



Case Report



Diagnostic bias during the COVID-19. A rare case report of salmonella typhi

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ABSTRACT

Introduction: In poor countries, due to the limited resources, mostly they prescribe medications without proper diagnosis. The aim of this report is to show diagnostic bias of COVID-19 case.

Case presentation: A 17-year-old male patient was presented to the Hospital with a fever up to 39 °C associated with rigor, sweating, generalized body pain, myalgia, fatigue, loss of appetite, headache, and multiple joint pain with no swelling and redness. The vital signs were steady on physical examination, except temperature which was 39 °C. The chest was clear, and the pulse rate was 90 beats per minute. The heart rate relative bradycardia and lungs were normal. Both a PCR test for COVID-19, and a viral assay ELISA were negative. After further investigations, the culture findings revealed the strong development of Gram-negative coccobacilli (*Salmonella* serotype Typhi) bacteria under the microscope, which was confirmed by using VITEK 2 to identify it. and treated with ciprofloxacin tab, two times per day for five days and amikacin ampule 500 mg IV every 24 hours for 10 days.

Discussion: Fever is a well-known sign of COVID-19 infection which has been observed in 83%–98% of patients with COVID19. As a result, it may be difficult to tell the difference between COVID-19 and other febrile infections, causing delays in diagnosis and treatment and may blind the physician from considering other febrile illnesses.

Conclusion: Physicians should construct more comprehensive differential diagnoses for people who experience fever, headache, or myalgia symptoms that are linked to a pandemic. COVID-19.

1. Introduction

Salmonella enterica subspecies *enterica* serovar Typhi causes typhoid fever (*Salmonella* Typhi). In low-resource settings, typhoid fever is a systemic infection that is a primary cause of death and illness [1]. Waterborne, foodborne, or significant person-to-person contact are all ways for the disease to spread [2]. Classically, typhoid fever is associated with prolonged fever with a step ladder pattern, gastrointestinal symptoms (like nausea, vomiting, diarrhea, or constipation), headache, fatigue, malaise, loss of appetite, and cough [3].

A novel coronavirus (SARS-CoV-2) is currently causing a severe pandemic of disease (termed COVID-19) worldwide, causing a global pandemic [4]. The majority of people infected with SARS-CoV-2 are asymptomatic or complain of pneumonia-like symptoms consisting of fever, cough, shortness of breath, and viral symptoms like myalgia, fatigue, and headache [5]. Also, the clinical spectrum of COVID-19 ranged from asymptomatic, mild, to moderate-severe, which might lead to death [6].

Fever, lack of appetite, nausea, headache, constipation, and sometimes diarrhea are symptoms of extensively drug-resistant typhoid fever,

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which are frequently non-specific and difficult to identify from other febrile disorders, including COVID-19 [7]. At the time of the COVID-19 pandemic, limited study had been done on typhoid fever diagnosis.

Medication is frequently provided in low-resource countries without a proper diagnosis in such cases. Apart from the nonspecific symptoms of typhoid, they are similar to those of other diseases such as malaria, dengue fever, and COVID19 [8].

In the period of the COVID-19 pandemic, a high index of suspicion for non-COVID-19 illnesses that can cause systemic disease and inflammation should be maintained [9]. The aim of this report is to describe a diagnostic bias COVID-19, after which proper diagnosis was established as having typhoid fever. This report was written and used the SCARE criteria for case reports as a guideline [10].

2. Patient information

A 17-year-old male patient presented to the hospital with a five-day fever 39 °C. That was episodic, mostly at night, and associated with rigor, sweating, generalized body pain, myalgia, fatigue, loss of appetite, headache, and multiple joint pain with no swelling and redness. The patient had no skin rash, redness, or swelling, did not have a pet or domestic animal at home. He also had mild central abdominal pain, colicky in nature, associated with mild, non-bloody diarrhea four times a day, with no bloody vomiting. He also had a mild dry cough that began one week after the onset of his symptoms, but he had no shortness of breath, was not smoking or drinking alcohol, and lived in a rural area, so his medical history did not indicate that he had a major disease. He had not had any previous abdominal surgery or trauma. Then he was approached with pyrexia of unknown origin. He did not eat Kurdish cheese, which is made from unpasteurized milk. None of his family members developed the same condition, but history revealed that he drank tap water and ate food on the local street during the 12 days before the onset of fever. Physician outside the hospital suspected a mild case of COVID-19 and treated for five days based on the COVID-19 standard care.

3. Clinical finding

The vital signs were stable during the physical examination, except temperature which was 39 °C. The pulse rate and blood pressure were 118bpm, 120/80 mmHg, respectively. SpO2 was 97%. The chest was clear, and the pulse rate was 90 beats per minute. The heart rate relative bradycardia and lungs were normal. He had poor skin turgor and appeared to be dehydrated. A part mild splenic enlargement and there was no palpable enlargement of the liver.

4. Diagnostic assessment

The following tests were done to differential diagnosis of fever; a PCR test for COVID-19, and a viral assay ELISA (Biotek) for detecting antibody IgM anti-SARS-CoV-2 was also done, the results for both tests were negative. ESR (erythrocyte sedimentation rate) to rule out rheumatological disease, vasculitis and malignancy, which was 17, serological test for Brucella was done by using Brucella agglutination titer, which was negative (<25 IU/mL). CBC to exclude hematological disease, which was normal, CRP, and D-Dimer were 43.94 mg/L and 0.29 µg/mL, respectively. Echocardiography had been done to exclude cardiac vegetation for IE (Infective Endocarditis), it showed no vegetation and was normal. Procalcitonin for evidence of bacterial infection, which was high at 0.319, abdominal ultrasound, which showed mild splenomegaly size (14 cm on long axis), urinary bladder wall at 8 mm (cystitis), and HRCT of the chest was normal. Blood was sent for bacterial culture and patient treated by paracetamol and ceftriaxone and the patient return home, after seven days the patient came back and the culture findings revealed the strong development of Gram-negative coccobacilli (*Salmonella* serotype Typhi) bacteria under the microscope, which was

confirmed by using VITEK 2 to identify it. The VITEK 2 AST-N325 card was used to detect antimicrobial drug susceptibilities according to the Clinical Laboratory Standards Institute's criteria. (bioMérieux). *Salmonella enterica Typhi* was found resistant to ampicillin, trimethoprim-sulfamethoxazole, cefazolin, cefuroxime, cefoxitin, and ceftriaxone. But Susceptible to ertapenem, meropenem, amikacin, gentamicin, tigecycline, ceftazidime, ciprofloxacin, and piperacillin.

Based on the results of the culture and antibiotic sensitivity tests, he was treated for 10 days, and the patient's follow-up convalescent COVID-19 antibody remained negative. After 10 days, the patient was fully recovered with no symptoms.

5. Therapeutic intervention

The patient outside hospital suspected a mild COVID-19 and treated with clexane vial one time per day and ceftriaxone vial 1 gm twice per day for five days but fever, sweating, myalgia, and headache continued. After diagnosis, the previous treatment was stopped and treated with ciprofloxacin tab 500 mg, two times per day for five days and amikacin ampule 500 mg IV every 24 hours for 10 days. The patient recovered clinically after 10 days on amikacin antibiotics.

6. Discussion

In low- and middle-income countries, typhoid fever is a public health hazard., killing around 200,000 deaths per year [11]. *Salmonella Typhi* is spread by contaminated water, undercooked foods, and infected patients, and is more common in regions with overpopulation, social disorder, and inadequate sanitation [12]. The present case is infected by contaminated food and water. Access to efficient antibiotic medication at the right time is critical for avoiding consequences including intestinal perforation and death. As a result, the worrying emergence of antibiotic resistance in *Salmonella Typhi* is anticipated to impair clinical outcomes [13]. In Pakistan and other low- and middle-income countries, extensively drug-resistant (XDR) typhoid fever is a severe public health problem., particularly during the COVID-19 epidemic, when excessive azithromycin usage may cause havoc [7]. Ampicillin, trimethoprim sulfamethoxazole, and chloramphenicol were the first-line therapies for typhoid. Multidrug-resistant (MDR) *S. Typhi* strains have been commonly documented since fluoroquinolones (ciprofloxacin, gemifloxacin, levofloxacin, and moxifloxacin) became the favored therapy in areas where MDR infections are prevalent. When alternative treatments are not available, ceftriaxone, a third-generation cephalosporin, and azithromycin, a macrolide, are drugs used nowadays to treat typhoid fever. However, isolated instances of *S. Typhi* resistant to ceftriaxone or azithromycin have lately been documented [14].

In the present case, resistance to the first line and low response to the second line, also resistance to the third line of ceftriaxone, which was used before proper diagnosis, therefore, the treatment was a failure. Typhoid symptoms can range from acute to severe and appear between 0 and 36 days following the disease's beginning [8]. Many typhoid patients have a generic febrile illness that is not clinically identified as typhoid [15]. Also, fever is a well-known sign of COVID-19 infection which has been observed in 83%–98% of patients with COVID19. As a result, it may be difficult to tell the difference between COVID-19 and other febrile infections, causing delays in diagnosis and treatment and may blind the physician from considering other febrile illnesses [16]. Furthermore, the present case depends on the clinical finding of fever, headache and myalgia previously diagnosed as COVID-19.

However, the presence of microbial assays such as real-time polymerase chain reaction or sequencing is the primary diagnostic technique for confirming COVID-19 infection (RT-PCR) [17]. But this tool has not always existed in the emergency departments, especially in low-income settings, so this might lead to biased diagnosis and, in turn, false treatment.

Due to symptom overlap with COVID-19, this condition, which

usually manifests with fever, headache, and myalgia, might be ignored, making diagnosis bias or the COVID-19 diagnostic technique more challenging. Fever is one of the most common symptoms of COVID-19 infection. Therefore, with the current epidemic, physicians must be more vigilant in recognizing other infections that appear with a prolonged fever. Malignancy, viral disorders, and rheumatological problems are among the differential diagnoses for chronic febrile sickness. A thorough medical history, including work, travel, and animal contact, may lead to the diagnosis of previously undiagnosed febrile diseases [16, 18]. The current case history helped physicians to suspect Typhoid fever.

A study in Brazil, they showed how the spread of the Zika virus during the pandemic, which is similar clinically to COVID-19, aggravates the problem of misdiagnosing the condition and leads to improper treatment [19].

Also, a study from Pakistan showed how during the COVID-19 pandemic, the mutual differential diagnosis between COVID-19 and typhoid was challenging for physicians, due to the fact that they were relying on clinical diagnosis in most cases, which makes the diagnosis challenging. Beyond that, the diagnostic tools for typhoid fever in low-income settings, such as the Widal test and Typhidot, have low sensitivity and specificity [7].

When symptoms are compatible with a current global pandemic virus, it is difficult to identify the real underlying cause without adequate diagnosis testing, and it is critical to rule out alternative possibilities [8,20].

7. Conclusion

Physicians should establish more complete differential diagnoses for individuals who have symptoms of fever, headache and myalgia that correlate with pandemic COVID-19.

8. Provenance and peer review

Not commissioned, externally peer-reviewed

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No source to be stated.

Ethical approval

Approval is not necessary for case report in our locality.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Jeza M.Abdul Aziz, Nguyen Tien Huy, Tareq Al-Ahdal, Muhammad Jabar Rashid, Rebwar Hassan Khdir, Mohammed I.M. Gubari, participated in the design of the study, literature review, writing the manuscript, final approval of the manuscript. Saman Kaka Abdullah, Kosar Shirwan Tahir, Zardasht Muhammad Hamarashid, contributed in the managing, follow up the patient, edited and approved the final manuscript.

Registration of research studies

According to the previous recommendation, registration is not

required for case report.

Guarantor

Jeza M.Abdul Aziz is the Guarantor of submission

Declaration of competing interest

There is no conflict to be declared.

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