CASE REPORT

A case of multisystem inflammatory syndrome in children presenting as systemic onset juvenile idiopathic arthritis

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Abstract

Multisystem inflammatory syndrome in children (MIS-C) is a rare and serious COVID-19 manifestation characterised by generalised inflammatory response including inflammation of the heart, blood vessels, lungs, kidneys, brain, skin, eyes and gastrointestinal system. Children usually present with fever lasting for 24 hours or more along with other symptoms such as abdominal pain, vomiting, diarrhoea, skin rash, red eyes, and swelling of the lips, tongue, hands and feet. Children with MIS-C usually have negative results for a current infection with COVID-19 but positive antibody results indicating that these children were infected with the COVID-19 virus in the past.

We present the case of a 12-month-old girl with multisystem inflammatory syndrome presenting as systemic-onset juvenile idiopathic arthritis (SoJIA) and positive Covid-19 PCR. She was treated successfully with Dexamethasone and Naproxen.

Keywords: Multisystem inflammatory syndrome in children, Covid-19, systemic-onset juvenile idiopathic arthritis (SoJIA).

DOI: https://doi.org/10.47391/JPMA.11-1984

Introduction

Multisystem inflammatory syndrome in children (MIS-C) is a rare and serious COVID-19 manifestation characterised by generalised inflammatory response including inflammation of the heart, blood vessels, lungs, kidneys, brain, skin, eyes, and gastrointestinal system. Children usually present with fever lasting for 24 hours or more along with other symptoms such as abdominal pain, vomiting, diarrhoea, skin rash, redness of the eyes, and swelling of the lips, tongue, hands and feet. Children with MIS-C usually have negative results for a current infection with Covid-19 but positive antibody results indicating that these children were infected with the Covid-19 virus in the past.[1]

This is a hyper inflammatory condition characterised by elevated serum inflammatory markers (CRP, ESR, ferritin) along with considerably abnormal coagulative (INR, PT, D-dimers, Platelets), and cardiac (troponin T/I, pro BNP) markers. Children can have abnormal echocardiogram with depressed ejection fraction, myocardial dysfunction and coronary artery aneurysm.[2] Children with Kawasaki disease (KD) and toxic shock syndrome (TSS) are also considered to have MIS-C. KD is a vasculitis and TSS is a potentially lethal disease derived from the release of bacterial toxins. Both present with multisystem involvement with high fever, mucocutaneous inflammation, shock-like condition and haemodynamic instability.[3]

Systemic onset juvenile idiopathic arthritis is another rare autoimmune mediated inflammatory condition involving many systems which can lead to the lethal condition called macrophage activating syndrome (MAS). It presents with fever, transient cutaneous eruptions and diffuse erythematosus or urticaria-like lesions, variable arthritis (mono-, oligo- or polyarthritis) affecting the small and large joints, adenopathy, hepatosplenomegaly and elevated inflammatory markers.[4]

We present an unusual case of a 12-month-old baby girl who had overlapping symptoms of MIS-C and systemic onset JIA with COVID-19 PCR positivity.

Case Summary

A 12-month-old baby girl presented in the emergency department on June 26, 2020 at the Children's Hospital, Pakistan Institute of Medical Sciences with high grade fever, excessive irritability and multiple joint swellings. She was all well two weeks back when she developed intermittent, high grade fever, which was partially relieved on taking antipyretic drugs. It was associated with generalised macular evanescent rash that became prominent with fever and faded away later on. There was no history of flu, cough, loose motion, vomiting, ear discharge and yellow discolouration of the skin and sclera. For last five days she had developed swelling of bilateral dorsum of hands and feet, left ankle, and left elbow. On examination she was irritable and febrile having temperature of 102°F, pulse rate 124 beats/minute, respiratory rate 26 breaths/minute, with bilateral conjunctival injection, strawberry tongue, bilateral swelling of the dorsum of hand with peeling of skin (Figure-1). Her left elbow was swollen and tender without overlying skin changes (Figure-2). Her abdomen was

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Figure-1: Peeling of skin and oedema of hand.

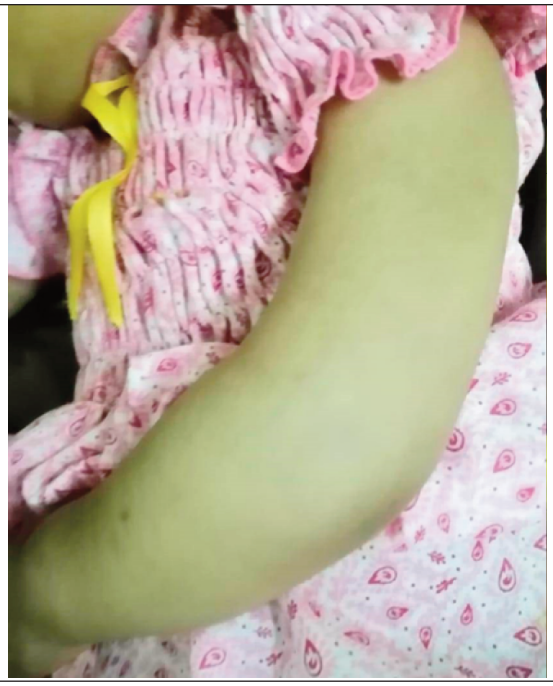

Figure-2: Elbow swelling

distended with central umbilicus, the liver was palpable 3cms below the subcostal margin and spleen was palpable 3cms below the left subcostal margin. The rest of the systemic examination, i.e. that of central nervous system, respiratory, and cardiovascular system, did not reveal any abnormal findings. She was initially admitted to the medical ward where investigations were done. In laboratory investigations, complete blood count revealed: total leukocyte count (TLC) 25,000/uL(4,000-10,000/ uL) with 11% lymphocytes and 88% neutrophils, haemoglobin 11.2 g/dl(13-17g/dl), platelet count 857,000/uL (150,000-450,000), serum ferritin level 8000 ng/mL (7–140), C-reactive protein (CRP) 100 mg/L (below 10.0), erythrocyte sedimentation rate (ESR) 140 mm/hr (0 and 20), D-dimers 3000 ng/ml (less than 400), alanine aminotransferase (ALT) 167 IU/L (upto 42), aspartate aminotransferase (AST) 121 IU/L (upto 35), serum total bilirubin level 0.2 mg/dl (upto1.0), international normalised ration (INR) 1.2, serum sodium (Na) 137 m.mol/l (135-145), serum potassium(K) 3.7 m.mol/l (3.5-5) and blood urea nitrogen (BUN) was 18 mg/dl (12-50). Her echocardiogram, antinuclear antibodies (ANA) and rheumatoid factor (RF) were normal.

As she was having overlapping symptoms of systemic onset JIA and MIS-C, she was sent for Covid-19 PCR and it turned out to be positive. She was then shifted to the infectious diseases unit to be isolated in the Covid-19 designated unit and injectable Dexamethasone and oral Naproxen were started. She became afebrile on day 3 of Dexamethasone, inflammatory markers came down on day 5 along with relieve in joint swelling. She was discharged after two consecutive negative COVID-19 PCRs. Her echocardiogram at admission and four weeks post discharge were normal. Till her recent follow-up she was well, playful and active.

Written informed consent was taken from the child's parents for reporting this clinical case.

Discussion

Since the start of the COVID-19 pandemic it was believed that this deadly virus does not affect children as much and as badly as it affects adults. But after some time this condition called multisystem inflammatory syndrome in children (MIS-C) which is considered a serious consequence of COVID-19 was observed in paediatric age group. With slight differences, CDC, UK, and WHO have similar case definitions,[5] though the case definition is preliminary as it can be changed when more data becomes available on this condition. According to WHO, children and adolescents less than 19 years of age who have fever for more than three days and two out of five clinical features i,e, 1) rash or non-purulent bilateral conjunctivitis or mucocutaneous inflammation, 2) hypotension or shock, 3) cardiac dysfunction or coronary artery involvement, 4) deranged coagulation, 5) gastrointestinal symptoms along with elevated inflammatory markers and no obvious cause of inflammation with evidence of COVID-19 infection either by RT-PCR, antigen test or serology, or likely contact with patients with COVID-19.[1] For case definition all criteria have to be there. This syndrome should also be considered in children with features of typical or atypical Kawasaki Disease (KD) or toxic shock syndrome. According to American Heart Association, for classic KD the child should have fever for ≥ 5 days along with four of the following five criteria: 1) Erythema of oral and pharyngeal mucosa/ cracking of lips/strawberry tongue, 2) Polymorphous exanthema, 3) Bilateral bulbar conjunctivitis (without

exudates), 4) Erythema and oedema of the hands and feet and/or periungual desquamation, and 5) Cervical lymphadenopathy (≥1.5 cm diameter), usually unilateral.[6]

Our child fulfilled the criteria for MIS-C with KD-like presentation but the clinical features against this condition were hepatosplenomegaly with arthritis. Although cases have been reported of reactive arthritis with corona virus in adults,[7,8] hepatosplenomegaly could not be explained in this condition. These features could fit in with the clinical diagnostic criteria of SoJIA. According to the International League of Associations for Rheumatology (ILAR), for diagnosing SoJIA there should be documented fever every day for at least three consecutive days and reoccurring over a period of at least two weeks, along with either two major criteria or one major criterion and two minor criteria. The rash (evanescent and erythematous) and arthritis constitute the major criteria while minor criteria include 1) generalised lymphadenopathy and/or hepatomegaly and/or splenomegaly, 2) serositis, 3) arthralgia, and 4) leukocytosis (≥ 15,000/mm^3) with neutrophilia.[9] Our child fulfilled two major and two minor criteria as she had rash with arthritis hepatosplenomegaly with leukocytosis (25,000) and 88% neutrophils.

The final diagnosis of overlapping syndrome of systemic onset JIA and MIS-C was made as our patient met the diagnostic criteria of both the conditions. COVID-19 has been reported with rheumatoid arthritis in adults but not in children.[10] To our knowledge, this is the first case of overlapping syndrome of MIS-C and SoJIA in paediatric age group. Arthritis is associated with many viral infections such as hepatitis B and C, rubella, parvovirus, and alphaviruses. In fact, 1% of arthritis is virus related.[11] The scenario is different with corona virus as it is often associated with arthralgia but not typical clinical arthritis.[12] Moreover, respiratory viruses are believed to trigger inflammatory response in patients susceptible to develop rheumatoid arthritis.[13] That is why work up for JIA were initially conducted and when inflammatory bio markers turned out to be high the sample was sent for PCR. When it came out positive MIS-C was considered and the child was started on NSAID and steroid. The child responded well to anti-inflammatory therapy and become symptom- free in three days.

Conclusion

There is a possible co-relation between COVID 19 and systemic-onset juvenile idiopathic arthritis. SARS CoV 2 could be a triggering factor for systemic-onset juvenile idiopathic arthritis but more reports are needed to establish this relationship.

Disclaimer: None.

Conflict of Interest: None.

Funding Disclosure: None.

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