A Case report: Initial diagnostic and management of MIS-C in Community hospital

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Abstract

Coronavirus disease (COVID-19) is an infectious disease that occurred in December 2019 [1], caused by SARS-CoV-2 virus. It can be curable without a specific treatment [2]. At present COVID-19 is spreading all over the world and transmitted in children and adults but the signs and symptoms of COVID-19 are less in children than adults [3-5]. Therefore, it has been found that children may have a history of COVID-19 infection, making them miss the complication of COVID-19 known as the Multisystem inflammatory syndrome in children (MIS-C), which necessarily requires patients' medical history, physical examination, and specific laboratory test results that are limited and different according to capacity of each hospital.

This case is reported in order to serve as an early detection of MIS-C in community hospitals in which laboratory investigation and primary management can be sent according to hospital capacity before patients are referred to tertiary care hospitals.

Introduction

COVID-19 in an infectious disease caused by the SARS-CoV-2 virus giving rise to mild to moderate respiratory symptoms. It can be cured without a specific treatment in general population without clinical and risk factors[6]. The MIS-C is a complication found among young and adolescent patients with a history of COVID-19 infection. There is a case report and case series related to MIS-C in pandemic area of COVID-19 from Europe and North America with some clinical features similar to Kawasaki disease and toxic shock syndrome, leading to multiple organ failure and shock [7]. A theory reminding that this group of diseases is possibly associated with COVID-19 is when an initial lab test is performed and positive serology is detected among the majority of patients[7]. The diagnosis of MIS-C was performed among individuals aged < 21 years present with fever**, laboratory evidence of inflammation***, and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); and no alternative plausible diagnoses, positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms [7]. Systematic review report from March - June 2020 identified 783 cases of MISC and 55% of them were boys and the median age was 8.6 years. The clinical manifestation was noted as gastrointestinal symptoms (71%)

***Fever ≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours*

****Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin.*

including abdominal pain (34%) and diarrhea (27%), cough, and upper respiratory tract symptoms, 4.5 % and 9.6% respectively[3].

As for initial immunomodulatory treatment, the first line is Intravenous immunoglobulin (IVIG) dosing is 2 gm/kg based on ideal body weight, with maximum dose of 100 gm. Cardiac function and fluid status should be assessed before IVIG is given. In some patients with cardiac dysfunction, IVIG may be given in divided doses (1 gm/kg daily over 2 days). Methylprednisolone 1-2mg/kg/day or another steroid at equivalent dosing may be used. Many studies showed that patients treated with IVIG and methylprednisolone had a lower risk of treatment failure, improved cardiac function, shorter duration of ICU stay, and reduced rates of treatment escalation compared to children who received IVIG alone.[9]

The treatments of refractory disease (defined as persistent fevers and/or ongoing and significant end-organ involvement) are high dose Methylprednisolone 10-30 mg/kg/day or high dose Anakinra or Infliximab 5-10 mg/kg IV. Infliximab should not be used in patients with MIS-C and features of macrophage activation syndrome. [9] MIS-C is considered a group of signs and symptoms affecting several organs and systems. However, this syndrome should be taken into consideration by finding causes and other diseases that are able to occur frequently because once MIS-C is diagnosed, patients are able to be treated with appropriate medications in a timely manner.

Case report

There is a case report of a patient with SARS-CoV-2 related MIS-C with cardiogenic shock diagnosed at community hospital and was referred to the main tertiary care hospital in Phuket, Thailand.

A previously healthy 10-year-old boy underwent a treatment at community hospital on 5th April 2022 due to having fever for 6 days with abdominal pain, nausea, vomiting, and diarrhea. He used to have a treatment at a clinic and was diagnosed with acute gastroenteritis, then underwent a symptomatic treatment but he did not get better. The patient had a history of COVID-19 infection on 28 February 2022. He had low grade fever with a runny nose and productive cough then was diagnosed by COVID-19 rapid antigen testing and received symptomatic treatment with home isolation for 10 days. He did not have a record of having COVID-19 vaccination.

According to the physical examination, vital signs at admission showed a fever (body temperature 38.4 °C), tachycardia (pulse rate 130 beats/minute), tachypnea (respiratory rate 26 times/minute) and hypotension (blood pressure 88/42 mmHg). His body weight and height are 46 kilograms and 146 centimeters respectively (Weight for height is 36 kilograms). The significant positive findings from the physical examination were injected conjunctiva with limbal sparing **(Figure 1).** According to an abdominal examination, the patient had pain when pressing on the epigastric area, and hepatosplenomegaly was not found.

According to the primary physical examination, the patient was diagnosed with bacterial gastroenteritis with moderate dehydration and was admitted to community hospital. A primary treatment was performed by giving normal saline 500 ml (15ml/kg) loading in 30 minutes then continue 5% dextrose in normal saline rate 100 ml/hour and Ceftriaxone 2 grams intravenously. Initial lab test results found anemia (hemoglobin of 11.3 mg/L and hematocrit of 32.6%), Leukocytosis (white blood cell 21030 leukocytes/mm^3) with 97% polymorphonuclear and lymphopenia 2% lymphocytes (Calculated absolute lymphocyte count (ALC)=420 lymphocytes/mm^3). The chemistry showed hyponatremia (Na 130 mmol/L) with hypokalemia (K 2.9 mmol/L), Chloride 90 mmol/L, Bicarbonate 22 mmol/L, Alanine transaminase 49 U/L, Alanine aminotransferase 43 U/L, Albumin 3.4 mg/dl. The urine analysis showed urine specific gravity 1.015, urine albumin/sugar negative, WBC 1-2 cells/HPF and RBC negative

On the following day, the patient still had fever (body temperature 37.5-38.2 °C), tachypnea (respiratory rate 28 beats/minute), tachycardia (pulse rate 110-120 beats/minute) and borderline hypotension (SBP 90-100) with still complained of abdominal pain. An electrocardiogram showed sinus tachycardia. Chest x-ray found increase cardiomegaly **(figure 2)**. Besides, computerized tomography of whole abdomen was performed for differential diagnosis but there was no evidence of acute appendicitis or others.

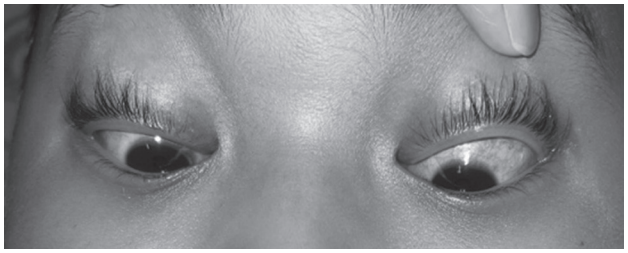

Figure 1 injected conjunctiva with limbal sparing

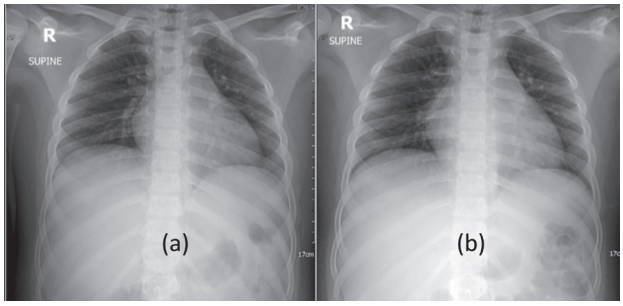

Figure 2 **(a)** Chest x-ray on 5th April 2022 (first day of admission) compare with **(b)** Chest X-ray on 6th April 2022 that showed increase CT-ratio (Cardiomegaly)

Moreover, additional lab test that could be performed at the community hospital was carried out, i.e., inflammatory marker test showed Erythrocyte Sedimentation Rate (ESR) 136 mm/hour, including cardiac marker, high sensitivity Troponin I 79.7 pg/ml. Based on such information, they were initially diagnosed as SARS-CoV-2 related Multisystem inflammatory syndrome in children with cardiogenic shock. Finally, the fluid was decreased to 50% maintenance and Dopamine 10 mcg/kg/min was given for raised blood pressure and the patient was referred to the main tertiary care hospital.

At the tertiary care hospital, SARS-CoV-2 Antibodies (anti-nucleocapsid) IgM/IgG test result was submitted; IgM negative, IgG 186.4 AU/ml, since the patient did not get COVID-19 vaccination. It was confirmed that the patient was actually had COVID-19 infection in the past. In addition, additional inflammatory marker tests were performed and an increased C-reactive protein (CRP) 85 microgram/L was found. Hypoalbuminemia (2.8 g/dL), high Lactate Dehydrogenase (325 U/L) were also detected. Additional biomarker for heart failure was performed and found an increased NT-proBNP; 10371 pg/ml. The earlier mentioned laboratory tests supported the diagnosis of SARS-CoV-2 related MIS-C. An echocardiogram was performed that showed normal cardiac function.

The treatments given to the patient included IVIG 1gm/kg/dose drip in 10 hours for 2 days because of volume overload status, Methylprednisolone 60 mg/day for 3 days then oral Prednisolone. After the patient took the aforementioned medications, fever and cardiogenic shock were resolvable; Dopamine could go off within 1 day after receiving the treatment. Aspirin 81 mg/day and Enalapril 2.5 mg/day were given. Inflammatory marker values were monitored, i.e. decreased CRP to 49.60 on the 2nd day, and to 10.32 on the 5th day after the treatment and <10 at one week after being discharged from the hospital. 1 month follow up, Echocardiogram was normal, then pediatrician stopped Prednisolone and Aspirin.

Discussion

MIS-C is a group of syndrome considered complications from getting infected with COVID-19 that is currently spreading across the world. MIS-C leads to severe problems through cytokine storms to numerous vital organs, such as heart, lung or kidneys. Importantly, in some cases, it can lead to permanent damage or death [10]. This report mentioned a male child

patient who was taken to the hospital with a fever and abdominal pain showing many differential diagnoses. Once patients come with such signs and symptoms, it is necessary to differentiate diseases frequently found, such as acute appendicitis, acute gastroenteritis. However, under the current situation, MIS-C should be taken into consideration due to the spread of COVID-19, especially in children who have or do not have a medical record of COVID-19 infection as they probably had asymptomatic infection before.

MIS-C is diagnosed based on persist fever more than 24 hours with a vital organs involvement together with lab investigation, for this patient, the diagnosis included low absolute leukocyte count, neutrophilia, hyponatremia, elevate inflammatory marker including hypoalbuminemia, anemia that fit this patient, compared to the diagnosis criteria both from CDC**** [8], Thai guideline [11] and American College of Rheumatology Clinical Guidance[9] to ensure the patient is referred to the tertiary care hospital in a timely manner with the least complications.

The overlapping syndrome between Kasawaki disease and MIS-C features suggest the same pathophysiology that could be responded to the same treatment - IVIG and glucocorticoid [12]. Some studies found the use of IVIG together with methylprednisolone was better than the use of IVIG alone, based on the necessity of the use of second dose IVIG. [9][13] This patient received IVIG and methylprednisolone, contributing to feeling better with low fever from the first day accordingly. In conclusion, the laboratory in a community hospital, for example, is limited and cannot diagnose MIS-C, but we should be aware of the disease in young and adolescent patients to alleviate complications and long-term damage.

Acknowledgement

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Reference

1. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutierrez-Ocampo E, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis. 2020;34:101623.
2. Coronavirus disease(COVID-19). Health Topic. World Health Organization. Available from: https://www.who.int/health-topics/coronavirus.
3. Radia T, Williams N, Agrawal P, et al. Multi-system inflammatory syndrome in children & adolescents (MIS-C): a systematic review of clinical features and presentation. PaediatrRespir Rev. 2021;38:51–7.
4. Cai J, Xu J, Lin D, Yang Z, Xu L, Qu Z, et al. A Case Series of children with 2019 novel coronavirus infection: clinical and epidemiological features. Clin Infect Dis. 2020. Epub 2020/03/01
5. Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. PediatrPulmonol. 2020;55: 1169-74.
6. COVID-19 Treatments and Medications. Centres for Disease Control and Prevention. Available from: https://www.cdc.gov/coronavirus/2019-ncov/your-health/treatments-for-severe-illness.html
7. Stephen Freedman, Shana Godfred-Cato, Richard Gorman, Rakesh Lodha, Lynne Mofenson, Srinivas Murthy, et al. Multisystem inflammatory syndrome in

***** CDC ; Centers for Disease Control and Prevention*

children and adolescents temporally related to COVID-19. World Health Organization. Available from: https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19
8. Information for Healthcare Providers about Multisystem Inflammatory Syndrome in Children (MIS-C). Centres for Disease Control and Prevention. Available from: https://www.cdc.gov/mis/mis-c/hcp/index.html
9. Henderson LA, Canna SW, Friedman KG, et al. American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With SARS-CoV-2 and Hyperinflammation in Pediatric COVID-19: Version 3. Arthritis Rheumatol. 2022;74:e1-e20.
10. Pruthi S, Acosta AJ, Arora AS, et al. Multisystem inflammatory syndrome in children (MIS-C) and COVID-19. Mayo Clinic. 2020. Available from: https://www.mayoclinic.org/diseases-conditions/mis-c-in-kids-covid-19/symptoms-causes/syc-20502550
11. Samkoses R, Chotpitayasunondh T, Chokephaibulkit K, et al. Guideline for diagnostic and treatment of Multisystem inflammatory Syndrome in Children; MIS-C and Hyperinflammation in Pediatric COVID-19 in Thailand. 2565;3:2-13.
12. Ahmed M, Advani S, Moreira A, et al. Multisystem inflammatory syndrome in children: A systematic review. EClinicalMedicine. 2020;26: 100527. Available from: 10.1016/j.eclinm.2020.100527
13. Ouldali N, Toubiana J, Antona D, et al. Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone With Course of Fever in Multisystem Inflammatory Syndrome in Children. JAMA. 2021;325:855–864.

การวินิจฉัยและการรักษาภาวะมิสซีเบื้องต้นในโรงพยาบาลชุมชน

สุทธิกิต พิกุลผล, กัญญาภัค สิงห์ดำ

บทคัดย่อ

โรคติดเชื้อไวรัสโคโรนา (COVID-19) เป็นโรคติดเชื้อระบบทางเดินหายใจ ซึ่งถือกำเนิดขึ้นเมื่อช่วงเดือนธันวาคม 2563[1] เกิดจากเชื้อก่อโรคไวรัสซาร์ส-โควี-2 (SARS-CoV-2 virus) ซึ่งในผู้ป่วยทั่วไปสามารถรักษาหายได้ โดยไม่จำเป็นต้องใช้ยารักษาเฉพาะ[2] ปัจจุบันโรคติดเชื้อไวรัสโคโรนากำลังระบาดไปทั่วโลก สามารถติดต่อได้ทั้งในเด็กและผู้ใหญ่ โดยในผู้ป่วยเด็กมักแสดงอาการน้อยกว่า[3-5] จึงอาจพบผู้ป่วยเด็กที่มีประวัติการติดเชื้อไวรัสโคโรนา โดยที่ไม่มีอาการแสดงมาก่อนได้ เป็นเหตุให้พลาดการวินิจฉัยภาวะแทรกซ้อนที่เกิดขึ้นภายหลังการติดเชื้อ คือ ภาวะมิสซี (The multisystem inflammatory syndrome in children : MIS-C) โดยการวินิจฉัยโรคดังกล่าว จำเป็นต้องอาศัยการซักประวัติ ตรวจร่างกาย และผลตรวจทางห้องปฏิบัติการพิเศษ ซึ่งอาจมีข้อจำกัดที่แตกต่างกันตามศักยภาพและบริบทของแต่ละโรงพยาบาล

รายงานผู้ป่วยเรื่องนี้ จัดทำขึ้นเพื่อชี้ให้เห็นถึงความสำคัญของการวินิจฉัยและการรักษาภาวะมิสซีเบื้องต้นในโรงพยาบาลชุมชน ที่มีข้อจำกัดในการส่งผลตรวจทางห้องปฏิบัติการและข้อจำกัดของยา ก่อนการส่งต่อผู้ป่วยเพื่อไปรักษาในโรงพยาบาลที่มีศักยภาพสูงกว่าต่อไป

โรงพยาบาลป่าตอง