Case Report

A pre-COVID case of multisystem inflammatory syndrome leading to fatal outcomes in a young woman

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ABSTRACT

Multisystem inflammatory syndrome (MIS) in adults involves severe complications, which include cardiovascular, cerebrovascular, and neural systems, in response to viral infections or vaccines. In this report, we describe a MIS-like clinical picture long before the COVID-19 pandemic in a 32-year-old woman, who was initially diagnosed with reactive sacroiliitis and soon after with myositis. After about 2 months, the patient developed dilated cardiomyopathy and congestive heart failure, leading to stroke. Brain imaging revealed an increased left middle cerebral artery infarct, increased midline shift, and right basal ganglia bleed, requiring decompressive craniectomy and mechanical ventilation. The patient became unresponsive and comatose and was discharged from the hospital at the family's request. During about 2 months of home care, the patient continued to be in a deep coma, developed bedsores over the body and gangrene of her lower limbs, and eventually died. This tragic case highlights the necessity of intense monitoring and assessments that should lead to early and accurate diagnosis, coupled with concurrent and prophylactic treatments to avoid fatal complications due to disease cascades following an MIS-like clinical syndrome.

Key words: Congestive heart failure, Dilated cardiomyopathy, Glucocorticoids, Immunoglobulins, Multisystem inflammatory syndrome, Steroids

Multisystem inflammatory syndrome in children (MIS-C) is a hyperinflammatory syndrome, in response to COVID-19 infection or vaccine, often presented with persisting fever, mucocutaneous manifestations, gastrointestinal and cardiac involvement, together with lymphopenia and elevated inflammatory and cardiac markers as the main clinical features [1]. MIS-C was first identified in children and described by the UK Royal College of Paediatrics and Child Health and subsequently by the Centers for Disease Control and Prevention in 2020 [2]. Soon after, the multisystem inflammatory syndrome in adults (MIS-A), with the involvement of multiple systems, was reported [3-5]. A diverse range of symptomatology of MIS-A includes cardiac dysfunction (myocarditis, myopericarditis, or arrhythmia), rash, and non-purulent conjunctivitis with secondary findings of thrombocytopenia, shock, and new neurological signs [6]. While cardiovascular involvement has been reported in both MIS-C [7] and MIS-A [8] cases, neurological complications such as stroke have been reported mainly in adults [9]. Clinicians may often miss the diagnosis of MIS during the early manifestations of the disease as it can mimic other disorders with similar symptoms. Failure to reach an accurate diagnosis and start appropriate treatment before the symptom cascades progress can lead to fatal consequences in patients with MIS.

Here, we present a case of MIS that led to fatal complications including dilated cardiomyopathy (DCMP), pulmonary embolism, congestive heart failure (CHF), stroke, coma, and eventual death of a young woman in India. Although the nature of the viral infection that triggered the syndrome and further complications was unknown, it was not related to COVID-19 as the clinical picture described in this report occurred several years before the pandemic.

CASE REPORT

A 32-year-old married female, with an average body mass index and without any past and family history of major medical illnesses, was presented at the outpatient department of a multispecialty hospital in India (several years ago in early February). The chief complaint recorded at that time by a consultant rheumatologist was severe back pain for the past 1 month (since early January),

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for which she was reportedly on steroids and other medications. The nature of back pain was non-radiating and dull, localized over the lower back with an intensity of 7–9 out of 10 on the pain scale. The severe pain was often associated with nausea. The patient also complained of swollen fingers and pain in the muscles and joints, mostly in the lower limbs, following a brief episode of fever possibly due to an unknown viral infection for which no major treatment was sought. Clinical reports from the hospital showed that rheumatoid factor (RF) was 32, which was higher than the normal range (<15 IU/mL), possibly indicating rheumatoid arthritis or inflammatory disorders.

On physical examination, a tender sacroiliac joint was noted. Her blood pressure was 130/95. She was provisionally diagnosed with reactive sacroiliitis, which is an inflammation of the sacroiliac joints in reaction to an infection in another area of the body.

She was further advised to get admitted as an inpatient, prescribed intravenous analgesics, and tested for a magnetic resonance imaging (MRI) of the sacroiliac joint and blood work. MRI report of axial and coronal T1, T2, short tau inversion recovery sections of both sacroiliac joints noted small hyperintense signals at the inferior aspect of the left iliac bone and edema in the left gluteal muscles. Vertebral bodies and discs, spinal canal, conus and cauda signals, and both sacroiliac joints were reportedly normal in the scan. The patient was further advised for a bone scan.

The patient was then prescribed these medications for a month, along with a request for further follow-ups: (i) Gabapentin, (ii) Vitamin D3/Cholecalciferol (60,000 IU) once a week; (iii) Pantoprazole 40 mg daily (before breakfast); and (iv) Etodolac 300 mg (after breakfast).

During the follow-up visit a month after the initial visit (in early March), the rheumatologist at the hospital reported that the patient had transient swelling of the joints but did not have sinusitis or any other allergic manifestations. Her blood pressure was 142/108. Sacroiliitis and HLA-B27 status were reportedly negative. RF and antistreptolysin O status were also shown as negative. The patient was referred for additional blood tests to evaluate creatinine-kinase, anti-cyclic citrullinated peptide, and antinuclear antibodies. The patient was advised to stop the gabapentin but continue with all other medications (i.e., Vitamin D3, Pantoprazole, and Etodolac) that were prescribed during the previous visit. The biochemistry test, done after 6 days of the follow-up visit, showed that the creatine phosphokinase level was 776 IU/L, which was beyond the normal range (25–192 IU/L). While the nerve conduction study showed no abnormalities, the needle electromyography tests were suggestive of a mixed pattern (predominantly myopathic in the right biceps and neurogenic in bilateral vastus lateralis and left tibialis anterior regions). Based on these reports and observation, a provisional diagnosis of myositis was made, and the patient was admitted as an in-patient for further investigations, which included a screening pack, activated partial thromboplastin time (APTT), international normalized ratio (INR), prothrombin time, and myositis profile. In addition, biopsies of the right thigh and right sural nerve were also ordered. Two of the medications, pantoprazole 40 mg, and etodolac 300 mg, were continued.

In late April, the patient was hospitalized following an acute onset of severe shortness of breath and was diagnosed with pulmonary embolism and treated with thrombolysis. During this episode, she was diagnosed with DCMP with a left ventricular ejection fraction (EF) was 22%. After she recovered from pulmonary embolism, she was discharged home. Following this event, within a span of 1 week (in early May), the patient was admitted to the cardiac intensive care unit (ICU) with the chief complaint of severe shortness of breath (class III), which was relieved by standing or sitting up (orthopnea). The EF was only 30%. She developed congestive cardiac failure due to DCMP with a left ventricular apical clot. After 2 days of her recent admission (in early May) due to CHF, the patient developed a sudden onset of altered sensorium with right-sided weakness due to an ischemic stroke with signs of aphasia. She was not provided thrombolytic therapy because her INR was high. Therefore, only conservative treatment was provided. Her MRI scan showed a large left middle cerebral artery (MCA) infarct with a midline shift, and the computed tomography scan revealed increased bleeding within the cranium. As clinical deterioration was observed, a decompressive craniectomy under general anesthesia was performed and the patient was shifted to the ICU and put on mechanical ventilatory support for the next 9 days (until mid-May). Six days after the craniectomy, the patient developed a fever and was evaluated for ventilator-associated Enterococci and *Klebsiella* infections. The patient became unresponsive and comatose, and the scores on the Glasgow coma scale were Eye-1, Verbal-1, and Motor-2. Soon after (during mid-May), the patient was discharged against medical advice based on the request from the patient's family to provide her with home-based care. Physical examination on the day of discharge described her as afebrile, moderately built, and nourished, along with puffiness of the face and bilateral pitting pedal edema. Other parameters were: SpO_2 (blood oxygen level)- 95%; heart rate- 114/min; blood pressure- 130/90; respiratory rate- 30/min; heart- S1 and S2 present; lungs- bilateral crepitations present; per abdomen (P/A)- soft; history of drug allergy- none. The patient was prescribed a list of medications on discharge (Table 1).

Following discharge, the family provided home care to the patient who was completely on assisted living. Medications were provided as prescribed by the medical team on discharge. Food, mainly in liquid form, was administered through the Ryles (feeding) tube. However, the patient's health deteriorated day by day. Throughout the time under home care, the patient remained in a deep coma and was completely unresponsive to verbal commands and external stimuli. Gradually, the patient developed bedsores over the body and gangrene in her lower limbs. Eventually, after about 9-weeks of home care, the patient died. All these phenomena occurred over 12 years ago in India, where the author of this article was trained and worked as a physician. This case report covers only the salient clinical history of our patient,

Table 1: A list of medications prescribed to the patient on final discharge from the hospital

Medication	Generic name	Dosage	Route	Frequency	Indication
Tab. Aztor	Atorvastatin	80 mg (1 tab)	RT	Once daily night	Dyslipidemia
Inj. Nootropil	Piracetam	3 g	IV	4 times daily	Cerebrovascular accident
Inj. Levipil	Levetiracetam	500 mg	IV	Twice daily	Seizure prophylaxis
Inj. Clexane	Enoxaparin	40 mg	SC	Once daily	DVT prophylaxis
Inj. Zosyn	Piperacillin and tazobactam	4.5 g	IV	4 times daily	Antibiotic
Tab. Nucarnit	Levo-carnitine	500 mg	RT	Twice daily	Coronary artery disease
Tab. Ivabrad	Ivabradine	5 mg (½ tab)	RT	Twice daily	Coronary artery disease
Tab. Lanoxin	Digoxin	0.25 mg	RT	Once daily	Congestive cardiac failure
Tab. Shelcal HD	Calcium and Vitamin D3	500 mg	RT	Once daily	Calcium supplement
Inj. Fendrop	Fentanyl	5 mL	IV	Hourly	Scalation
Inj. Targocid	Teicoplanin	400 mg	IV	Once daily	Antibiotic
Inj. Pan	Pantoprazole	40 mg	IV	Twice daily	Gastritis
Inj. MVI	Vitamins A, B1, B2, B5, D3	1 amp	IV	Once daily	Vitamin supplement
Syp. Duphalac	Lactulose	30 mL	RT	Twice daily	Constipation

Tab.: Tablets, Inj.: Injections, Syp.: Syrup, mg: Milligram, gm: Gram, mL: Milliliter, amp: Ampule, RT: Ryles tube, IV: Intravenous, SC: Subcutaneous, DVT: Deep venous thrombosis

whose clinical outcome at the end was tragic but debatable as to whether a better clinical outcome is a possibility in this case.

DISCUSSION

This tragic case report briefly narrates the fatal sequelae of an MIS-like presentation, which quickly gave rise to cardiac and neural complications such as DCMP, CHF, and stroke followed by decompressive craniectomy, coma, and eventual death. We are not aware of any previous publication describing clinical complications of an MIS-like picture similar to our case before the COVID-19 pandemic. We found a post-COVID case report similar to our case with MIS-related complications in a 55-year-old woman who presented with fever, multiple ischemic strokes, thrombocytopenia, elevated inflammatory markers, and multiorgan dysfunction a few days after COVID-19 illness in India [9], the patient, unlike in our case, responded well to treatments using immunomodulatory medications and steroids and showed better outcome [9]. Therefore, there is a possibility that early and accurate diagnosis, coupled with concurrent and prophylactic treatments, such as intravenous immunoglobulin along with adjunctive steroid therapy, may have led to better clinical outcomes in our patient, although predicting severe complications of MIS might be challenging in many cases.

Although the diagnostic category of MIS in children and adults was introduced and has been applied only since 2020 to describe the clinical sequelae of COVID-related complications in children [10] and adults [3,11], there is a possibility that MIS-like cases were present in response to other viral infections before the COVID-19 pandemic as our case report suggests. As seen in our case, both cardiovascular [7,8] and neurological [9] complications of MIS or other inflammatory diseases have been widely reported in the literature. While differential diagnoses may include other hyperinflammatory diseases, including Kawasaki disease (KD), KD shock syndrome, adult-onset Still disease, and the macrophage activation syndrome, which share similar clinical features to MIS [8], we provisionally attribute the sequelae of cardiac and stroke manifestations in our case to MIS although our patient's symptoms started after an unknown viral infection. While MIS is reportedly a dangerous complication in response to natural infection or vaccination for SARS-CoV2, its pathophysiology is likely linked to a primed immune system and antibody-dependent enhancement [6]. Further, it is unclear whether there is a genetic pre-disposition or other factor that confer risk in otherwise healthy young adults.

A preliminary diagnosis considered in our case was myositis, characterized by inflammation of the muscles causing pain and weakness, which does have an association with ischemic stroke [12]. Another possible differential diagnosis may include a mixed connective tissue disease (MCTD), whose "classic" symptoms include the Raynaud phenomenon (reduced blood flow to fingers, toes, ears, and nose, causing sensitivity, numbness, and loss of color in these areas), swollen "sausage-like" fingers, inflamed joints and muscles, and pulmonary hypertension (high blood pressure in the blood vessels of the lungs) [13]. Regardless of the precision in diagnosis, the inflammatory and autoimmune syndromes do require a generic pattern of treatment, such as intravenous immunoglobulins, glucocorticoids, and interleukin-6 or 1RA inhibitors, alongside steroids, to avoid severe complications and death. In essence, a multi-prong approach in diagnosis and treatment should be deemed a requirement in the clinical management of MIS-like and other immunological disease spectrum. While it is debatable whether the disease cascade could have been prevented or arrested in this case by specific treatment strategies, this tragic case highlights the necessity of intense and continued monitoring and assessments that can facilitate early and accurate diagnostic formulation alongside the established treatments in MIS-like clinical syndrome.

CONCLUSION

This case report describes a complex inflammatory syndrome and its sequelae several years before the COVID-19 pandemic in a 32-year-old woman, who initially presented with symptoms of possible viral-induced inflammation. The cascade of complications that followed within a span of 5 months included severe shortness of breath, pulmonary embolism, DCMP, CHF, and stroke, leading ultimately to severe coma and death. This case report emphasizes the importance of early and accurate diagnosis along with appropriate treatment of MIS to avoid fatal outcomes.

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