Multisystem inflammatory syndrome in children (MIS-C) caused a rare presentation of ataxia and papilledema; A case report

hesam nabavizadeh[1], Rafat Noeiaghdam[1], Leila Johari[1], Hamidreza Ghasemirad[2], and Reza Moshfeghinia[1]

[1]Shiraz University of Medical Sciences
[2]Shahid Sadoughi University of Medical Sciences and Health Services

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Running title: a multi-system inflammatory syndrome in children (MIS-C) with ataxia and papilledema

Abstract:

Background: Multisystem inflammatory syndrome in children (MIS-C) is observed with severe signs of COVID-19. Some reports indicated the effect of MIS-C on the neurological manifestations of the children.

Case presentation: A 13-year-old Iranian boy was transferred to the emergency department of Shiraz, Iran in May 2022 from a deprived area with fever, generalized skin rashes, palmar erythema, vomiting, vomit, and diarrhea. Severe conjunctivitis, photophobia, headache, and ataxia were also observed on the day of admission. His neurological manifestations were improved by the treatments including high-dose methylprednisolone and intravenous immunoglobulin (IVIG). He was discharged nine days after the admission.

Conclusions: Because of the low presence of ataxia and papilledema in MIS-C after COVID-19, as far as we know, we presented the first study of this presentation.

Keywords: Multisystem inflammatory syndrome; COVID-19; Ataxia; Papilledema

Background:

Multisystem inflammatory syndrome in children (MIS-C) is observed in children with severe signs of COVID-19. MIS-C is known as a multisystem inflammation in individuals below 21 years with the presentation of organ involvement (at least two organs out of 4 including heart, skin, eye, and gastrointestinal organs), laboratory signs of inflammation, fever, and being in contact with a COVID-19 patient or SARS-COV2 confirmed by laboratory tests (1). The incidence of neurologic symptoms like headache, meningitis, encephalopathy, photophobia, fever, and rarely papilledema and ataxia was 13–21% in MIS-C patients (2). Ataxia contains an absence of coordination of muscle movements including eye movements abnormality, gait abnormality, and speech changes. Some types of ataxia like acute post-infectious cerebellar ataxia can take place among children after bacterial or viral infections (3). Papilledema is known as swelling of optic nerves as a result of high intracranial pressure, which leads to nerve damage and vision loss. It may be a hallmark of pseudotumor cerebri. Pseudotumor cerebri is known for the elevation of lumbar puncture (LP) opening pressure, normal Magnetic Resonance Imaging (MRI) findings, and abducens palsy but other normal neurological exams. High intracranial pressure may be induced by inflammatory disorders like Kawasaki disease and systemic lupus erythematosus (4). As far as we know, we reported the first case of MIS-C presented by papilledema and ataxia, simultaneously.

Case presentation:

A 13-year-old Iranian boy without any underling disease was transferred to the emergency department of Shiraz, Iran in May 2022 from a deprived area with the symptoms of fever since 5 days ago, generalized skin rashes, palmar erythema, nausea, vomiting, and diarrhea. Severe conjunctivitis, photophobia, headache, and ataxia were also observed on the day of admission. He was moved to the pediatric intensive care unit (PICU) for additional management. His vital signs were blood pressure of 114/57 mmHg, pulse rate of 111 PR/min, respiratory rate of 20 RR/min, the body temperature of 37.8 centigrade, and oxygen saturation of 96% without oxygen supplements at rest in the room. Polymerase Chain Reaction (PCR) was negative for COVID-19 but the serology IgG and IgM test was positive. No signs of respiratory disorder were observed. In the physical examination, conjunctivitis, loss of vision, and strawberry tongue were seen. The sounds of the heart and lungs were bilaterally clear.

Inflammatory markers were elevated in the first days of admission. Full laboratory results were summarized in Table 1.

Table 1-The detailed laboratory tests by day of admission

Test
Hemoglobin, g/dL
Hematocrit, %
White blood cell, cells per mm
Neutrophil, %
Lymphocyte, %
Platelet, cells per mm
CRP, <6 mg/L
ESR, mm/h
Albumin
CPK, mcg/L
D-dimer, µg/mL
Procalcitonin
Troponin I
Fibrinogen level, mg/dL
Blood culture
Urine culture
Sodium, mEq/L
Potassium, mEq/L
Albumin
Creatinine, mg/dL
BUN, mg/dL
AST, U/L
ALT, U/L

CRP indicates C-reactive protein; ESR, Erythrocyte sedimentation rate; CPK, Creatine phosphokinase; LDH, Lactate dehy

Because of the involvement of three main organs (brain, skin, and gastrointestinal organs), the diagnosis of Multisystem inflammatory syndrome in children (MIS-C) was suspected. brain MRI and retinal nerve fiber layer (RNFL) thickness and optic nerve head (ONH) analysis were reported with the signs of papilledema and flattening of the posterior globe (Figure 1 and 2), and the sonography of kidneys showed marked parenchymal thinning and cortical damage. The echography showed minimal pericardial effusion and trivial tricuspid and pulmonary valve regurgitation. Lumbar Puncture (LP) was performed on the patient. The result showed opening pressure of 40 cmH2O. The pressure of CSF was 30 cmH2O. Protein of 28, sugar of 65, and 0 cell count were also observed.

Figure 1- Magnetic Resonance Imaging (MRI). The signs of papilledema and flattening of the posterior globe

Figure 2- Optic nerve head (ONH) and retinal nerve fiber layer (RNFL) - signs of papilledema

As the result, high dose methylprednisolone for 3 days and acetazolamide were started for the patient. Due to loss of vision, high opening pressure in LP, eye problems, papilledema, and ataxia treatment with high-dose methylprednisolone 30 mg/kg three times a day and Intravenous Immunoglobulin (IVIG) IV stat in 10-12 hours (2gr/kg), ciprofloxacin eye drop, ceftriaxone 1gr Intravenous (IV) per 12 hours, intravenous acetaminophen (Apotel) 650 mg IV stat, were started for the patient. After these chain of therapies 10 days after the admission, the headache and ataxia of the patient were disappeared, the vision became better than before and the ophthalmology reports were shown no signs of papilledema. He was discharged with the treatment of prednisolone 15mg four times a day for three days, acetazolamide 250mg, and betamethasone, and ciprofloxacin. At the day of discharge ESR and CRP were reduced but the count of WBC was elevated.

Discussion and Conclusions:

The prevalence of neurologic symptoms in MIS-C is not completely clear in the past articles, but it may be about 20% in complicated cases (5, 6). MIS-C has some neurological manifestations like encephalopathy, reduced reflexes, muscle weakness, and headaches; (7). In a study showing neuroimaging presentations in children, encephalopathy with SARS-CoV-2, acute encephalomyelitis-like changes of the brain, and myelitis were also the common presentations. Corpus callosum reversible changes was observed in MIS-C patients in some cases, but cerebrovascular disorders in children were less than adults (8). Ataxia is not common in the presentation of MIS-C. Even though acute ataxia is commonly presented in children, it is rare in SARS-COV2 patients. This rare happening can be related to children's relative resistance to the severe types of COVID-19. Cerebellar ataxia is common in children 2-5. 9 years old as an uncommon age range for COVID-19 infection. It might take place because of immunosuppression or chronic diseases conditions (9). Further investigations are needed to investigate the presence of ataxia in MIS-C children after COVID-19.

As far as we know, we reported the first case of ataxia in a MIS-C patient with the presentation of other rare manifestations like papilledema. Akçay et al. reported a rare case of cerebellitis in a MIS-C patient. The signs of nystagmus, ataxia, and dysarthria were observed in the child. But the patient wasn't complicated with the signs of eye problems (10).

Due to ataxia and headache in our case, the patient underwent brain MRI and CSF assessment by LP. Papilledema were observed in MRI of our patient as a rare presentation of MIS-C. LP was abnormal in about one fourth of the past studies' investigations (11). CSF assessment revealed high opening pressure (40 cmH2O) and elevation of the pressure of CSF (30 cmH2O). The etiology of this high pressure in MIS-C patients is not still completely clear (12). Additionally, high opening pressure caused by immunomodulatory treatment earlier than LP could be mistaken as a result of MIS-C instead of aseptic meningitis (13). But because of starting pulse therapy with methylprednisolone after LP, one of the reasons for high pressure could be because of the presence of MIS-C. In our patient, abnormal circulation of CSF might lead to papilledema and ataxia, simultaneously.

The results of kidney sonography revealed marked parenchymal thinning and cortical damage. The level of ferritin was 506.2 at the fourth day of admission. High level of ferritin is significantly associated with acute kidney injury. As an inflammatory marker it is also observed in hepatitis. The levels of ALT and AST were significantly high at the fifth day of admission. Due to statistical analysis, the prevalence of hepatitis and acute kidney injury were 49% and 25%, respectively (14).

In spite of reduction of neutrophil, ESR and CRP after the treatment, the WBC count increased significantly. It might be because of the role of methylprednisolone as a glucocorticoid in the elevation of WBC count after the treatment (15).

Due to rare presence of ataxia and papilledema in MIS-C after COVID-19, as far as we know, we presented the first study of this presentation. Neurologic symptoms, especially Pseudotumor cerebri, should be kept in

mind in MIS-C patients, and for prevention of vision loss even in mild cases of MIS-C treatment also should be started immediately.

Declarations

Ethics approval and consent to participate

The authors confirm that they have obtained all proper patient consent forms. The patient has consented for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed. Also, a signed and consent form was received from the patient in Persian. All methods were performed in accordance with the ethical standards in the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images

Availability of data and materials

All data an materials of the study are available by corresponding author

Competing interests

The authors declare that they have no competing interests

Funding:

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Authors' contributions

ShN and RN saw the case for the first time and realized its specialness and completed its information with the cooperation of LJ. RM and HG did the work of writing and reviewing the literature and collecting information, also ShN managed all the steps as the professor and supervisor of team. All authors read and approved the final manuscript.

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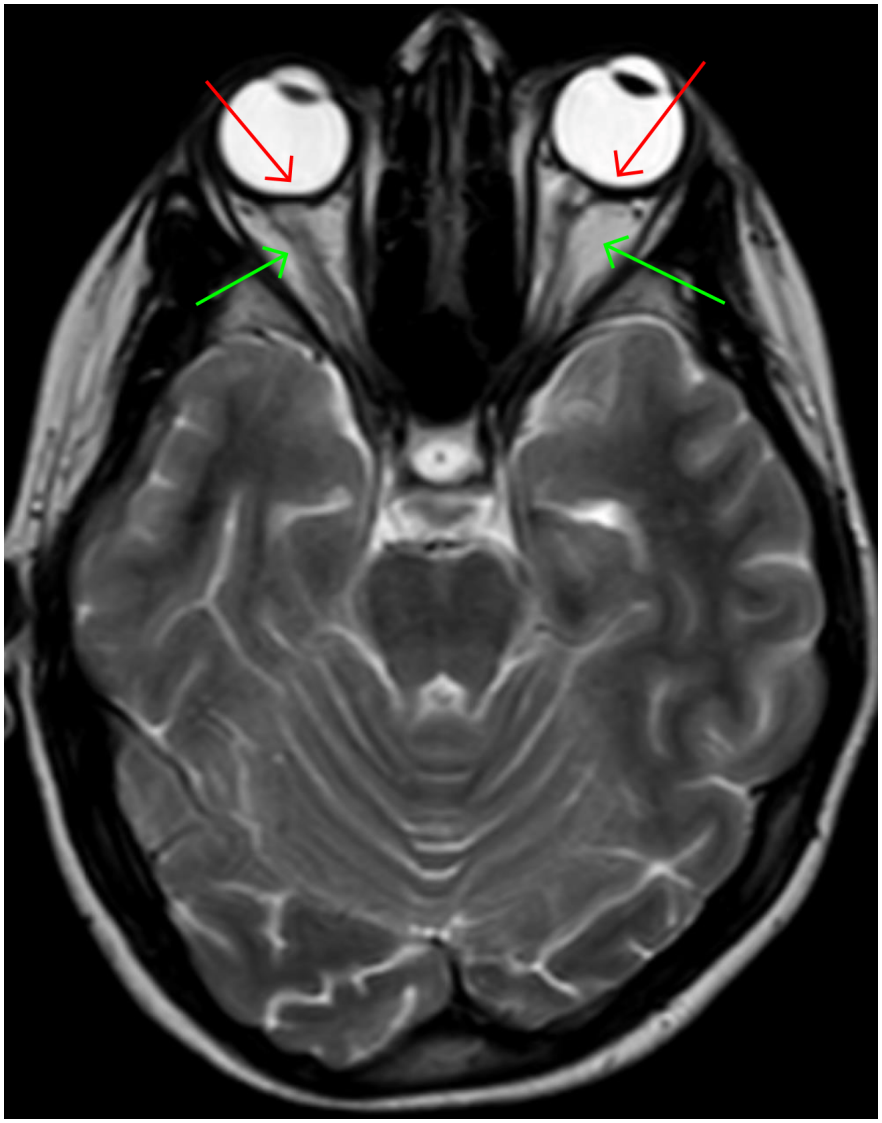

Figure 1- Magnetic Resonance Imaging (MRI). The signs of papilledema and flattening of the posterior globe. flattening of the posterior sclera (red arrows) and distention of the perioptic nerve (green arrows)

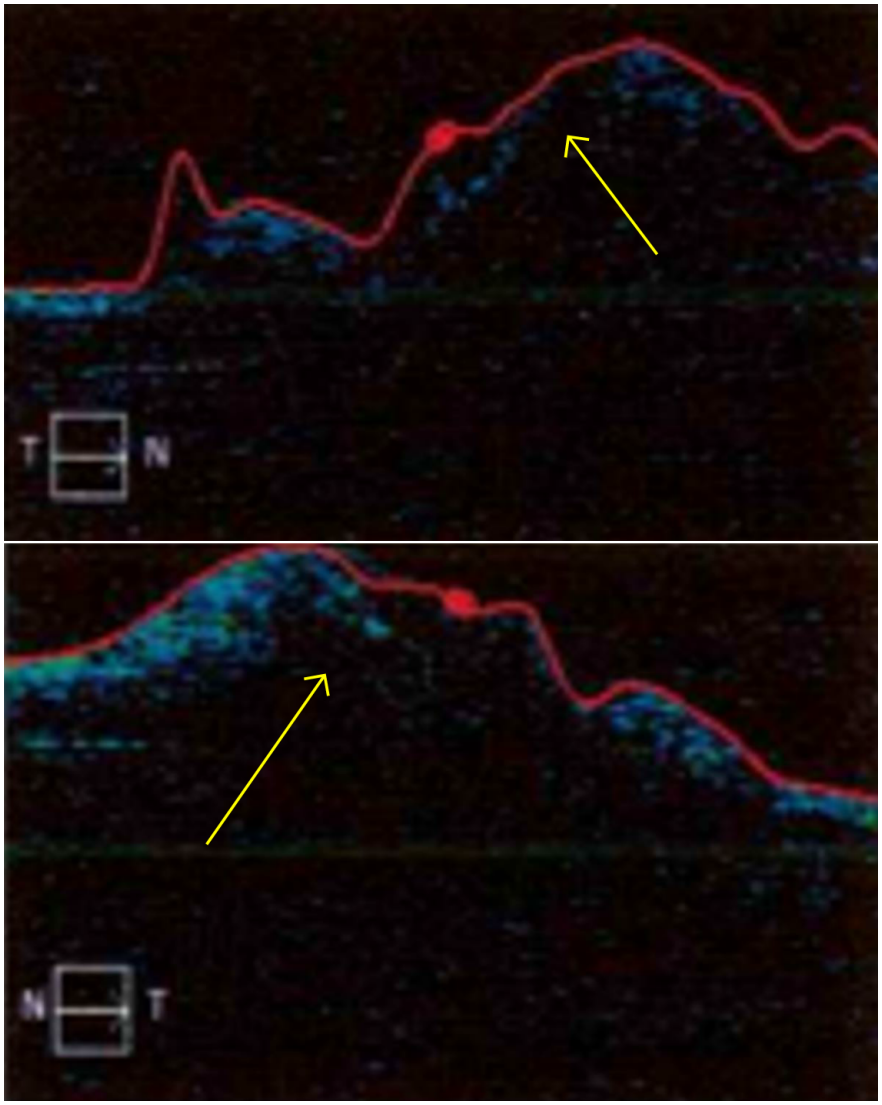

Figure 2 . Optic nerve head (ONH). The signs of papilledema. cross-section of the optic nerve head shows swelling of the nerve fibre layer (right, up; left, down)