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Case Report: Possible Vertical Transmission of *Bartonella bacilliformis* in Peru

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Abstract. A 22-day-old male was admitted with a 2-day history of irritability, dyspnea, jaundice, fever, and gastrointestinal bleeding. A thin blood smear was performed, which showed the presence of intraerythrocyte bacteria identified as *Bartonella bacilliformis*, and subsequently, the child was diagnosed with Carrion's disease. The diagnosis was confirmed by specific polymerase chain reaction. The child was born in a non-endemic *B. bacilliformis* area and had not traveled to such an area before hospitalization. However, the mother was from an endemic *B. bacilliformis* area, and posterior physical examination showed the presence of a wart compatible with *B. bacilliformis* in semi-immune subjects. These data support vertical transmission of *B. bacilliformis*.

Bartonella bacilliformis is an endemic pathogen from Andean areas at 600–3,000 m above sea level (masl), and its presentation has two phases. The first phase (acute phase) is the so-called Oroya Fever, in which the pathogen invades the red blood cells, causing severe anemia that may lead to death, especially in the absence of antibiotic treatment. Indeed, mortality rates had reportedly been as high as 90% in the pre-antibiotic era.[1,2] Oroya Fever mostly affects previously non-exposed people.[3] Thus, young children are especially affected by this illness.[3,4] In the second phase of the illness, which may occur weeks to months after the acute phase (but may be present in the absence of previously described acute phase symptoms), the bacteria cause an abnormal proliferation of endothelial cells, producing the so-called Peruvian wart.[3,5] Additionally, the presence of healthy carriers, which may act as a natural bacterial reservoir, has also been described.[6]

Natural transmission is mediated by a sandfly (different members of the *Lutzomyia* genera) bite, but vertical and post-transfusion transmissions have also been proposed as possible routes of infection.[7–10]

In this report, a neonatal case of Oroya Fever from a non-endemic coastal area of Peru is presented, and the possible routes of transmission are discussed.

A 22-day-old male child was attended at the Hospital Regional Eleanor Guzman Barron (HREGB; Nuevo Chimbote, Peru) after 2 days of evolution of irritability and breathing difficulty, jaundice, fever, and gastrointestinal bleeding as reported by the mother. The child presented a fever of 38.4°C, and biochemical analysis showed hyperbilirubinemia (total bilirubin: 45.8 mg/dL; conjugate bilirubin: 13 mg/dL), creatinine levels of 1.7 mg/dL, and an erythrocyte count of 12% with hemoglobin levels of 4 g/dL. Despite no reports of *B. bacilliformis* in the area of the child's origin, the thin blood smear showed the presence of coccoid (90%) and bacillar (10%) forms, leading to the diagnosis of Oroya Fever. During hospitalization, severe red blood cell hemolysis and digestive hemorrhage made a blood transfusion from the mother necessary because of the lack of a blood bank.

Seven days after hospital admission, the child presented worsening clinical evolution, including hepatosplenomegaly and renal insufficiency, leading to his transfer to the Intensive Care Unit of the Instituto Nacional de Salud del Niño (INSN; Lima, Peru), in which an additional pericardic effusion was observed on cardiac echography. After admission to the INSN, the initial diagnosis of Oroya Fever was confirmed by direct blood polymerase chain reaction (PCR) (Figure 1) as previously described and posterior bacterial culture in 5% blood agar plates incubated at 28°C in 5% CO_2.[11,12] The microorganisms were further identified as *B. bacilliformis* by amplification and sequence of the *16s ribosomal RNA* (*rRNA*) gene both directly from blood samples and from growing microorganisms.[12]

After 10 days in the Intensive Care Unit, the child was transferred to the Infectious Diseases Department, in which concomitant pneumonia was also diagnosed.

During the stay in the INSN, the child was treated with ciprofloxacin, ceftazidime, ampicillin, and vancomycin following the schedule and dosages presented in Table 1; however, during the previous stay in the HREGB, no data regarding the precise therapeutic schedule were recorded. The child received four additional packed red cells transfusions of 50 mL each, leading to a rise in hematocrit and hemoglobin levels from 25% and 8 g/dL (day 14 after first attendance) to 48% and 11 g/dL (day 43 after first hospitalization), respectively. After successful treatment, the neonate was discharged from the INSN 44 days after the first hospitalization.

In this case, several severe complications were observed, including pericarditis effusion and digestive hemorrhage as well as pneumonia. These complications have been previously described as relevant complications of severe Oroya Fever, especially in children.[13]

A questionnaire given to the mother revealed her origin as Huaraz, an endemic area of Carrion's disease. Interestingly, during the third trimester of pregnancy, the mother presented a febrile syndrome, which was documented as a urinary tract infection and treated with an unspecified antibiotic plus paracetamol. In the questionnaire, the mother reported the presence of a wart, which was visually compatible with endothelium proliferation of *B. bacilliformis*, but no additional analyses or molecular determinations were made. These data strongly suggest that, in this case, vertical transmission of Carrion's disease took place, especially considering the history of the mother, including a personal relationship with

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TABLE 1
Antibiotic schedule

AA	HREGB* (days 1†–6)	INSN – Intensive Care Unit (days 7–16)	INSN – Infectious Diseases Department (days 17–44)
CIP		35 mg/12 hours	
CAZ			170 mg/8 hours; 180 mg/8 hours
AMP		160 mg/6 hours	
VAN			40 mg/6 hours

AA = antibacterial agent; AMP = ampicillin; CIP = ciprofloxacin; CAZ = ceftazidime; VAN = vancomycin.
*No data about antibiotic treatment have been recovered from records of the HREGB.
†Length of hospital stay in days.

an endemic area, a gestational episode of fever, and the presence of a wart, in addition to the fact that the illness incubation time varies from 7 days to several months. Thus, possible external infection can probably be ruled out.[13]

Three other methods of transmission should also be considered: natural (sandfly bite), transfusion, or breastfeeding. Nonetheless, although infection transmitted by transfusion could be ruled out in this case, because transfusion was done after the diagnosis of the disease in the neonate, a sandfly bite or breastfeeding transmission could not be ruled out. However, we need to note that this transfusion with maternal blood resulted in an increase in the neonate bacterial burden, playing a role in the aggravation of the clinical presentation, which led to the child's transfer to the INSN. Regarding the transmission of *Bartonella* by breastfeeding, to the best of our knowledge, it has not been described to date, but in the absence of specific data, this possibility should be considered. With respect to a sandfly bite as the cause of the episode presented, this is unlikely, because Nuevo Chimbote is on the Peruvian coast, and the presence of these vectors has not been reported in this area (Lutzomyia vectors are located in areas higher than 600 masl). However, stable or unstable introduction of illness transmission vectors, which may result in the development of vector-borne diseases, has been largely described.[14] Thus, possible sporadic introduction of Carrion's disease vector in the area cannot be discarded. Furthermore, possible visits by relatives from Huaraz, who may act as involuntary vector carriers, should also be considered.

Infection by *B. bacilliformis* during pregnancy has often been related to serious maternal or fetal complications, including miscarriage, fetal death, or pre-term birth among others.[15] Mother-to-child transmission was first proposed by Tomas de Salazar in 1858,[9] and it was also reported by both Malpartida[7] and Colareta[8] in the mid-1930s. Nonetheless, a bibliographic search showed very little data on the vertical transmission of *B. bacilliformis*, being mainly limited to sporadic cases showing or suggesting this route of transmission. Tuya and others[16] reported the case of a 19-day-old child presenting Oroya Fever with 30% parasitemia, in which the mother also presented a positive thin blood smear. Tarazona and others[13] reported a pre-term child with a mother presenting verrucous lesions, in which blood samples from the child collected at 90 minutes after birth resulted in a positive *Bartonella* culture.[8] Regarding other *Bartonella* spp., to our knowledge, only perinatal transmission of *B. vinsonii* ssp. *berkhoffii* and *B. henselae* has been reported,[17] which strongly suggests vertical transmission. Additionally, it is of note that vertical transmission of members of the *Bartonella* genus has been observed in naturally infected rodents.[18]

This quasiabsence of data regarding the vertical transmission of *B. bacilliformis* might be because of the lack of reports in article format; also, it could be because the population at risk lives in remote rural areas, in which health facilities have many limitations, including the lack of diagnostic tools other than microscopy, which is strongly expertise-dependent. Social attitudes and practices may also result in delays or non-attendance to health centers during pregnancy or after childbirth. All of these factors may lead to an underestimation or misdiagnosis of mother-to-child *B. bacilliformis* transmissions.[19] However, early adequate antibiotic treatment of pregnant women with *Bartonella* infection is effective to avoid or limit both maternal illness complications and fetal/newborn

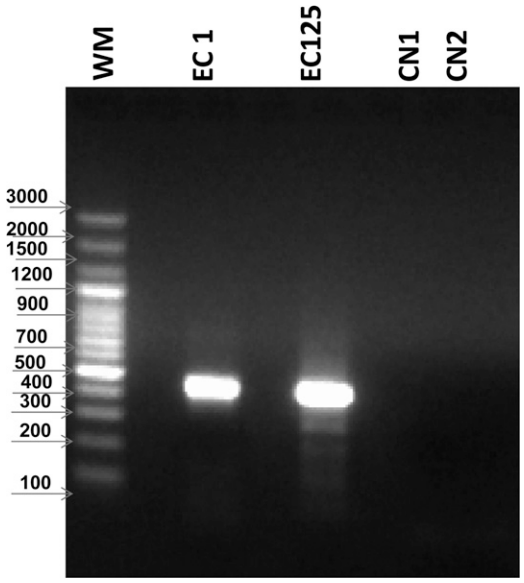

FIGURE 1. Direct blood PCR detection of *B. bacilliformis*. CN = negative control; EC1 = positive control; EC125 = amplification of DNA extraction from neonatal blood; WM = molecular weight marker.

involvement,[13] and it may, therefore, obviate or diminish vertical transmission.

In summary, these data suggest the vertical transmission of *B. bacilliformis*, reinforcing the need for early detection and treatment of infected pregnant women.

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