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Unraveling a diagnostic challenge: malaria in an 8-year-old female misdiagnosed as dengue

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Abstract

This case study presents a young female patient from Santo Domingo, Dominican Republic, who was misdiagnosed multiple times before being accurately diagnosed with malaria. This case highlights the challenging diagnosis of malaria in non-endemic regions like the Dominican Republic, where cases are rare and often overlooked due to migration patterns, such as those from Sub-Saharan Africa. The patient initially presented with concerns of asthma, persistent high fever suspected to be dengue, and hypogastric abdominal pain lasting several hours. Upon examination, she was found to be alert but mildly dehydrated, with vital signs indicating a heart rate of 102 bpm, a respiratory rate of 24 breaths per minute, a temperature of 38 ºC, and a blood pressure of 100/60 mmHg. Her physical examination was largely unremarkable except for the noted abdominal pain upon deep palpation in the hypogastrium. After a series of diagnostic tests, malaria was confirmed, and the patient was treated with antimalarial medication and supportive care, resulting in significant clinical improvement. She was subsequently discharged with follow-up care instructions. This case underscores the importance of considering malaria in the differential diagnosis, even in regions where it is not typically endemic. The findings from this case highlight the importance of region-specific strategies and innovations, such as gene drive technology, in controlling malaria. The socio-economic impact of malaria, particularly in poverty-stricken areas, and the influence of urbanization on disease spread, further complicate its management. This case demonstrates the need for healthcare professionals to be vigilant and adaptable, taking into account various factors, including socio-economic conditions and migration, when diagnosing and treating vector borne diseases like malaria.

Keywords

Malaria, Dengue, Case report, Non-endemic, Dominican Republic, Plasmodium, Misdiagnosis, Hypogastric pain, Hypnozoites, Overlapping symptoms

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Introduction

Malaria and dengue are two common febrile illnesses in tropical and subtropical regions (1) that often present with overlapping symptoms, complicating diagnosis (2). Both diseases share symptoms such as fever, chills, headache, and muscle pain, making it easy to misdiagnose one for the other, especially in regions where both are non-endemic. Malaria, caused by the *Plasmodium* species, may present with additional symptoms like anemia, jaundice, and cerebral malaria in severe cases (3). Dengue, a viral infection transmitted by *Aedes* mosquitoes, can be accompanied by retro-orbital pain, rash, and joint pain, sometimes progressing to severe forms like dengue hemorrhagic fever or shock syndrome (4, 5). The host immune response plays a crucial role in combating Malaria, with immunoglobulins (Ig) being key players in the body's defense. Various types of immunoglobulins, including IgG, IgM, and IgA, contribute to this response, each with unique functions. IgG antibodies are essential for neutralizing parasites, providing long-lasting immunity (6). On the contrary, IgM antibodies typically indicate recent infections and can enhance inflammation, potentially leading to severe disease manifestations. Diagnosing malaria becomes further complicated by other mosquito-borne diseases, such as dengue. Serological tests for dengue rely on detecting specific immunoglobulins, particularly IgM and IgG, to determine the presence of an infection (7). However, these tests may not necessarily indicate a current dengue infection due to the potential for cross-reactivity with other flaviviruses, leading to false-positive results. This overlap can create diagnostic confusion, especially in regions where malaria and dengue co-circulate (8). In non-endemic areas, such as Santo Domingo in the Dominican Republic, malaria is frequently misdiagnosed due to its rarity and the focus on more common illnesses like dengue (9). Healthcare providers often rely on hemograms that can overlook malaria while focusing on differential diagnoses like stress-related illnesses or dengue (10).

Concurrent infections of dengue and malaria, while rare due to the different habitats of their vectors and the activities of different carrier mosquitoes, have been documented in African countries. Numerous instances of concurrent infections between the dengue virus (DENV) and the malaria protozoans *Plasmodium falciparum* and *Plasmodium vivax* have since been reported (11). The symptoms of each infection may mask those of a simultaneous second infection, resulting in delays in treatment and in severe complications. Notably, *Plasmodium knowlesi* has emerged as a common cause of malaria in Malaysia, associated with one of the highest rates of mortality (7). Some areas with high rates of both malaria and dengue are those in Southeast Asia. The rate of infection for febrile patients is about 0.99% (12). The manifestations of concurrent malaria and dengue are high fever and myalgia. Overall, concurrent malaria and dengue infection are uncommon. The malaria mosquito vector mainly is endemic to rural areas while the dengue mosquito vector is endemic to urban areas. Thus, overlap is uncommon. Additionally, the concurrent infection can be overlooked since it is easy for one diagnosis to be made without taking into account a possible second diagnoses (12).

Patient Information

The patient was an 8-year-old female from Santo Domingo, who was presented by her mother with symptoms of fever and abdominal pain. There was no indication that the patient had traveled near the border with Haiti, and no one specifically asked about recent travel history at the time of admittance. This is an important point, as recent travel to areas where malaria is more prevalent could have influenced the diagnostic process and treatment decisions. The patient's history did not suggest recent exposure to high-risk malaria zones, which delayed the consideration of malaria in the differential diagnosis (13). She had a history of asthma but was in good general condition until five days prior to admission when she developed a fever (39-39.5°C) and abdominal pain in the hypogastric region. The patient's hypogastric pain was a key factor in the initial diagnosis of dengue, as abdominal pain is a common warning sign of severe dengue, often related to liver or gastrointestinal involvement. However, hypogastric pain can also occur in malaria due to splenic or liver enlargement (14). This overlap in symptoms contributed to the diagnostic challenge, as both dengue and malaria can present with similar abdominal discomfort. Ultimately, the pain added to the complexity of distinguishing between the two diseases in this case. Initial home management included acetaminophen, with transient improvement, but persistent fever led to an emergency room visit and subsequent discharge. The patient was not fever-free on discharge, since her vital signs included a temperature of 38°C, a heart rate of 102 l/m, a respiratory rate of 24 r/m, and a blood pressure of 100/60 mmHg. With the onset of abdominal pain, she returned to the emergency room, leading to her admission. Her medical history included asthma, two prior hospitalizations, no surgeries, transfusions, or medications, and a complete vaccination schedule as informed by her mother. The patient was hospitalized two prior times due to episodes of stomach pain and consistent fever. The patient was worried that the symptoms indicated recurring or unresolved underlying conditions, possibly linked to infections or inflammatory processes, that warranted medical intervention. In both instances, the recurrent fever and abdominal pain raised concerns about the potential for serious conditions such as viral or bacterial infections, gastrointestinal dysfunction, or other systemic inflammatory responses, necessitating hospitalization for closer monitoring and treatment. Typhoid fever was ruled out in this case based on the patient's clinical presentation and laboratory findings. While typhoid shares some overlapping symptoms with conditions like malaria and dengue—such as fever and abdominal pain—the patient did not exhibit hallmark signs of typhoid, such as a stepwise fever pattern, rose-spot rash, or significant gastrointestinal symptoms like diarrhea or constipation (15, 16). Laboratory testing, particularly blood cultures, further supported the exclusion of typhoid. The blood culture was negative after 48 hours, and the thick blood smear confirmed the presence of hematozoa, leading to a malaria diagnosis. The family history revealed healthy parents and no significant medical conditions among grandparents or siblings. The patient had reported abdominal pain that was ongoing for hours, of moderate intensity, predominantly

hypogastric, unmanaged, with no improvement. The patient's mother reported that at the beginning of the clinical picture, she observed and managed fever spikes.

Clinical Findings

On physical examination, the patient was alert, febrile, and eupneic, with mild dehydration. Her vital signs were notable for a heart rate of 102 bpm, a respiratory rate of 24 breaths per minute, a temperature of 38 ºC, and a blood pressure of 100/60 mmHg. The assessment of her head, eyes, nose, mouth, ears, chest, lungs, abdomen, genitals, extremities, skin, and neurological functions were all within normal limits, except for abdominal pain on deep palpation in the hypogastrium. The initial diagnosis was suspected dengue with alarm signs, and treatment included a gentle diet, hydration, acetaminophen, and frequent monitoring. In this case, dengue fever was initially suspected due to the patient's clinical presentation and the regional prevalence of dengue in Santo Domingo. She had a high fever (39-39.5°C), which is a sign of dengue, persisting for five days despite home management with acetaminophen. Her pain localized to the hypogastric region, a symptom that can occur in dengue, particularly in cases involving complications of dengue with alarm signs. Lastly, despite her history of asthma, her respiratory rate was normal, and she was eupneic, ruling out any immediate respiratory involvement and strengthening the suspicion of a febrile illness like dengue. However, persistent high fever and rising platelets necessitated further testing, leading to a positive result for hematozoa, indicative of malaria.

Table 1. Timeline of patient care

Date	Description
05 January, 2020	Gentle diet, Sol Harlac (5MG/Kg/H), Acetaminophen SOS (15MG/KG/DOSE), Hemogram, SV+BH+DMH+ C/4HOURS
06 January, 2020	In the event of a high fever lasting more than 6 days and rising platelets, which are currently not alarming signs, other possible diagnoses are considered. Carry out: PCR, TGO, TGP, Blood culture, Urinalysis, Thick drop, Malaria, Hepatitis, Sepsis
07 January, 2020	Suspend Sol Harlac, Mixed Sol 0.33% (1500ml/M²SC/24h) Carry out : Bilirubin, Urea, Creatinine, Chloroquine 150MG C/24 H, Primaquina 15MG Single dose, Notify the epidemiology department
08 January, 2020	Preliminary blood culture (negative in 48 hours), Continue with the same medication, No fever spikes, Discharged with outpatient management

Diagnostic Assessment

Given the persistence of high fever and abdominal pain, laboratory tests were conducted including a complete blood count and platelet count. Laboratory diagnosis of malaria typically involves identifying malaria parasites in a blood smear, with PCR being a confirmatory test in cases of ambiguous results

(17). Rising platelet levels led to further testing, including polymerase chain reaction (PCR) and blood culture, which confirmed hematozoa. Imaging and specific surveys were not detailed in this case, as the combination of PE and lab testing provided enough information to establish the proper diagnosis. The primary diagnostic challenge was distinguishing between dengue and malaria, as both were present with overlapping symptoms such as fever. Initial thoughts led to the diagnosis of dengue due to the regional prevalence and clinical presentation. However, the lack of improvement and lab results necessitated a reevaluation of the diagnosis. Treatment included a gentle diet, hydration, acetaminophen, and frequent monitoring. However, persistent symptoms and lab findings led to the final diagnosis of malaria. With treatment using chloroquine and primaquine, the patient showed significant improvement. Malaria's prognosis is generally favorable with timely and appropriate treatment. In a documented malaria report from 2020, early treatment of uncomplicated malaria generally leads to a good prognosis and full recovery. Research has shown that patients treated in the early stages of the parasite cycle had better recovery outcomes than patients treated in the later stages where malaria became more life-threatening (18). However, delays in diagnosis or treatment could have led to more severe complications. The absence of complications and the patient's continued improvement after treatment indicated a positive prognosis.

Therapeutic Intervention

Appendix 1 presents the treatment algorithm that the patient underwent in terms of care as well as possible tests and treatments if the patient hypothetically got dengue instead of malaria. On 05 January 2020, an 8-year-old female patient was admitted with symptoms including fever and abdominal pain. To ensure proper nutrition while minimizing gastrointestinal distress, she was placed on a gentle diet. Intravenous hydration was started with Sol Harlac at 5 mg/kg/hour to address dehydration and support recovery. To manage fever and provide symptomatic relief, acetaminophen was administered as needed (SOS) at 15 mg/kg/dose. Monitoring of blood parameters was done through laboratory tests, including a hemogram. Vital signs, blood pressure, hydration status, and dehydration levels were monitored at four-hour intervals. Given high fever for more than six days, with an increasing trend of platelets, further diagnostic workup was indicated on 06 January 2020. After suspecting dengue, tests performed included polymerase chain reaction (PCR), transaminase levels (TGO, TGP), blood culture, urinalysis, and a thick blood smear. These investigations were undertaken in pursuit of differentials such as malaria, hepatitis, and sepsis.

By 07 January 2020, the patient's hydration solution was adjusted to Mixed Sol 0.33% at 1500 ml/m² body surface area per 24 hours to better meet her needs. Extra laboratory tests were performed to assess liver and kidney function by measuring bilirubin, urea, and creatinine levels. Upon confirmation of malaria, treatment was adjusted accordingly. Chloroquine was administered at a dosage of 150 mg/day during the chronic phase as an antiparasitic; a single dose of primaquine, 15

mg, was given for hypnozoites and to prevent relapses. The case of malaria was also reported to the epidemiology department for public health monitoring.

On 08 January 2020, this represented a preliminary blood culture that had turned negative after 48 hours with no secondary bacterial infection and normal vital signs. As there was no spike in fever and the symptomatic improvement was appreciable, the medication regimen remained unchanged. The patient was discharged with an outpatient management plan that included scheduled follow-up visits to monitor recovery and prevent potential relapses.

Follow-up and Outcomes

Some clinician and patient-assessed outcomes included regular monitoring of vital signs and symptomatic relief. The patient initially presented with a five-day history of fever and abdominal pain, prompting emergency room visits and subsequent admission. The initial suspicion of dengue was considered due to the fever's pattern and associated abdominal pain. Follow-up diagnostic tests, such as PCR, blood cultures, and urinalysis, were critical in determining the final diagnosis of malaria, initially suspected to be dengue. These tests revealed the presence of Plasmodium parasites, confirming malaria. Intervention adherence and tolerability were evaluated through frequent assessments of vital signs and patient-reported symptom relief, particularly focusing on hydration and acetaminophen management. The patient was placed on a gentle diet and received intravenous fluids to manage dehydration. Adverse and unanticipated events included a persistent high fever and worsening abdominal pain, which led to additional testing and a change in the initial diagnosis. The patient's response to the prescribed treatments, including Chloroquine and Primaquine, was closely monitored, ensuring that no further complications arose. The persistence of fever despite initial management highlighted the need for further diagnostic testing. After confirming a diagnosis of malaria, treatment adherence was ensured through careful administration of medications and follow-up evaluations. The patient showed improvement in symptoms, with no further fever spikes, indicating successful intervention and management. Post-discharge, no further fever spikes were reported, indicating successful intervention and management. Regular follow-up visits were scheduled to ensure the patient's continued recovery and to monitor for any potential relapse or complications. A treatment algorithm is presented in Appendix 1.

Discussion

The clinical case of an 8-year-old female patient presenting with fever and abdominal pain, later diagnosed with malaria, aligns with the literature on malaria's clinical presentation, diagnosis, and management. Strengths of this case approach include thorough evaluations such as PCR, blood cultures, and urinalysis, which were critical in confirming malaria after initially suspecting dengue. Frequent monitoring and checkups ensured the patient was well-rested and stable, highlighting the importance of broad differential diagnosis in non-endemic areas. Close monitoring of vital signs and symptomatic relief ensured prompt response to adverse events, leading to effective

management with Chloroquine and Primaquine. However, there was a delay in considering malaria as a diagnosis, only after several days of high fever and worsening symptoms was this diagnosis made, which underscores a limitation. This case emphasizes the necessity for rapid diagnostic tools and timely clinical suspicion in non-endemic regions to prevent complications. While the diagnostic workup was thorough, empiric treatment with antimalarial medication prior to confirmation could have led to unnecessary side effects, such as nausea, dizziness, or even more severe reactions associated with medications like Chloroquine and Primaquine. Such side effects, especially in pediatric patients, highlight the need for judicious use of antimalarial drugs and emphasize the importance of confirming the diagnosis before initiating treatment (19). Additionally, an algorithmic approach recommending simultaneous testing for both dengue and malaria in endemic or non-endemic areas where both diseases are plausible would be more appropriate (20). This approach avoids unnecessary medication while ensuring that prompt treatment is available once the diagnosis is confirmed. In this case, the eventual combination therapy of Chloroquine and Primaquine proved effective, as supported by the case, which stresses the importance of early diagnosis and appropriate treatment. The rationale for concluding malaria was based on the patient's persistent fever despite initial management for suspected dengue, with eventual positive diagnostic tests confirming malaria. This approach underscores the value of combining diagnostic tools with clinical knowledge for successful outcomes.

Conclusion

Healthcare providers must be cognizant of malaria and its potential threats, particularly in patients presenting with fever in non-endemic areas. While timely and accurate diagnosis supported by comprehensive testing and vigilant monitoring is essential, it is equally important to avoid initiating antimalarial treatment without confirmation, given the risks of side effects and contributing to drug resistance. A balanced approach involving rapid diagnostic tools, clinical suspicion, and simultaneous testing for diseases like dengue and malaria would lead to more effective and targeted treatment strategies. By utilizing the lessons learned in this case, such as careful differential diagnosis and the algorithmic approach to testing, healthcare systems can improve the efficiency and effectiveness of future treatments, ensuring better outcomes for patients while minimizing unnecessary risks.

Informed Consent

Consent was provided by the Dominican physician to publish the case. No personal information was included in the study.

References

1. World Health Organization. “Malaria.” World Health Organization. WHO, December 4, 2023. https://www.who.int/news-room/fact-sheets/detail/malaria.

2. Gebremariam TT, Schallig H, Kurmane ZM, Danquah JB. “Increasing Prevalence of Malaria and Acute Dengue Virus Coinfection in Africa: A Meta-Analysis and Meta-Regression of Cross-Sectional Studies.” *Malaria Journal.* 22(1), 2023. https://doi.org/10.1186/s12936-023-04723-y.

3. Cleveland Clinic. “Malaria: Symptoms, Treatment, Causes, Prevention and Signs.” Cleveland Clinic, May 18, 2022. https://my.clevelandclinic.org/health/diseases/15014-malaria.

4. CDC. “Clinical Features of Dengue.” Dengue, June 5, 2024. https://www.cdc.gov/dengue/hcp/clinical-signs/index.html.

5. Centers for Disease Control and Prevention. “Transmission.” CDC, September 26, 2019. https://www.cdc.gov/dengue/transmission/index.html.

6. Triller G, Scally SW, Costa G, Pissarev M, Kreschel C, Bosch A, Marois E, et al. “Natural Parasite Exposure Induces Protective Human Anti-Malarial Antibodies.” *Immunity.* 47(6), 1197-1209, 2017. https://doi.org/10.1016/j.immuni.2017.11.007.

7. Chong SE, Zaini RHM, Suraiya S, Lee KT, Lim JA. “The Dangers of Accepting a Single Diagnosis: Case Report of Concurrent Plasmodium Knowlesi Malaria and Dengue Infection.” *Malaria Journal.* 16(2), 2017. https://doi.org/10.1186/s12936-016-1666-y.

8. Kingston R, Routledge I, Bhatt S, Bowman LR. “Novel Epidemic Metrics to Communicate Outbreak Risk at the Municipality Level: Dengue and Zika in the Dominican Republic.” *Viruses.* 14(1), 162, 2022. https://doi.org/10.3390/v14010162.

9. Garcia M, Bonilla L, Alvarez B. “Dominican Republic | CDC Yellow Book 2024.” wwwnc.cdc.gov, May 1, 2023. https://wwwnc.cdc.gov/travel/yellowbook/2024/itineraries/dominican-republic.

10. Keys H. “Following Misdirection and Multiple Malaria in Santo Domingo, Dominican Republic.” *Science & Technology Studies.* 35(2), 52-71, 2022. https://doi.org/10.23987/sts.110326.

11. Selvaretnam A, Sahu PS, Sahu M, Ambu S. “A Review of Concurrent Infections of Malaria and Dengue in Asia.” *Asian Pacific Journal of Tropical Biomedicine.* 6(7), 633-638, 2016. https://doi.org/10.1016/j.apjtb.2016.05.008.

12. Wiwanitkit V. “Concurrent Malaria and Dengue Infection: A Brief Summary and Comment.” *Asian Pacific Journal of Tropical Biomedicine.* 1(4), 326-327, 2011. https://doi.org/10.1016/s2221-1691(11)60053-1.

13. CDC. “Haiti | CDC Yellow Book 2024.” wwwnc.cdc.gov, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/itineraries/haiti.

14. Wilson S., Jones FM, Mwatha JK, Kimani G, Booth M, Kariuki HC, et al. “Hepatosplenomegaly Associated with Chronic Malaria Exposure: Evidence for a Pro-Inflammatory Mechanism Exacerbated by Schistosomiasis.” *Parasite Immunology.* 31(2), 64-71, 2009. https://doi.org/10.1111/j.1365-3024.2008.01078.x.

15. Cleveland Clinic. “Typhoid Fever: Symptoms, Causes, Treatments.” Cleveland Clinic, September 7, 2022. https://my.clevelandclinic.org/health/diseases/17730-typhoid-fever.

16. CDC. “Clinical Guidance for Typhoid Fever and Paratyphoid Fever.” Typhoid Fever and Paratyphoid Fever, 2024. https://www.cdc.gov/typhoid-fever/hcp/clinical-guidance/index.html.

17. CDC. “Evaluation and Diagnosis.” Malaria, April 24, 2024. https://www.cdc.gov/malaria/hcp/clinical-guidance/evaluation-diagnosis.html.

18. World Health Organization. “World Malaria Report 2020.” www.who.int, 2020. https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2020

19. Global Malaria Programme (GMP). “WHO Informal Consultation on Fever Management in Peripheral Health Care Settings: A Global Review of Evidence and Practice.” Who. int, 2024. https://www.who.int/publications/i/item/9789241506489.

20. Konstantinos M, Hin S, Müller P, Wipf N, Thomsen E, Coleman M, et al. “Converging Human and Malaria Vector Diagnostics with Data Management towards an Integrated Holistic One Health Approach.” *International Journal of Environmental Research and Public Health.* 15(2), 2018. https://doi.org/10.3390/ijerph15020259.

Appendix 1. Treatment Algorithm