Case Report

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The COVID trap: pediatric diagnostic errors in a pandemic world

<https://doi.org/10.1515/dx-2020-0150>

Received November 21, 2020; accepted July 14, 2021;
published online August 5, 2021

Abstract

Objectives: The COVID-19 pandemic has introduced strains in the diagnostic process through uncertainty in diagnosis, changes to usual clinical processes, and introduction of a unique social context of altered health care delivery and fear of the medical environment. These challenges created a context ripe for diagnostic error involving both systems and cognitive factors.

Case presentation: We present a series of three pediatric cases presenting to care during the early phases of the COVID-19 pandemic that highlight the heightened potential for diagnostic errors in the pandemic context with particular focus on the interplay of systems and cognitive factors leading to delayed and missed diagnoses. These cases illustrate the particular power of availability bias, diagnostic momentum, and premature closure in the diagnostic process.

Conclusions: Through integrated commentary and a fishbone analysis of the cognitive and systems factors at play, these three cases emphasize the specific influence of the COVID-19 pandemic on pediatric patients.

Keywords: cognitive bias; COVID-19; diagnostic error; multisystem inflammatory syndrome in children.

Introduction

Diagnostic errors are increasingly recognized as a preventable source of patient harm [1]. Prior analyses of diagnostic

errors have categorized the majority of these as involving either system factors, cognitive factors, or both [2, 3]. Specifically, ambient work conditions, organizational culture, emotionally charged situations, fatigue, stress, and organizational culture can all affect the immediate decision-making process and contribute to diagnostic errors [1, 4–7]. Over the last 18 months, the coronavirus disease 2019 (COVID-19) pandemic has introduced marked and rapid changes in the structures and processes of health care delivery, levels of fatigue and stress, work environment adaptations, and a novel disease entity. These changes highlight the complex context in which clinical decision making occurs and encourages us to examine the direct and indirect effects of a global pandemic on the diagnostic process, with particular focus on the interplay between cognitive and systems factors.

Early in the course of the pandemic, Gandhi and Singh presented a framework for eight types of anticipated diagnostic errors in the setting of the coronavirus disease 2019 (COVID-19) pandemic [8]. However, this framework was described from the lens of adult patients and acute COVID-19 disease rather than pediatrics. While many of these error types can apply to pediatrics, there are distinct considerations for pediatric diagnosis during the COVID-19 pandemic, particularly the recognition of multisystem inflammatory syndrome in children (MIS-C). MIS-C is a rare hyperinflammatory condition reported in children and temporally associated with prior SARS-CoV-2 exposure with features that can resemble many other more common pediatric conditions. We have outlined the basic case definition for MIS-C [9] and a list of alternative plausible differential diagnoses in Table 1 to highlight these similarities. As an emerging disease with an evolving case definition, the true incidence of MIS-C is difficult to estimate [10]. However, a recent cohort study using enhanced SARS-CoV-2 surveillance data estimated the incidence of MIS-C to be 316 persons per 100,000 SARS-CoV-2 infections [11]. As of June 2021, there have been over 4,000 reported cases of MIS-C in the United States and 37 deaths attributed to MIS-C [9]. It is estimated that approximately 60% of children with case definition confirmed MIS-C in the

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Table 1: MIS-C case definition and alternative plausible diagnoses.

MIS-C case definition	Alternative plausible diagnoses
Patient <21 years presenting with: <ul style="list-style-type: none"> – Fever – Inflammation – Clinically severe illness requiring hospitalization – Multisystem (≥ 2) organ involvement 	<ul style="list-style-type: none"> – Toxic shock syndrome – Sepsis syndrome – Rickettsial disease (i.e. Rocky Mountain Spotted Fever) – Severe bacterial infections (e.g. pyelonephritis, meningitis) – Systemic viral infections <ul style="list-style-type: none"> – Epstein–Barr virus – Adenovirus – Disseminated herpes simplex virus (HSV) – Staphylococcal scalded skin syndrome – Stevens Johnsons Syndrome – Kawasaki disease – Systemic juvenile idiopathic arthritis
AND	
No alternative plausible diagnoses	
AND	
Evidence of current or recent SARS-CoV-2 infection by PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within 4 weeks prior to the onset of symptoms.	

United States require intensive care according to estimates as of July 2020 [12].

Here we present three cases of children with acute illnesses in the early months of the COVID-19 pandemic, illustrating the particular risk of diagnostic error in that context. These cases serve as potent reminders of how the diagnostic uncertainty of a new disease entity, as well as system changes from a public health crisis such as a pandemic, can further expose our vulnerability to diagnostic error. Details of the cases have been altered as appropriate to protect patient privacy.

Case presentation

Case 1

A previously healthy 6-year-old male presented to the Emergency Department (ED) of a large children's hospital located in the mid-Atlantic region of the United States in May 2020 with approximately 3 days of fever, bilateral lower extremity pain with inability to walk, rash, diarrhea, and vomiting. At presentation, the patient appeared irritable but alert. Vital signs were notable for temperature of 38.6 °C, mild tachycardia, and elevated blood pressure for age. His exam was notable for dry, cracked lips, erythematous tongue, injection of nasal mucosa, erythematous rash of groin and left arm, and tenderness to palpation of the large muscle groups in the lower extremities. Documentation intermittently

describes migratory joint pain with palpation and range of motion; however, documentation of the joint exam was missing or less detailed in different clinician notes during a similar time period. Initial laboratory studies revealed a normal white blood cell count with 88% neutrophils on differential, mild anemia, and mild thrombocytopenia. Inflammatory markers were high with erythrocyte sedimentation rate of 49 mm/h (reference range: 0–20 mm/h) and C-reactive protein of 52 mg/dL (reference range: 0.0–0.9 mg/dL). He was also noted to have mild hyponatremia and mildly elevated liver enzymes. The laboratory-developed nasopharyngeal multiplex reverse-transcription polymerase chain reaction (PCR) for respiratory viruses was negative and SARS-CoV-2 nasopharyngeal PCR was negative. He was started on vancomycin, ceftriaxone, and clindamycin. He was also given one dose of doxycycline.

The patient was initially admitted to the general pediatrics floor, but due to concerns of hyponatremia and need for ongoing clinical assessment, he was rapidly transferred to the pediatric intensive care unit (ICU). He did not have any hemodynamic instability. Due to suspicion of MIS-C as a diagnosis, Rheumatology was the first consult team to be called. Immunomodulatory therapies (intravenous immunoglobulin and steroids) were discussed, but not initiated. Notably, the initial differential diagnosis documented in the ED was broad and included atypical Kawasaki, MIS-C, streptococcal or staphylococcal toxic shock syndrome, bacterial sepsis, and tick-borne illnesses. However, with each transfer (from ED to general floor to

ICU) the documentation increasingly focused on MIS-C as a working diagnosis.

Around 12 h after admission, bilateral knee radiographs were obtained that revealed unilateral right knee effusion. Orthopedics was consulted and performed an arthrocentesis with synovial fluid analysis revealing 125,139 white blood cells with 73% neutrophils. An ultrasound of the bilateral hips was obtained and revealed unilateral left hip effusion. He was taken for operative washout of the left hip and right knee joints. The Infectious Diseases team was consulted at about 16 h after admission. Blood cultures and synovial cultures from left hip and right knee grew *Streptococcus pyogenes* and he was diagnosed with invasive group A streptococcal disease presenting with multiple septic joints and likely toxin-mediated rash without shock.

Case commentary

This case presents a series of systems factors and cognitive factors (depicted in Figure 1) that contributed to delayed diagnosis of invasive group A streptococcal disease with septic arthritis. Of the systems factors noted, we see potential for improvement in communication systems to buffer the inherent pitfalls of telephone consultation and multiple transfers including potential loss of critical case information, reliance on communicated physical exam findings rather than primary exam, and misunderstanding of key findings.

This case highlights important cognitive factors contributing to delayed diagnosis including availability bias,

premature closure, anchoring, diagnostic momentum, and confirmation bias [13]. This patient presented to the hospital at a time when MIS-C, a new clinical entity, was being reported; several children at this hospital had already been treated for the syndrome. Although MIS-C was still a rare diagnosis and a diagnosis of exclusion, the heightened interest in this emerging disease likely contributed to a tendency to recall more easily this diagnosis, set the stage for anchoring bias, and led to premature closure on this as the primary working diagnosis. Furthermore, many features consistent with severe infections such as group A streptococcal disease (hyponatremia, fever, rash, gastrointestinal symptoms, myalgias, and elevated laboratory markers of inflammation) were similar to features of MIS-C allowing for a confirmation bias effect and less emphasis on less consistent features (such as specific joint pain, erythrodermic rash). Anchoring on MIS-C also led to less focus on the initial chief complaint, refusal to walk in the setting of fever, which in pediatrics should trigger concern or septic arthritis and requires prompt time-sensitive surgical management.

The particular power of availability bias over clinician differential diagnosis building is palpable in the narrative of this case. The context of the pandemic appeared crucial to driving the diagnostic momentum seen in this case and leading to premature closure on MIS-C. While, ultimately, the patient received appropriate antimicrobials and operative debridement of the affected joints, the time lapse still highlights areas of improvement in our diagnostic process, particularly as related to the pandemic.

Figure 1: Fishbone diagram analysis of cognitive and systems factors contributing to diagnostic error.

Case 2

A 6-day-old full-term female infant born via spontaneous vaginal delivery was admitted to the pediatric ICU in June 2020 for respiratory and fulminant liver failure. The initial working diagnosis was acute COVID-19 vs. MIS-C. Prenatal history was notable for maternal group B streptococcus positive status. Two months prior to delivery, the mother had been diagnosed with COVID-19 by SARS-CoV-2 PCR in the setting of self-limited respiratory symptoms. The mother was noted to have a positive SARS-CoV-2 PCR without symptoms on screening at time of admission to the labor and delivery unit. After delivery, the neonate was tested for SARS-CoV-2 via PCR and was found to be negative. She was discharged from the newborn nursery on day of life (DOL) 2 without complications.

On DOL 5, the baby's parents noted that she had decreased oral intake and activity for which they sought medical care. At the time of presentation to a local ED, the baby was noted to be ill-appearing with progressive apnea requiring intubation. Blood cultures were obtained and she was treated empirically with ampicillin, gentamicin, and acyclovir. Initial laboratory findings were notable for severe acidosis (pH <6.9), normal white blood cell count with 22% premature neutrophils on differential count, elevated liver enzymes with aspartate transaminase of 2,638 U/L (reference range: 30–140 U/L) and alanine aminotransferase of 318 U/L (reference range: 5–45 U/L), and quickly developed signs of disseminated intravascular coagulation. She was transferred to a large children's hospital for further care.

Upon arrival at the children's hospital, additional laboratory studies revealed markedly elevated ferritin (>200,000 ng/mL; reference range: 99.6–717.0 ng/mL) and continued impaired renal function and liver failure. Due to concern for SARS-CoV-2 infection with secondary hemophagocytic lymphohistiocytosis triggered by the anti-viral inflammatory process, the hospital's specialized multidisciplinary consultation team for immune dysregulation was consulted. As a result of this consultation and concern for hemophagocytic lymphohistiocytosis, dexamethasone was given on DOL 6. Later that day, herpes simplex virus (HSV) PCR from serum was positive and a diagnosis of disseminated neonatal HSV disease was made. Further steroid administration was held and the neonate was continued on IV acyclovir.

Of note, concerns for neonatal COVID-19 continued; a total of four SARS-CoV-2 PCRs were collected from both nasopharyngeal and tracheal aspirate sources from DOL 2 through DOL 6, all of which were negative. Despite

these test results, she remained on expanded, COVID-19 transmission-based precautions for about 24 h.

Case commentary

In this case, systems factors contributed to diagnostic delay and erroneous decision to administer steroids, which are contraindicated in disseminated neonatal HSV disease. Specific opportunities were identified for improved communication, as the patient required multiple transfers of care (both between and within hospitals) and telephone (rather than in-person) subspecialty consultation. Local SARS-CoV-2 disease activity likely contributed to availability bias of a SARS-CoV-2 related diagnosis. In particular, we highlight the focus on positive maternal SARS-CoV-2 testing, prior maternal mild COVID-19 disease, documentation of high suspicion for COVID-19 in transfer notes of the neonate, and repetitive SARS-CoV-2 PCR testing of the neonate despite negative results. These factors originate from new processes of routine testing for SARS-CoV-2, the existence of the COVID-19 pandemic, and the emergence of MIS-C that does require immunomodulatory therapy (in contrast to neonatal HSV disease) and led to the cognitive factors of availability bias, diagnostic momentum, leading to premature closure, and continued confirmation bias [13].

This case builds on the availability bias seen in case 1 and particularly highlights the interplay of communication systems (including transfer notes and telephone consultations) with cognitive factors of diagnostic momentum and confirmation bias (Figure 1). The mutual reinforcements of systems and cognitive factors in this case suggests opportunities for systems level interventions to counteract cognitive bias in the diagnostic process. While this case occurred during the COVID-19 pandemic, these interactions are not unique to this moment.

Case 3

A 3-year-old male presented to a community ED in the mid-Atlantic United States in April 2020 with septic shock after 10 days of pale appearance, nosebleeds, fever, and altered mental status with hallucinations. Prior to ED presentation there had been one telephone encounter (two days prior) and one ambulatory clinic visit (one day prior), both of which resulted in a working diagnosis of a viral syndrome. Notably, this clinic visit was identified to be a “drive-through” visit with minimal provider contact. The patient's

parents also expressed hesitation in seeking medical care due to fear of exposure to COVID-19 in the healthcare setting. During the ED visit and ICU admission at the community hospital, he was diagnosed with acute B-cell lymphoblastic leukemia with severe pancytopenia (white blood cell count <2 K/uL, hemoglobin <3 g/dL, and platelets <5 K/uL) and septic shock secondary to group G streptococcal bloodstream infection with subsequent hyperkalemic cardiac arrest. He was transferred to a tertiary care children's hospital two days after initial presentation for continued management of multiorgan system failure. Several days later, due to the severity of neurologic injury in the setting of cardiac arrest, the decision was made to withdraw life-sustaining measures.

Case commentary

This case presents a striking array of systems factors, primarily related to seeking care in the setting of a pandemic and with active shelter-in-place orders (Figure 1). In the diagnostic error model presented by Gandhi and Singh, the avoidance of seeking healthcare due to the pandemic and fear of exposure to COVID-19, could be classified as a variant of "acute collateral" [8]. These concerns of COVID-19 exposure may have contributed to this child's delayed diagnosis of acute leukemia, which in turn likely resulted in a more severe disease presentation with septic shock, severe tumor lysis syndrome, and death. The ultimate outcome highlights downstream effects of necessary public health measures, shifts in alternative modes of care (i.e. phone and telehealth appointments), and patient and family perceptions of the healthcare field and media communication surrounding safety and the pandemic.

The cognitive factors at play in the outpatient visits with this case emphasize the typical cognitive biases that can happen even in the absence of a pandemic including availability bias and premature closure on a diagnosis that does not fit all the presenting symptoms [13]. Additionally, there may be an added contributor of "wellness bias," particularly in the case of a previously healthy child in the ambulatory pediatric clinic setting that may prevent consideration of more serious etiologies for presenting symptoms [14, 15].

Discussion

In this case series, we reviewed three cases that demonstrate the potential for diagnostic error in pediatric patients during the COVID-19 pandemic. Our review highlights three key themes in the factors leading to diagnostic error: (1) the

pandemic as a context for increasing diagnostic uncertainty and with associated cognitive biases of anchoring bias, availability bias, and diagnostic momentum, (2) rapid changes of local clinical practice processes of care related to COVID-19 pandemic, and (3) unique social environment changes introduced by the COVID-19 pandemic leading to adaptations in routine medical care delivery and hesitancy to approach the medical environment.

In the spring of 2020, COVID-19 was a rapidly emerging disease entity in the United States. The constantly evolving understanding of this disease process contributed to heightened diagnostic uncertainty, particularly in the early phases of the pandemic. We have found the pediatric experience with COVID-19 particularly challenging from a diagnostic standpoint as many children with acute COVID-19 often have minimal to no attributable symptoms [16]. Furthermore, the emerging clinical syndrome of MIS-C, thought to be a post-inflammatory disease related to SARS-CoV-2 infection, is characterized by signs and symptoms that overlap with many other more common severe pediatric diseases including bacterial sepsis, toxin-mediated disease, and viral syndromes other than COVID-19. In one study reviewing cases undergoing evaluation for potential MIS-C at a large children's hospital, 14 of 39 cases were given a non-SARS-CoV-2 infection as a diagnosis either in addition to or instead of MIS-C [17]. Because our understanding of MIS-C is evolving and the condition remains a diagnosis of exclusion, consideration of MIS-C in a differential diagnosis likely presented additional opportunities for diagnostic uncertainty. While diagnostic uncertainty has been difficult to define and measure, it is thought to impact the clinical decision-making process and potentially lead to diagnostic errors [18–20]. Strategies to counteract cognitive biases by utilizing slower thinking rather than heuristics in contexts of heightened risk may be helpful in decreasing the likelihood of anchoring and premature closure; however, studies of cognitive debiasing strategies, reflective practice, and feedback as tools to prevent error have had mixed results [21–23]. Interestingly, disease-specific interventions have shown more promise from an evidence-base and implementation standpoint [22]. Feedback systems, akin to those used in patient safety domains, have also been suggested to promote learning from prior diagnostic errors or near misses and address related systems factors [24–26] and are included in the National Academy of Medicine diagnostic process outcomes framework [1]. Further discussion of systems-level strategies targeting diagnostic error can be found in a narrative review by Singh et al. [27]. The literature and our experiences with the cases illustrate the complex nature of diagnostic errors, suggesting that there

may not be one generalizable solution. Addressing diagnostic errors is likely to require a creative approach in learning from themes shared by near misses and errors that could subsequently prevent similar pitfalls [2, 28].

The pandemic has also necessitated changes in the clinical processes of care that may have impeded communication and thus affected the diagnostic process as noted in each of our cases. These include new screening processes for SARS-CoV-2 prior to admission, changing hospital consultation models surrounding COVID-19 and related diagnoses, use of technology to conduct some in-hospital evaluations, and alternative work environments and models (i.e. increased telephone consultation). These processes were also rapidly changing to adapt to our constantly evolving knowledge, likely contributing to the cognitive load, increased stress, and increased fatigue of physicians and other healthcare professionals during this time as well as vulnerabilities in communicating these changes in processes. Recognition of the increased cognitive load that may come with other situations of heightened strain such as time, limited bed capacity, and decreased provider availability can be analogous and similarly impede the diagnostic process [4, 6, 7]. By recognizing these situations of rapid process change and potential information overload, we can identify potential interventions to streamline and reduce waste in these processes so we minimize preventable strains on the medical decision-making process [7].

Finally, the early phases of the COVID-19 pandemic introduced a unique social environment with shelter-in-place orders and rapid shifts to alternative modes of accessing healthcare (i.e. telehealth, phone calls) in effort to limit exposures. In case 3, we saw the potential impact of these conditions in delaying in-person care due to desire to limit exposures to the medical environment. An analysis from the Netherlands demonstrated a decrease in cancer diagnoses in March and April 2020 as compared to the period of time prior to the pandemic [29]. This effect was most pronounced with skin cancers and the consequence of such delays on patient outcomes is currently unknown. Delays in care have also led to decline in routine childhood immunizations [30], another indication that there are barriers and hesitations to seeking care temporally correlated with COVID-19 pandemic emergency declaration. The Centers for Disease Control and Prevention issued a Morbidity and Mortality Weekly Report on this issue in June 2020 to highlight avoidance of care and barriers to seeking care as a concern during the pandemic and suggest continuing public outreach through diverse platforms [31]. These messages can emphasize the importance of continuing medical care for those with chronic conditions, seeking medical care for

acute conditions, as well as describing precautions taken by healthcare facilities to reduce exposure risk.

Our case series was limited by the information available to us by chart review or involvement in a case. There are many clinicians involved in one patient's care and it is difficult to determine the weight of each of these individuals in the diagnostic process. Furthermore, as in many cases of analyzing diagnostic error, our information about the patient and family factors are limited. This is particularly highlighted in case 3, in which the patient had a delayed presentation to both telephone and in-person care. We are limited by the information gathered upon entering the medical system and what the patient's family was able to communicate about the sequence of events prior to seeking care. However, we do not have extensive information about the cognitive factors at play for the patient's family that influenced the prior visits and timing of seeking care.

In summary, we highlight three cases of diagnostic error in pediatrics during the COVID-19 pandemic with focus on the cognitive and systems factors at play in each. These cases illustrate how the pandemic holds a magnifying glass to the vulnerabilities of our diagnostic process. We should seize this opportunity to test improvements to these shortcomings while they are more visible and build a more robust diagnostic system.

Acknowledgments: We would like to thank Drs. Katherine M. Laycock, MD, Laura A. Vella, MD, PhD, Audrey R. Odom John, MD, PhD, and Jeffrey S. Gerber MD, PhD, MSCE for their thoughtful suggestions to the manuscript.

Research funding: Dr. Fatemi received funding from the Gordon and Betty Moore Foundation (GBMF7276) as part of the Society to Improve Diagnosis in Medicine (SIDM) Fellowship in Diagnostic Excellence.

Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: Authors state no conflict of interest.

Informed consent: Not applicable.

Ethical approval: Not applicable.

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