Multisystem inflammatory syndrome in adults in Hong Kong: two case reports

Abram JY Chan[1] *, MB, BS, FHKAM (Medicine), **Judianna SY Yu**[2], MB, BS, FHKAM (Medicine), **Alwin WT Yeung**[2], MB, BS, FRCP, **HP Shum**[3], MB, BS, MD, **KC Lung**[1], MB, BS, FRCP

[1] *Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China*
[2] *Department of Medicine and Geriatrics, Ruttonjee and Tang Shiu Kin Hospitals, Hong Kong SAR, China*
[3] *Department of Intensive Care, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China*

* Corresponding author: cjy548@ha.org.hk

This article was published on 16 Apr 2024 at www.hkmj.org.

Hong Kong Med J 2024;30:173–5
https://doi.org/10.12809/hkmj2310676

Case presentations

Case 1

A 51-year-old Chinese woman presented to Pamela Youde Nethersole Eastern Hospital on 29 September 2022 with a 1-week history of intermittent fever and confusion. She enjoyed good past health and had received three doses of Comirnaty vaccine with the last dose administered on 18 February 2022. She was first symptomatic and with a positive rapid antigen test for coronavirus disease 2019 (COVID-19) on 2 September 2022. She recovered after 8 days without the need for antiviral therapy. Respiratory samples over the initial 4 days of admission were negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR). Magnetic resonance imaging of the brain on 30 September 2022 revealed focal cytotoxic oedema in the splenium of the corpus callosum, possibly indicative of encephalitis or encephalopathy (Fig a). Chest X-ray on admission revealed diffuse right lung opacities (Fig b). The chest symptoms of the patient deteriorated with bilateral involvement and increased need for oxygen support, and she was transferred to the intensive care unit with use of a high-flow nasal cannula. She was intubated on 2 October 2022 as oxygenation was suboptimal. Lumbar puncture was unremarkable. Chest X-ray on 5 October 2022 showed dense bilateral opacities (Fig c), and computed tomography of the thorax on 5 October 2022 showed bilateral pulmonary consolidations and diffuse ground glass opacities. She also developed anaemia (haemoglobin level: 7.9 g/dL) and thrombocytopenia (platelet count: 78 × 10^9/L). She was in a hyperinflammatory state with ferritin level of 14057 pmol/L, C-reactive protein level of 273 mg/L, lactate dehydrogenase level of 1081 IU/L, and persistently elevated D-dimer level of >8000 ng/mL. Immunoglobulin G antibody level against SARS-CoV-2 receptor-binding domain on 3 October 2022 was 34 225.34 AU/mL. The patient was otherwise haemodynamically stable. Electrocardiogram showed sinus rhythm and high-sensitivity troponin I level was only mildly elevated (19.7-119 ng/L).

BioFire FilmArray Pneumonia Panel for endotracheal aspirate detected 10^5 copies/mL of *Staphylococcus aureus* while *mecA/C* gene was not detected, and culture also grew scanty methicillin-sensitive *S aureus*. Cytomegalovirus DNA PCR was negative. Repeated respiratory samples including nasopharyngeal/throat swabs, sputum and endotracheal aspirate did not detect SARS-CoV-2 RNA. *Pneumocystis jirovecii* pneumonia PCR was negative as was sputum for acid-fast bacillus smear/c/st. Autoimmune workup including antinuclear antibody, antineutrophil autoantibodies and immunoglobulin pattern was negative. The patient was initially prescribed empirical meningitis treatment with intravenous ceftriaxone 2 g Q12H and intravenous acyclovir 500 mg Q8H, and antimicrobials were switched to piperacillin-tazobactam on 2 October 2022 after cerebrospinal fluid results excluded meningitis. Her condition continued to deteriorate while on antibiotics.

The patient was suspected of having multisystem inflammatory syndrome in adults (MIS-A) and was started on intravenous methylprednisolone and intravenous immunoglobulin (IVIG) from 5 October 2022. She was initially given a daily dose of methylprednisolone 0.5 g for 3 days and IVIG 20 g for 5 days. She gradually improved with decreased oxygen requirement and ventilatory support and was extubated on 7 October 2022. There was significant improvement in inflammatory markers with C-reactive protein level decreased to 30.8 mg/L, ferritin level decreased to 4746 pmol/L, and lactate dehydrogenase level decreased to 526 IU/L at the end of treatment. Serial chest X-ray showed radiological improvement with decreased bilateral opacities (Fig d) and near-resolution of chest X-ray upon discharge (Fig e) 16 days after starting MIS-A treatment. She completed a 9-week course of steroids with full recovery. A repeated magnetic resonance imaging of the brain was scheduled 7 months after discharge to monitor her progress, which showed resolution of previously noted oedema in the splenium of the corpus callosum.

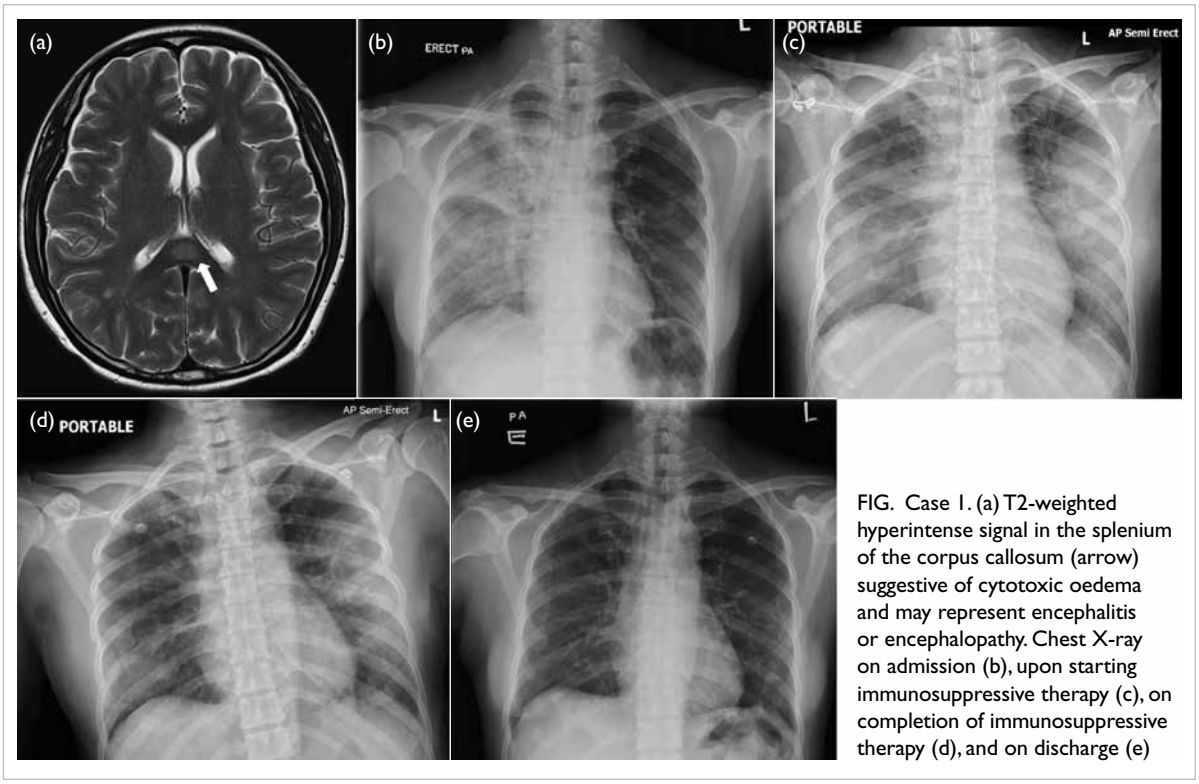

FIG. Case 1. (a) T2-weighted hyperintense signal in the splenium of the corpus callosum (arrow) suggestive of cytotoxic oedema and may represent encephalitis or encephalopathy. Chest X-ray on admission (b), upon starting immunosuppressive therapy (c), on completion of immunosuppressive therapy (d), and on discharge (e)

Case 2

A 39-year-old Malawian man presented to Ruttonjee and Tang Shiu Kin Hospitals on 1 November 2022 with a history of fever since 29 October 2022. He had had confirmed COVID-19 infection with nasopharyngeal swab SARS-CoV-2 PCR positive on 7 October 2022 but recovered without the need of antivirals. He had a history of malaria 21 years ago but no travel history over the last 2 years. He otherwise enjoyed good past health apart from obesity (body weight: 120 kg; body mass index: >30 kg/m^2). He had received two doses of CoronaVac and one dose of Comirnaty vaccines with the last dose administered on 2 March 2022. His fever persisted and he was noted to have bilateral conjunctivitis and petechiae over the throat. Electrocardiogram later revealed new atrial fibrillation and serial echocardiograms showed accumulation of pericardial effusion and worsening left ventricular ejection fraction of 30%. He had acute liver failure with elevated parenchymal enzyme level (alanine transaminase level: 1079 IU/L), coagulopathy (international normalised ratio: 2.61), hyperammonaemia (serum ammonia level: 108 μmol/L), and hyperlactatemia (lactate concentration: 6.65 mmol/L). He also developed acute kidney injury (creatinine level: 256 μmol/L, estimated glomerular filtration rate: 26 mL/min/1.73 m^2) and thrombocytopenia (platelet count: 35×10^9/L). He was transferred to the intensive care unit for further management on 6 November 2022. He was in a hyperinflammatory state with ferritin level of 131 351 pmol/L, C-reactive protein level of 442 mg/mL, lactate dehydrogenase level of 7710 IU/L, and persistently elevated D-dimer level of >8000 ng/mL. Immunoglobulin G antibody level against SARS-CoV-2 receptor-binding domain on 6 November 2022 was >40 000 AU/mL. He was haemodynamically stable throughout his admission.

The patient was suspected of having MIS-A and was commenced on intravenous methylprednisolone (0.5 g for 6 days) and IVIG (20 g for 5 days) on 8 November 2022. His fever subsided soon after steroids were given, with resolution of organ failure. He was discharged 11 days after starting MIS-A treatment with prednisolone 40 mg twice daily. Repeated echocardiogram on 16 November 2022 prior to discharge showed significant improvement with left ventricular ejection fraction of 55% and decreased pericardial effusion of up to 1.1 cm in thickness. He had no further episodes of atrial fibrillation. He was last seen 4 weeks post-discharge and remained well on a tapering dose of prednisolone. He remained well and was eventually weaned off immunosuppressants in early October 2023.

Discussion

The Centers for Disease Control and Prevention case definition for MIS-A was developed through expert opinion and states that the patient should be aged ≥21 years, have been hospitalised for at least 1 day or died as a result, and fulfilled certain clinical and laboratory criteria with no more likely alternative diagnosis.[1] Case 1 did not fulfil these primary clinical criteria for MIS-A. Nonetheless she exhibited the neurological and haematological components of the secondary clinical criteria and also met the laboratory criteria with no other cause identified. Fulminant pulmonary involvement is unusual since pulmonary involvement has been used to distinguish MIS-A patients from patients with severe COVID-19 infection.[2] Chronologically the patient developed fulminant pneumonitis 3 weeks after her initial COVID-19 infection, within the commonly described 2- to 5-week interval between onset of typical COVID-19 symptoms and onset of MIS-A, that likely represented a post-acute phenomenon rather than part of the initial infection. A case series in the United States also reported that MIS-A patients may have pulmonary involvement and require mechanical ventilation when compared with multisystem inflammatory syndrome in paediatric patients.[3] Although 86% to 89% of MIS-A patients have one or more cardiovascular abnormalities,[4] the lack of cardiac involvement in this patient with otherwise compatible clinical features should not have excluded the diagnosis of MIS-A.

Case 2 fulfilled the Centers for Disease Control and Prevention case definition as well as having markedly deranged liver and renal function. Despite his impaired left ventricular ejection fraction, there was no shock or congestion to explain the deranged liver and renal function. Both liver and renal function recovered with immunosuppression, suggesting reversibility with treatment of the hyperinflammatory state. Such hepatic involvement has been reported in a case in Croatia[5] and renal involvement has been reported previously, albeit usually associated with shock.[2]

Both cases responded rapidly to methylprednisolone and IVIG. This treatment regimen was with reference to the guidelines published by the National Institutes of Health and extrapolated from multisystem inflammatory syndrome in children data.[6] Case 2 had a longer course of methylprednisolone based on body weight and higher level of inflammatory markers. Steroid tapering was initiated afterwards and continued for at least 2 months in both our patients. Further studies would be helpful to guide the management for MIS-A.

Author contributions

All authors contributed to the concept or design of the study, acquisition of the data, analysis or interpretation of the data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

The patients were treated in accordance with the Declaration of Helsinki. Verbal consent for treatments, procedures and for publication has been obtained from the patients.

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