 mg/dL). Initial venous blood gas showed respiratory alkalosis, Ph (7.54), CO2 (26.6 mmHg/L), and HCO3 (26.2 mmol/L); therefore, the patient was admitted to the Pediatrics ICU as a case of SARS-COV-2 with MIS-C. According to the Saudi MOH guidelines protocol for the treatment of MIS-C, ceftazidime, vancomycin, IVIG 2g/kg/dose, methylprednisolone (10mg/kg/dose), enoxaparin, tocilizumab, aspirin, and favipiravir were initiated. After a single dose of IVIG the patient began to improve; fever decreased on the second day of admission. During admission to PICU, despite the sufficient hydration & chemistry of the blood, the patient demonstrated a reduction in the blood pressure with wide pulse pressure (98/35). Therefore, the patient was administrated norepinephrine to maintain the blood pressure; moreover, potassium chloride was given to correct the hypokalemia; then patient became stable and improved, so norepinephrine weaned gradually after that patient shifted to an isolation room in the general pediatric ward. Then, he stayed in PICU for five days & a full hospital stay about eight days. Finally, he discharged home in good condition with a tapering dose of prednisolone and aspirin with cardiology and nephrology outpatient department's (OPD) follow up regarding persistent respiratory alkalosis and hypokalemia with renal ultrasound to exclude renal diseases.

DISCUSSION

Our patient fulfilled the CDC criteria in terms of MIS-C [4]. Evidence of current or recent SARS-CoV-2 infection is confirmed by reverse transcription-polymerase chain reaction (RT-PCR), serology test, or exposure to a suspected or confirmed COVID-19 case within the four weeks before the onset of symptoms. We considered our patient as a case of MIS-C, and we follow the Saudi MOH

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guideline for treating MIS-C by pulse therapy of methylprednisolone (ranging from 2 to 30 mg/kg/day), intravenous immunoglobulin, 1 to 2 grams/kg, enoxaparin, tocilizumab, aspirin, and favipiravir.

MIS-C occurs as the delayed latent reaction to SARS-CoV-2 that triggers the immune system to generate antibodies that are the responsible cause of cytokines storm [6]. We assumed that the cytokines storm contributes to metabolic acidosis of SARS-CoV-2 patients; however, our patient's presented by persistent respiratory alkalosis associated with hypokalemia and hypotension with wide pulse pressure despite adequate hydration. All of these indicators raised our suspicion of other underlying diseases affecting the acid-base balance, especially renal diseases such as Barrter syndrome and Gitelman syndrome (GS) [7,8]. Further investigations are needed to elucidate the pathophysiological mechanism of MIS-C in relation to other associated inherited renal diseases in pediatrics ages group.

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Table 1: Clinical and laboratory characteristics

Investigations	**Reference Range**	**Patient Result**	
		Initial	**Final**
Complete blood count			
Total white blood cells	4.5-13.5 $\times 10^3/\mu L$	9.41	23.93
Neutrophil count	**1.5-8.5** $\times 10^3/\mu L$	8.36	22.18
Lymphocyte count	**1.5-6.5** $\times 10^3/\mu L$	0.71	1.48
Hemoglobin	12.5-13.7 g/dL	9.9	9.4
Platelets	150-350 $\times 10^3/\mu L$	136	210
Biochemistry			
Random serum glucose	7-200 mg/dL	84.7	130
Creatinine	44-88 µmol/L	53	53.08
Urea	1.7-7.1 mmol/L	4.2	3.0
calcium	2.1-2.5 mmol/L	2.27	1.96
sodium	135-145 mmol/L	132	139
Potassium	3.5-5 mmol/L	4.11	3.3
Chloride	97-107 mmol/L	93.0	99
Magnesium	0.63-1.05 mmol/L	1.00	0.87
Phosphorus	0.78-1.42 mmol/L	1.36	1.2
LDH	100-190 units/L	306	213
Total serum bilirubin	0.2-1.5mg/dL	0.460	
Direct bilirubin	0.0-0.2 mg/dL	0.242	

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Albumin	34.0-50.0 g/L	29.0	29.2
AST	13-35 unit/L	38.2	15
ALT	10-30 unit/L	19.9	20
Alkaline phosphatase	100-320 units/L	91.0	74
Blood Gases			
pH	7.35-7.45	7.544	7.435
Hco3	21-28 mmol/L	26.2	24.6
PCo2	35-45 mmHg/L	27.6	36.7
Coagulation Profile			
PT	11.0-13.5 seconds	11.8 sec.	
PTT	30-40 seconds	37.8 sec.	
INR	0.8-1.1	1.03	
Inflammatory Markers			
ESR	0.0-20 mm/hour	77	
C-RP	0.0–0.9 mg/dL	>27.0	
Ferritin	7-140 ng/mL	438.4	
Cardiac enzymes			
Troponins	<0.2ng/ml	NOT TAKEN	
CKMB	0-25U/L	33.4	
Cultures, Serology			
COVID-19 PCR	Positive twice		
Blood culture	Negative		
Urine Culture			
Cytomegalovirus antibodies			
Epstein-Barr virus antibodies			
Herpes Simplex Virus Antibodies			