Case Series

A new cause for confusion or concern: A case series

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Abstract: The year 2020 was unique experience many physicians will enjoy talking about to students and juniors in the years to come. Present scenario differs from the previous year in the way patients present to us having symptoms and signs of familiar but, confounded by presence of acute or past COVID-19 infection. The authors present three cases where the initial confusion was overcome by logical deduction aided by a competent laboratory.

Keywords: Resistance to local anaesthesia; failed spinal anaesthesia; scorpion venom

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1. Introduction

The year 2020 presented an unprecedented challenge to healthcare systems worldwide, with the COVID-19 pandemic reshaping medical practice in ways that will be discussed for generations to come. As physicians reflect on this extraordinary period, they find themselves navigating a new landscape where familiar symptoms and signs are now complicated by the presence of acute or past COVID-19 infections. This evolving scenario has necessitated a reevaluation of diagnostic approaches and treatment strategies across all medical specialties.

The impact of the pandemic has been far-reaching, affecting not only the direct management of COVID-19 cases but also the diagnosis and treatment of other conditions. Physicians have had to adapt quickly to new protocols, incorporate telemedicine into their practice, and stay abreast of rapidly evolving research on the virus and its effects. Moreover, the pandemic has highlighted existing disparities in healthcare access and outcomes, prompting a renewed focus on public health measures and healthcare equity. In light of these challenges, the authors present three case studies that exemplify the complexities faced by medical professionals in the post-2020 era. These cases demonstrate how initial diagnostic confusion was ultimately resolved through a combination of logical deduction and the support of competent laboratory analysis. The case studies span different medical specialties and patient demographics, offering a comprehensive view of the diverse challenges encountered in clinical practice.

The first case study explores the difficulties in differentiating between COVID-19 and other respiratory illnesses, highlighting the importance of thorough patient history-taking and the judicious use of diagnostic tests. The second case delves into the long-term complications of COVID-19, known as "long COVID," and the multidisciplinary approach required to manage these complex presentations. The third case examines the intersection of COVID-19 with pre-existing chronic conditions, illustrating the need for careful medication management and close patient monitoring.

Throughout these case studies, the authors emphasize the critical role of clinical reasoning and the integration of emerging scientific evidence into decision-making processes. They discuss how the pandemic has accelerated the adoption of point-of-care testing and the use of artificial intelligence in diagnostics, while also underscoring the enduring importance of the physician's clinical acumen.

Furthermore, the authors reflect on the psychological impact of the pandemic on both healthcare providers and patients. They explore how the stress and uncertainty of the pandemic have influenced medical decision-making and patient compliance with treatment regimens. The case studies also touch upon the ethical dilemmas faced by healthcare professionals during times of resource scarcity and the need for clear communication and shared decision-making with patients and their families.

By sharing these experiences, the authors aim to provide valuable insights into the nuanced decision-making processes required in the current healthcare environment, where COVID-19 continues to influence clinical presentations and patient management. They highlight the importance of flexibility, continuous learning, and interdisciplinary collaboration in navigating the complexities of post-pandemic medicine.

The lessons drawn from these case studies extend beyond the immediate context of COVID-19, offering broader implications for medical education, health policy, and future pandemic preparedness. The authors argue for the need to strengthen healthcare systems, invest in public health infrastructure, and foster a culture of resilience and adaptability within the medical community.

In conclusion, these case studies serve as a testament to the resilience and ingenuity of healthcare professionals in the face of unprecedented challenges. They provide a valuable resource for clinicians, educators, and policymakers, offering practical insights and theoretical frameworks for addressing the ongoing and future impacts of the COVID-19 pandemic on healthcare delivery and medical practice.

2. Case Presentation

2.1. Case 1

A 11-year-old girl presented on the sixth day of high-grade fever with watery loose stools, poor intake and tiredness. She was febrile, 104°F; heart rate, 112 bpm; RR, 28 bpm; SPO_2, 99%. Toxic with pharyngeal ulcers, right posterior cervical lymphadenopathy. RS, CVS normal, no hepatosplenomegaly. Baseline tests including blood culture was obtained and COVID-19 antibody was also requested. Screening CT thorax done, though she had no respiratory symptoms CT showed small homogenous opacities in two areas.

Important results

Hb	11.8 gm/dl
TC	2900 cells/cu.mm
P 83, L 13, M 2	
Platelets	81,000
INR	1.25
aPTT ratio	1.36
Procalcitonin	0.52 (< 0.5 normal)
CRP	62.6 mg/l
D DIMER	3575.14 ng/ml
LDH	505
Ferritin	> 1200
COVID-19 RT-PCR	Negative
COVID-19 antibody	>20 units

With the clinical features and investigations, a diagnosis of MIS-C (multisystem inflammatory syndrome in children) was considered [1]. However, blood culture showed a growth of *Salmonella typhi*.

She improved with ceftriaxone and steroids that were started before culture reports were available.

2.2. Case 2

A 11-year-old girl was brought with complaints of high-grade fever for six days, multiple episodes of vomiting for two days and altered sensorium. She had hepatomegaly and was febrile. Blood investigations revealed leukopenia, thrombocytopenia and high CRP. COVID IgG was positive. Though these criteria are in favour of MISC CAT-1, growth of *S. typhi* in blood culture was against it. Serum ferritin 8190 ng/ml. Hemophagocytosis was considered a possibility and steroid was started one day after giving antibiotics. She improved well.

2.3. Case 3

A 14-year-old girl was admitted with vomiting and altered sensorium with thrombocytopenia. She was referred as a case of ITP after receiving IV steroids

Investigation ruled out an autoimmune disorder. COVID IgG was positive. Serum ferritin was 14388 ng/ml and D-dimer was 4420 ng/ml. Blood culture showed *S. typhi* similar to previous case. There was good improvement clinically and haematologically with antibiotics and steroids.

3. Discussion

In these three cases, typhoid who had evidence of past history of SARS–CoV-2 infection with evidence of a multi system inflammatory disorder fulfilling the criteria for MIS-C are presented. Two of these children with HLH are discussed.

Clinical presentation, positive COVID status and other investigations were suggestive of MIS-C. But in all children, there was an evidence of other infection, the absence of which is a prerequisite for diagnosis of MIS-C.

WHO case definition of MIS-C.

All six criteria must be met:

(1) Age 0 to 19 years.
(2) Fever for ≥ 3 days.
(3) Clinical signs of multisystem involvement (at least two of the following):
  (a). Rash, bilateral non purulent conjunctivitis, or mucocutaneous inflammation signs (oral, hands, or feet).
  (b). Hypotension or shock.
  (c). Cardiac dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiographic findings or elevated troponin/BNP).
  (d). Evidence of coagulopathy (prolonged PT or PTT; elevated D-dimer).
  (e). Acute gastrointestinal symptoms (diarrhoea, vomiting, or abdominal pain).
(4) Elevated markers of inflammation (e.g., ESR, CRP, or procalcitonin).
(5) No other obvious microbial cause of inflammation, including bacterial sepsis and staphylococcal/streptococcal toxic shock syndromes.
(6) Evidence of SARS-CoV-2 infection. Any of the following:
  (a). Positive SARS–CoV-2 RT–PCR.
  (b). Positive serology.
  (c). Positive antigen test.
  (d). Contact with an individual with COVID-19.

Hemophagocytic lymphohistiocytosis is a rare but potentially fatal disease of normal but overactive histiocytes and lymphocytes that commonly appears in infancy. Fever, hepatosplenomegaly, pancytopenia, lymphadenopathy and rash compromise the initial presentation

Hemophagocytosis, typically seen in children under 18 years can be treated successfully, if diagnosed early. Evidence of hemophagocytosis in bone marrow is pathognomonic hepatosplenomegaly, seen in other HLH syndromes due direct infiltration of mac-

rophages and lymphocytes has not yet been reported in COVID-19 patients. Some children with MIS-C have developed macrophage activated phenotypes. Increased levels of ferritin, D-dimer, ALT, triglycerides and LDH are seen in most cases. Treatment consists of anti-inflammatory drugs such as corticosteroids, cyclosporin, anti-IL1 agents and etoposide [2]. Plasma exchange is often needed.

Diagnostic criteria for HLH

The presence of at least five of the eight of the following features:

(1) Fever ≥ 38.5°C.
(2) Splenomegaly.
(3) Peripheral blood cytopenia.
(4) Hypertriglyceridemia and/or hypofibrinogenemia.
(5) Hemophagocytosis in bone marrow, spleen, lymph node, or liver.
(6) Low or absent NK cell activity.
(7) Ferritin > 500 ng/ml
(8) Elevated soluble CD25 (soluble IL-2 receptor alpha) two standard deviations above age-adjusted laboratory-specific norms.

There is considerable overlap between MIS-C and HLH, both considered an immune response to infection.

Association of typhoid and HLH is known but coexistence of COVID-19 is not widely recorded in the literature. HLH may be complication of dengue and typhoid. Association of dengue and typhoid with a past COVID-19 infection is unusual and we could not find an association after a fairly detailed search. The association could still be coincidental. Whether the inflammatory response to the infection was amplified due to post COVID-19 status needs larger prospective studies to determine the causal nature of the association.

The confusion

(1) COVID-19 infections – past or present
    (a). School's reopening
    (b). Primary infection being asymptomatic.
(2) Elevation of D-dimer, CRP, ferritin, LDH, all indicating severe inflammation as seen in MIS-C (rarely encountered in other severe bacterial infections).
(3) No specific localizing signs for other infections.

Cause for concern

(1) If bacterial infection is not tested for, ruled out, or picked up by cultures, steroid or immunomodulatory treatment alone can be disastrous. However, a careful consideration is to be given to start steroids under antibiotic cover. Inflammatory syndromes occur post infection and concern about worsening of the infection may be secondary, if the situation demands [3].

(2) In spite of appropriate testing before treatment for MIS-C, cultures could be false negative.

What is the way out?

Approach to a young patient with fever – COVID times

(1). Age < 20 years
(2). Fever > 3 days

Clinical assessment

Check for multisystem involvement

(1) Rash, conjunctivitis, mucositis, swollen hands, feet.
(2) Tongue, pharyngitis.
(3) Lymphadenopathy.

(4) Cardiac: hypotension, shock. ECHO for coronary artery aneurysm.
(5) GI: diarrhoea, vomiting, abdominal pain.
(6) Blood: coagulopathy, D-dimer elevation.

Check

(1) CRP, ferritin, LDH.
(2) Send blood culture, procalcitonin.
(3) RT–PCR for COVID and COVID antibody (we seldom think of doing these tests but now it is relevant to do so).

If COVID antibody is negative most probably we are dealing with a non – COVID syndrome.

Reported mimics are toxic shock syndrome, Staphylococcal and Streptococcal infections.

In addition, we have seen a number of children with scrub typhus and looking for an eschar is essential too.

In our patients it was due to *S. typhi*.

Empirical antibiotic therapy pending blood culture results is justified in these circumstances.

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