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Case report

Challenging Case of Multisystem Inflammatory Syndrome in a 19-Year Old Female: A Case Report

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Abstract

Introduction. In comparison to older adults, SARS-CoV-2, leads to a mild illness in children and young adults typically manifested with fever, cough and gastrointestinal symptoms. However, the multisystem inflammatory syndrome in children and young adults (MISC) emerged during the coronavirus disease in 2019 pandemic.

Case report. We report a challenging case of a 19-year old female patient with signs and symptoms of multisystem inflammatory syndrome and SARS-CoV-2 infection, most probably as a post infectious disease with onset between 2 to 4 weeks after the infection. Its clinical symptoms may have overlaped with classical Kawasaki disease (systemic vasculitis) or Kawasaki-like syndrome (atypical) with fever, gastrointestinal symptoms, rash, conjunctival injection, hypotension, sore throat, mucosal changes with a relative lack of severe respiratory disease, myocarditis, hypoalbuminemia and elevated inflammatory markers. And indeed, the clinical presentation of COVID-19 in young adults resembles Kawasaki disease with gastrointestinal manifestations to severe inflammation with myocarditis.

Conclusion. Timely diagnosis and proper treatment of the multisystem inflammatory syndrome and SARS-CoV-2 infection are real challenge requiring multidisciplinary approach and tertiary resources.

Keywords: coronavirus disease, young adults, pneumonia, pleural effusion, rash, Kawasaki like disease

Introduction

In comparison to older adults, SARS-CoV-2 in children and young adults leads to a mild illness typically manifested with fever, cough and gastrointestinal symptoms. Nevertheless, the multisystem inflammatory syndrome in children and young adults (MISC) emerged during the coronavirus disease in 2019 pandemic [1]. It seems to be a post infectious disease with onset between 2 to 4 weeks after infection. Its clinical symptoms overlap with classical Kawasaki disease (systemic vasculitis) or Kawasaki-like syndrome (atypical) with fever, gastrointestinal symptoms, rash, conjunctival injection, hypotension, sore throat, mucosal changes with a relative lack of severe respiratory disease, myocarditis, hypoalbuminemia and elevated inflammatory markers [2].

We report a challenging case of a young female patient with signs and symptoms of MISC and SARS-CoV-2 infection.

Case report

A 19-year old female patient, SARS-CoV-2 PCR positive, was admitted to the University Clinic of Nephrology - Skopje (Covid 19- dedicated ward for adults). Initial symptoms included sore throat and fever treated with antibiotics with no improvement. After two weeks with positive SARS-CoV-2 test she was admitted to our hospital due to blood in the stool, body rash, severe anemia, elevated liver enzymes, elevated D-dimer, hypotension, tachycardia and heaptomegaly. Before admission due to her symptoms and the difficulty of a diferential diagnosis, the patient was examined by a hematology and a gastro-entero-hepatology specialists.

Laboratory findings timeline during hospitalization is shown in Table 1. At admission the patient presented with marked anemia with hemoglobin level below 50g/l, elevated inflammatory markers as leukocytes, thrombocytes, ferritin and C reactive protein. Electrolytes were all lower than referent levels. Increased transaminase activity, hyperbilirubinemia and hypoalbuminemia indicated a possible liver affection. Virology

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Table 1. Biochemical findings during hospitalization

Parameter	December 18	December 22	December 28
Hb (g/l)	42	86	111
RBC (10^{12}/l)	1.4	2.2	3.8
WBC (10^9/l)	25.5	18.3	12.9
PLT (10^9/l)	724	547	465
Ferritin (ug/l)	840		450
AST (U/l)	39		27
ALT (U/l)	134	76	73
LDH (U/l)	696	400	320
Total protein (g/l)	36	55	57
Albumin (g/l)	19	28	32
Total bilirubin (umol/l)	53		18
Direct bilirubin (umol/l)	43		10
Sodium (mmol/l)	130		142
Calcium (mmol/l)	1.6	2.0	2.2
Potassium (mmol/l)	3.5		4.4
Iron (umol/l)	2.1	2.5	9
Glucoses (mmol/l)	6.3	4.5	5.6
Creatinine (umol/l)	57		56
C-reactive protein (mg/l)	107	55	4.8

Abbreviations: Hb-hemoglobin, RBC-red blood cells, WBC-white blood cells, AST-aspartate aminotransferase, ALT-alanine aminotransferase, LDH-lactate dehydrogenase, alkaline phosphatase

Table 2. Hemostasis during hospitalization

Date	PLT (10^9/l)	Htc	Prothrombin time (s) (9.8–14.2)	Activated partial (s) (27.9–29.1)	Thrombin time (s) (16.1–19.01)	d-dimers (0–500)
Dec,18	589	012	12	32	14	7923
Dec, 22	378	034	11.1	29	16.8	15679
Dec, 28	287	050	10.5	31.5	18.9	8076

Abbreviations: PLT – platelets, Htc – hematocrit

findings on acute Hepatitis B and C were negative. Hemostasis findings showed marked elevation of D dimers during the whole hospitalization as shown in Table 2.

Interdisciplinary approach defined the treatment including antibiotics, low molecular weight heparin, several blood and plasma transfusions, cryoprecipitate, somatostatin analogue, proton pump inhibitors and low dose corticosteroids. Considering high inflammatory markers and fever, antibiotics were administrated with consecutive worsening of the rash and in consultation with pulmologist, the therapy was stopped. The patient underwent serological tests to detect antibodies, complement activity, proteinuria and results were in referent levels (IgE 64IU/ml, IgA 1.2 g/L, IgG 5.9g/L, IgM 0.84 g/L, C3 1.5g/L, C4 0.29g/L, rheumatoid factor 10 IU/ml, proteinuria 0.6g/L…0.09g/D). Microbiological and laboratory markers for sepsis were also negative (Procalcitonin 0.2 ng/ml, sterile hemoculture).

The fever and inflammation subsided after treatment with corticosteroids. Due to repeated rectorrhagia, gastroscopy and colonoscopy were performed. The gastroscopy findings were multiple ulcers in esophagus and stomach. The colonoscopy showed multiple ulcers in colon indicative of Crohn's disease or enteropathy due to the coagulopathies. The patient underwent serological tests (antineutrophil cytoplasmic antibodies, antinuclear antibody, anti-double stranded DNA, anticardiolipin antibodies, antiphospholipid antibody) for systemic diseases due to suspicion for vasculitis, but the tests returned as negative. Computer tomography was performed with findings of viral pneumonia, bilateral pleural effusion and pericarditis. The patient was on minimal oxygen support, therapy continued, the condition gradually improved, and there was an improvement in the laboratory analyses (Table 1). The patient was discharged after 10 days in stabile health condition, afebrile, with corrected anemia, normal liver enzymes, inflammatory markers, no signs of active bleeding with recommendation to continue the therapy with corticosteroids, low molecular weight heparin and proton pump inhibitors.

Discussion

Since an arising cluster of pneumonia cases was first reported in Wuhan (China) in December, 2019, the COVID 19 pandemic caused by Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapidly spread worldwide. Children and adolescents presented a small proportion of COVID 19 cases. Starting from April 2020, there had been an abnormal increase in cases of Kawasaki-like disease and myocarditis in children. The cases were more frequent in places heavily affected by the SARS-CoV-2 epidemic (Italy, UK and US) [3]. Risk factors for developing severe disease among children infected with SARS-CoV-2

included age, viral load, and chronic comorbidities. The epidemic curve of the Pediatric Inflammatory Multisystem Syndrome (PIMS) cases followed that of COVID-19 with a lag time of 4-5 weeks, supporting the hypothesis of PIMS being a post-infectious manifestation [4].

Kawasaki disease is a systemic vasculitis in children and one of the leading causes of childhood acquired heart disease. There are similarities between these symptoms and Kawasaki disease, but also there are differences. The patients are older than in classical Kawasaki. In classical Kawasaki disease vomiting, diarrhea and abdominal pain are present in less than 18%, but gastrointestinal signs seem to be more present in COVID-19 linked Kawasaki like disease [2]. The virus has been detected in respiratory secretions, feces and blood. Also, these two could be different diseases with several presentations (ranging from Kawasaki disease, atypical Kawasaki disease, toxic shock syndrome and myocarditis) and different mechanisms (post-infectious reaction or cytokine storm as observed in adults with COVID-19).

One should differentiate between the "classical Kawasaki disease" triggered by COVID-19, atypical Kawasaki disease and a systemic inflammatory presentation similar to cytokine storm observed in adults. We can't rule out the implication of other factors, either infectious or environmental. Nevertheless, the incidence seemed to be low. WHO has developed a case definition and case report form for multisystem inflammatory disorder in children and adolescents [5].

Patients presenting with Kawasaki Disease and MISC can have similar symptoms, physical findings, and laboratory results, but they have different diagnostic criteria [6]. Children with MISC are usually older, have more symptoms consistent with clinical shock, have involvement of gastrointestinal and cardiovascular symptoms, and have lymphopenia with elevated inflammatory markers. Our patient's findings were in line with those of MISC rather than the Kawasaki disease. Because many cases met the diagnostic criteria of classic or incomplete Kawasaki disease, most reported MISC cases were treated using the standard protocol for Kawasaki disease, which is intravenous immunoglobulin with or without aspirin. A large proportion of MISC cases have a similar presentation to Kawasaki disease shock syndrome, mainly shock, so supportive and inotropic or vasoactive treatment should also be applied. Our patient also did not present with shock or the need of inotropes. Steroids have also been used to treat MISC. Many children with MISC also present with hypotension. If signs of shock are present, patients should be resuscitated with volume expansion using buffered or balanced crystalloids and should stay under close monitoring. Broad spectrum antibiotics are also appropriate because the clinical presentation (high C reactive protein, increased neutrophils) makes it difficult to exclude bacterial infection, but antibiotic treatment should be stopped once the infection has been excluded and the patient is clinically improved [3]. Inflammatory markers are useful for stratifying risk and monitoring response to therapy [7]. In our case, considering high admission inflammatory markers antibiotics were started, but immediately when infection was rolled out, only corticosteroids were administrated.

A hallmark of COVID 19 in adult and pediatric patients has been the coagulopathy [1,3]. Some patients have developed major vessel thrombosis. Although mechanisms underlying the coagulopathy in COVID 19 are still unknown, anticoagulant therapy (mainly heparin or a low molecular weight heparin) is currently recommended for patients with severe COVID 19. Many children with MISC have elevated D dimers which, in some institutions, is used as a guide for anticoagulant treatment, especially for those with a high concentration of D dimers. Our patient presented with coagulopathy, hemorrhagic syndrome and marked anemia requiring appropriate therapy. Hence, our patient belongs to the group of younger adults and according to the symptoms and laboratory parameters was supposed to have MISC. The patient had a good response to the therapy and she was completely cured.

Conclusion

The clinical presentation of COVID-19 in young adults resembles Kawasaki disease with gastrointestinal manifestations to severe inflammation with myocarditis. Physicians should be aware of the possibility of post COVID 19 inflammatory syndrome and MISC with all the potential for complications. Timely diagnosis and proper treatment of multisystem inflammatory syndrome and SARS-CoV-2 infection are real challenge requiring multidisciplinary approach and tertiary resources.

Conflict of interest statement. None declared.

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