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ID TEACHING CASES

Measles or Not Measles? That Is the Question!

Marina Kristy Ibraheim,[1] Hesham Awadh,[2] Ambreen Allana,[2] Luis Ostrosky-Zeichner,[2] and Cesar A. Arias[2-5]

[1]The University of Texas Health Science Center, McGovern Medical School, Houston, Texas, USA, [2]Department of Internal Medicine, Division of Infectious Diseases, The University of Texas Health Science Center, McGovern Medical School, Houston, Texas, USA, [3]Center for Antimicrobial Resistance and Microbial Genomics, University of Texas Health Science Center, McGovern Medical School, Houston, Texas, USA, [4]Center for Infectious Diseases, University of Texas Health Science Center, School of Public Health, Houston, Texas, USA, and [5]Molecular Genetics and Antimicrobial Resistance Unit, International Center for Microbial Genomics, Universidad El Bosque, Bogotá, Colombia

We present a diagnostically challenging case of a patient who presented with fever and rash during a measles outbreak. The diagnosis was complicated by the interpretation of the results of serological tests, which resulted in implementation of major preventive measures in the hospital. The patient was later confirmed to have murine typhus.

Keywords. measles; serological testing; typhus.

CASE

A 34-year-old Caucasian man living in Houston, Texas, presented to a local hospital 6 days after developing fatigue, malaise, odynophagia, rash, and recurrent high-grade fevers. One day prior, he had developed a generalized rash on his shoulders and trunk. These symptoms began once he and his family returned from a 3-day vacation in Destin, Florida, and Lake Charles, Louisiana. While on this trip, he had walked through high grass and swam at the beach. No other family members or close contacts reported similar symptoms. The patient denied sustaining any insect or tick bites; however, he had reported that his dog and home were infested with fleas and termites, respectively. His immunization status was up to date.

On admission, the patient had a temperature of 103°F and was tachycardic (107 beats per minute). His blood pressure (range) was 104/67 (85–110) mmHg (systolic blood pressure). Physical exam revealed an ill-appearing man with bilateral conjunctival injection and cervical lymphadenopathy. Skin examination revealed a diffuse, nonblanching maculopapular rash with petechiae on the trunk and bilateral upper and lower extremities (Figures 1 and 2). No mucocutaneous or urogenital lesions were noted. Laboratory evaluation demonstrated a white blood cell count of 3.1 ×10 k/μL, platelet count of 62 k/μL, hemoglobin of 14.1 g/dL, alanine transaminase of 100 U/L, aspartate aminotransferase level of 113 U/L, alkaline phosphatase level of 116 U/L, and total bilirubin of 0.8 mg/dL. Blood and urine cultures were negative. Serological studies yielded a positive Rubeola (measles) IgM antibody of 3.4 AU (>1.2 AU positive) and IgG antibody 6.2 AU (>1.10 AU positive).

At this stage, the main differential diagnoses included measles and murine typhus. Out of an abundance of caution due to the clinical picture and serologic studies, a decision was made to trigger a hospital-wide infection response involving implementation of airborne precautions and administration of intravenous immunoglobulin (IVIG) for postexposure prophylaxis to high-risk patients who were likely in contact with the patient. During this time, the patient began doxycycline 100 mg IV twice daily. Within 2 days of initiating treatment, the patient's clinical condition gradually improved. Episodes of fever and hypotension began to dissipate. His rash improved and resolved by the third day of treatment. His white blood cell count and platelet count doubled within 4 days of treatment. Further serological studies revealed a Rocky Mountain Spotted Fever IgM antibody titer of 3.53 (positive >1.10 index), IgG antibody titer of 1:256 (negative <1:64), typhus antibody titer of 1:256 IgM and IgG (active >1:64), confirming the diagnosis of murine typhus. Measles reverse transcription polymerase chain reaction (RT-PCR) testing from plasma, urine, and throat swab were negative, although these samples were obtained after the rash resolved.

DISCUSSION

The patient's case of *Rickettsia typhi* infection presented a unique diagnostic challenge due to its overlapping presentation with measles, an airborne viral illness that has become highly prevalent in recent years in both Texas and the United States [1]. In 2019 alone, 1249 cases of measles emerged in the United States, marking the highest annual incidence of measles in the country since 1992 [2]. Clinicians, keenly aware of the resurgence of measles, have become more vigilant. Diagnostic criteria for measles include fever (>101°F or >38.3°C) and the presence of conjunctivitis, cough, or coryza. Patients may develop a morbilliform, blanching, maculopapular rash. Koplik spots (1–3-mm papules on the buccal mucosa) can present before exanthem manifestation and are pathognomonic for the disease. The morbilliform rash typically appears 3–4 days after

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Correspondence: Cesar A. Arias, MD, PhD, 6431 Fannin St. MSB 2.112, Houston, TX 77030 (cesar.arias@uth.tmc.edu).

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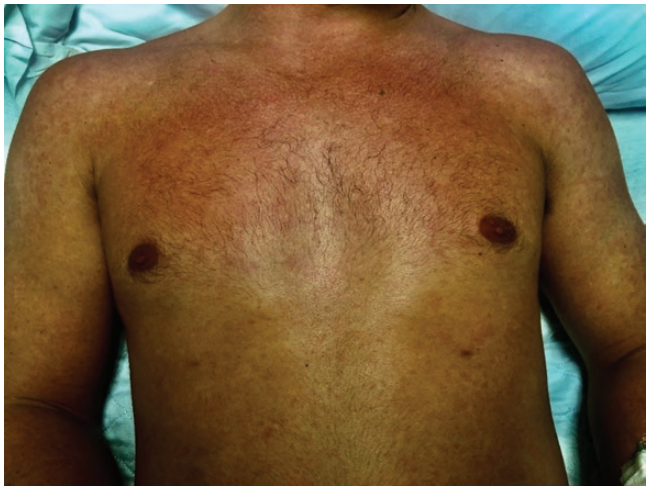

Figure 1. Blanching, maculopapular rash involving the chest, trunk, and bilateral upper extremities.

the onset of fevers, beginning on the face, and advances inferiorly, sparing the hands and feet [3]. These symptoms appear clinically similar to murine typhus, which has experienced a resurgence in Southeast Texas in recent years [4].

Murine typhus can be transmitted by cats, rats, or dog fleas [5–7]. In recent years, cases of murine typhus have clustered around the Harris County/Houston area, Tarrant County/Ft. Worth area, and Dallas County/Dallas area [4]. Symptoms of murine typhus manifest variably, but the classic triad includes fever, headache, and rash. Other symptoms include chills, malaise, myalgia, arthralgia, and vomiting. The rash of typhus, much like the rash of measles, is macular or maculopapular, coalescing on the trunk and sparing the hands and feet [8]. Based on these symptoms, there is overlap between measles and typhus. The geographic distribution of these diseases further complicated diagnosis in our case. While the patient's exposure to fleas and termites could point toward a murine typhus diagnosis, this factor alone does not sufficiently establish the diagnosis.

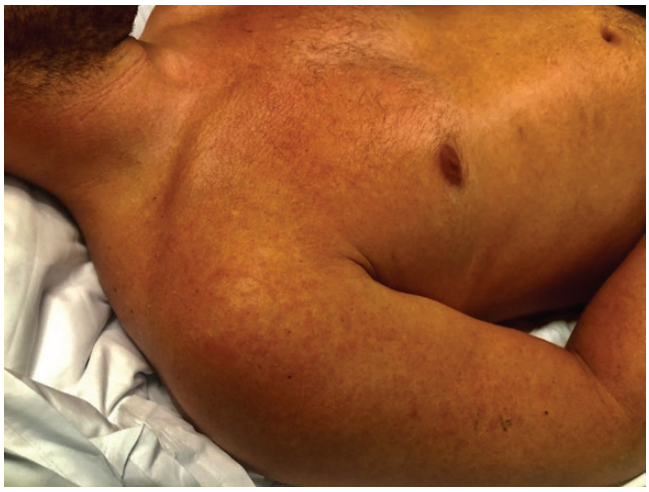

Figure 2. Maculopapular rash with petechial component on right upper extremity.

To differentiate between measles and typhus, clinicians often rely on laboratory testing. The most commonly utilized test for measles is the measles-specific immunoglobulin M (IgM) antibody. However, timing of testing is crucial (4 days after rash onset) to minimize false negatives [3]. Measles-specific IgG titers can be obtained, and a ≥4-fold increase 7–10 days after rash may suggest recent infection [9]. While serologic testing is generally helpful, false positives, as seen in our case, have been well documented. Indeed, false-positive antibodies have been previously reported in the setting of fever and rash and in infections like Parvovirus B19 virus or Epstein-Barr virus [10]. To circumvent this, clinicians can perform RT-PCR testing from serum, nasopharyngeal secretions, urine, and combined throat and nasal swabs. However, each must be obtained within 3 days, 4–7 days, 4–16 days, or 16 days after rash onset, respectively. Indeed, the timing is essential for maximizing the test's accuracy [11]. RT-PCR of serum samples can be performed optimally if obtained <3 days after exanthem manifestation. While we did perform RT-PCR testing, the patient had already improved clinically, and his rash had disappeared, decreasing the sensitive of the RT-PCR approach.

To test for *R. typhi*, clinicians can utilize serum IgG antibodies by indirect fluorescent antibody testing, and a ≥4-fold increase is diagnostic [9]. Leukopenia, thrombocytopenia, and elevated liver enzymes, although nonspecific, often occur in murine typhus, as seen in this case [8].

Doxycycline is the drug of choice for murine typhus, reducing fever duration by 1.5–4 days [12]. Without treatment, typhus can self-resolve within 12–21 days [12]. For pregnant women or patients who otherwise cannot tolerate tetracycline treatment, chloramphenicol can reduce the duration of fever to 2.5–4 days [12]. Quinolones are an option and demonstrate variable efficacy in the literature [1].

Distinguishing between murine typhus and measles remains clinically challenging to clinicians due to their similar presentations. Recent outbreaks of both diseases and challenges in serological interpretations have further complicated diagnosis, as demonstrated by this case. Taken together, this case emphasizes the importance of carefully assessing the patient's overall condition and utilizing laboratory tests to make appropriate therapeutic and infection control decisions in the setting of known outbreaks of infectious diseases.

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