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Case Report

# Bartonellosis (Oroya Fever, Peruvian Wart): A Case Report

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**Abstract:**

Bartonellosis (also called Carrión's Disease, Oroya Fever or Peruvian Wart) is caused by the bite of mosquitoes of the Lutzomyia genus belonging to the Psychoid family. They are nocturnal blood-sucking insects, with complete metamorphosis. About 450 species are known, distributed throughout the American continent, mostly in tropical and subtropical areas. In Ecuador, sporadic cases have been reported, with certain characteristics such as, for example, not presenting the blood phase and, in the eruptive phase, not being aggressive. Here, we present a unique case of a 13-year-old boy with a history of congenital heart disease, who presented a clinical picture of one year of evolution suggestive of dermatosis, characterized by papules and nodules that occasionally bleed. The mother reports living in an area of lush vegetation and being in contact with bites. The results of blood count, peripheral blood smear, liver function and coagulation: normal. Blood sample: Negative Bartonella spp. PCR biopsy ribC gene: Positive B. bacilliformis. This case demonstrates the importance of maintaining an entomo-epidemiological surveillance system in patients exposed to arthropod bites that allows for timely detection of cases in order to make a diagnosis and provide timely treatment.

**Key words:** bartonella infections; medical records; vector borne diseases; Ecuador

## Introduction

Human Bartonellosis is a biphasic bacterial infection caused by Bartonella bacilliformis. In 1993, American and European scientists found other species of bartonellae affecting humans and later others affecting only animals [1].

At the time of the Republic (1870-1906) a serious epidemic occurred during the construction of the Lima - La Oroya railroad (the highest in the world) in which thousands of workers (Chileans, Chinese, Bolivians, etc.) participated, of which more than 7,000 died, the disease being known as "Oroya Fever"; in some survivors appeared reddish dermal eruptions, which were given the name of Peruvian wart. This epidemic motivated great research interest in the international medical community [2].

The Peruvian medical student, Daniel Alcides Carrión, in 1885, investigated and established the clinical unity between Oroya fever and the Peruvian wart, thus becoming the martyr of Peruvian medicine. For this purpose, he inoculated the product of a verruca from a patient at the Hospital Dos de Mayo, in order to experiment in his own body, the development of the disease known as Peruvian wart [2,3].

In 1909, Alberto Barton, a medical microbiologist, discovered the etiological agent of Carrión's disease in the parasitized red blood cells of the anemic phase of the disease and described them as "end globular bodies", which was later catalogued as a bacterium identified with the name Bartonella bacilliformis in recognition of its discoverer [4].

Townsend, in 1913, identified the vector Lutzomyia verruca rum (popularly known as "titira" or "manta Blanca") as the transmitter of the disease, whose habitat is limited to the valleys of the Andean Mountain range of Colombia, Ecuador and Peru [3,4].

Lutzomyia's are nocturnal hematophagous insects, with complete metamorphosis. About 450 species are known, distributed throughout the American continent, mainly in tropical and subtropical zones. The optimum temperature where they develop fluctuates between 19ºC - 23ºC; the average life span of the mosquito is 50 to 60 days [5].

Among the clinical manifestations, two phases are described: the acute, septicemic, febrile or anemic stage, known as Oroya fever, and the

chronic, eruptive or Peruvian wart stage. It has an incubation period of 21 days (up to 7 months) [6].

The acute phase constitutes the malignant period of the infection, with abrupt or insidious onset, with chills, fever and sweating, joint and bone pain, hyperoxia, followed by severe anemia due to hemolysis, jaundice, hepatomegaly, lymph adenomegaly [7]. This phase may be less intense and, in some places, especially in Ecuador, it manifests very discreetly or goes unnoticed. It lasts between 2 to 4 weeks and the great majority of those who receive treatment recover. After an average of two months in this phase (which may not occur, particularly in natives of the endemic region) the Peruvian wart appears. The disease may not affect the skin in up to 45% of cases [8,9].

The chronic phase, eruptive or Peruvian wart, mainly affects children and adolescents, without a typical clinical picture of the acute hematic phase. Three types of lesions have been described: Miliary or papillary, represented by reddish papules, measuring < 3 mm, usually on the extremities. Subcutaneous nodules, with erythematous or normal overlying skin, scarce, located on the extensor surface of the extremities. The macular lesions are sometimes solitary neoformations, measuring 5 mm to 1-2 cm, erythematous, friable, sometimes pedunculated [9].

At the base of any of these lesions there is an epidermal collarette. The most common type of rash is milia, although different types may appear in the same patient. Miliary lesions are usually painless, whereas, the macular lesions may be painful and two thirds of the cases may bleed. Pruritus is variable. Spontaneously regressing lesions may also be observed, especially in children. Lesions in oral, conjunctival and nasal mucosa have been described. About 50% of patients with Peruvian warts are bacteremia. Without treatment, this phase persists from one month to one year, but the risk of becoming an asymptomatic reservoir is high, so in no case should the corresponding treatment be discontinued [9,10].

For diagnosis, in the febrile phase, the most useful technique is to obtain a blood smear (Giemsa-Wright staining). This method requires expertise. Sensitivity of 36% and specificity between 91 to 96% have been described; in the eruptive phase, the sensitivity of the smear is less than 10% [11].

Skin biopsy of the lesion remains the best method to confirm clinical suspicion in Peruvian wart. Histological alterations correspond to a hemangioid granulomatous reaction (telangiectatic granuloma). Other tests used are: PCR in blood and tissue samples and indirect immunofluorescence for the detection of antibodies [12].

Treatment depends on the stage of the disease: in cases of acute uncomplicated Bartonellosis, amoxicillin with clavulanic acid is recommended as first line therapy in pregnant women, children and adolescents under 14 years of age < 45 kg, at a dose of 40 mg/kg/day p.o every 12 hours for 14 days, and ciprofloxacin for adults and older, heavier children, at a dose of 500 mg p.o every 12 hours for 14 days; as second line therapy, chloramphenicol, cotrimoxazole and amoxicillin [13]. Regarding complicated acute Bartonellosis, as first line therapy, IV ciprofloxacin and ceftriaxone and in pregnant women ceftriaxone with chloramphenicol and as second line, combinations of ciprofloxacin and ceftriaxone with ceftazidime and amikacin [14]. Likewise, in chronic eruptive Bartonellosis (Peruvian wart), the first line treatment in all cases is Azithromycin, in children and adolescents <45kg 10 mg/kg/day p.o x 7 days, in > 45 kg and adults 500 mg/day p.o x 7 days and in pregnant women, 1 g/day once a week x 3 weeks. As a second line of treatment: rifampicin, erythromycin and ciprofloxacin, the latter not indicated in pregnant women [13,14].

On the other hand, it is important to perform a clinical control of the lesions after 14 days to evaluate the therapeutic response, if this is good (decrease in number, size and color > 90%) the treatment is concluded, if it is regular (decrease in number, size and color between 50 and 90%) the therapy is extended with 1g of Azithromycin in a single dose. If there is no response (decrease in number, size and color < 50%, or no change or new lesions appear), discontinue treatment and rotate second-line antibiotic [15]. In this study, we seek to report on a documented clinical case that allows us to identify the presence of Bartonella bacilliformis in a community of Ecuador.

## 2. Case Presentation

A male patient, 13 years, 3 months old. Origin: rural area, San Pedro del Villao Enclosure. Pedro Carbo District. Guayas Province. Pathologic history: congenital heart disease, seen at the outpatient Dermatology clinic due to a clinical presentation suggestive of dermatosis, characterized by papules and nodules that sometimes bleed, of one year of evolution. On physical examination she presented with failure to thrive, afebrile, and several reddish papules and dry crusts, scattered in the right retro auricular region and limbs. In addition, an angiomatous tumor with desquamative collaret, located at the level of the third metacarpophalangeal joint; in the right gluteal fold, neoformation, friable, sessile, covered with blackish crust.

**Figure 1: (A).** Reddish tumor with desquamative collarette. **(B).** Neoformation with necrotic crust in gluteal fold and miliary lesion. **(C).** Erythematous papules on fingers. **(D).** Spontaneously regressing lesion.

**Presumptive diagnoses:** Peruvian wart vs. bacillary angiomatosis.

**Tests performed:** Normal blood biometry and peripheral blood smear. Normal liver and coagulation tests. Negative blood cultures. Blood sample: Negative Bartonella spp; PCR Gen rib C in skin sample (skin biopsy): Positive B. bacilliformis.

**Treatment started:** Azithromycin 500 mg p.o x 7 days. On day 14, she received 1g of the same drug as extended therapy, due to an 80% decrease in lesions, achieving remission of the lesions with hypertrophic scarring at the biopsy site [10].

**Figure 2: (A).** Post-treatment lesion regression. **(B).** Post-treatment lesion regression.

### 2.1. Entomo-Epidemiological Activities

At the same time, the Epidemiological Surveillance team of the Hospital del Niño "Dr. Francisco de Icaza Bustamante" coordinated field actions with the Zonal and District teams of Health Coordinating Offices 8 and 5, respectively.

The entomological investigation consisted of placing CDC traps and capturing the vector in strategic locations in the house and surrounding areas. For this, we had the help of vector control personnel from Pedro Carbo Enclosure, who refer that this activity requires more time to complete the study, which would allow us to perform hourly activity and vector density.

It should be noted that, during field activities, by taking samples from relatives and neighbors, they reported that the patient frequented the area surrounding the house, which is adjacent to the mountain, a place where entomological research could be carried out in greater depth.

**Figure 3: (A).** Access to the San Pedro de Villao site. **(B).** Patient's home. **(C).** Stream.

The work team evaluated the ecosystem of the place and its surroundings. Pedro Carbo, is an enclosure located on the coast of Ecuador, near the province of Manabi. It is located at Km 63 of the Guayaquil-Manabí highway. The study area is located between 1°49'10" S and longitude 80°19'41 "W. The temperature at which the traps were placed fluctuated between 22 - 24o C and the relative humidity from 70 to 75%. The altitude of the site is 585 mts.

A great variety of exuberant vegetation, and houses surrounded by fruit trees (mango, tangerine, oranges and cotton) was observed. It shows the presence of permanent and semi-permanent bodies of water, such as streams, as well as animal tracks.

To evaluate vector density, traps were placed in the home and in two houses adjacent to the patient's home. In the remaining houses, three traps were placed per house (intradomicile, extra domicile and peridomicile). The traps were placed at 18:00HRS, for two consecutive days and removed HRS of the following day. Subsequently, they were sent to the National Vector Reference Center (CRNV) located at the Public Health Research Institute (INSPI- Quito) for classification and taxonomic identification of the species collected.

**Figure 4: (A).** Intra-domicile trap. **(B).** Peridomicile trap. **(C).** Extradomicile trap.

**Figure 5: (A).** Review of traps. **(B).** Surrounding house. **(C).** Surrounding river.

Eleven specimens belonging to the genus Lutzomia, and four species (cayennensis, gomenzi, sallesi and dysponeta) were taxonomically identified: none associated as a potential vector of B. bacilliformes.

## 3. Discussion

B. bacilliformis is an opportunistic pathogen that is rarely isolated in clinical specimens and even more rarely in human blood [1]. It is the etiologic agent of Carrion's disease or Oroya fever (acute phase of infection) and Peruvian wart (chronic phase of infection) [1,3,4]. The acute phase of the disease is severe, characterized by a massive invasion of the bacteria into the erythrocytes and consequently causes acute hemolysis associated with fever [7]. If the infection is not treated, the mortality rate can reach up to 85% [10]. However, infection caused by this bacterium is rarely reported [8,9]. The chronic phase is characterized by benign pruritic and bleeding rash lesions and other symptoms such as malaise and osteoarticular pain [9]. At the time of admission to the local hospital, the patient was afebrile, with several reddish papules and dry crusts scattered in the right retro auricular region and extremities as obvious symptoms. In addition, an angiomatous tumor located at the level of the third metacarpophalangeal joint; in the right gluteal fold, neoformation, friable, sessile, covered with blackish crust.

B. bacilliformis can be isolated from blood cultures and secretions from lesions in people from endemic areas. B. bacilliformis infections are a health problem in many rural areas of South America (Andean Cordillera) and for travelers visiting these regions. Outbreaks of bartonellosis have been reported in the mountainous regions of Peru, Ecuador, and Colombia [3,4]. Since entomological surveillance of species of the Lutzomia genus is not carried out regularly as a surveillance system in the country, it is likely that for various reasons such as occupation, as well as man-vector contact due to the proximity of homes to the resting places of the vector, cases and colonization of the bacterium will continue to occur [5]. Human Bartonellosis or Carrion's disease continues to be a public health problem that, despite prevention and control efforts, persists in Ecuador, especially in rural and low-income areas similar to the patient's origin.

The patient's lesions decreased and returned to normal after treatment with Azithromycin. It is important to recognize the timeliness and timely diagnosis, which allowed for treatment efficacy and early recovery of the patient. [6]. It should be noted that the identification of the species using the PCR technique Gen ribC facilitated the correct administration of the treatment. Likewise, the patient under study was caught in the chronic (eruptive) phase of the disease, which is consistent with what the literature indicates, that this phase mainly affects children and adolescents [12]. Likewise, the evolution was favorable once the treatment was established and completed, taking into consideration the underlying pathology. At present, the patient continues with subsequent controls with the specialty.

From the above, it must be considered that B. bacilliformis multiplies rapidly in human reservoirs during the acute phase of the disease and remains for prolonged periods in convalescent persons [9,10]. The existence of wild reservoirs has not been demonstrated, being the sick and untreated man the only known reservoir. It should be noted that minors tend to have benign lesions, few in number and with a popular or miliary appearance, which can even involute spontaneously (becoming healthy carriers) [13].

In this regard, the current incidence of Bartonellosis shows seasonal and geographic variations, with an increase in cases during the rainy season. In addition, the lack of knowledge of the population and the difficulty in early diagnosis contribute to the spread of the disease. Addressing and reaching the correct diagnosis of Bartonellosis requires a comprehensive approach that includes the training of health professionals, access to laboratory tests, solid entomological and epidemiological surveillance, and continuous research to understand the reality of the country and consequent public education [14].

It is essential that governments and health institutions continue to invest in education, entomo-epidemiological surveillance and medical care programs to effectively address this disease that affects vulnerable communities.

## Conclusion

There is currently a great silence about Carrion's disease, probably due to the low prevalence of cases at the national level in recent years.

In view of the above, it is imperative to raise awareness among the inhabitants of the localities where Lutzomia cohabits with human beings of the importance of knowing about this disease, which has special characteristics, especially in the infant population.

## Ethical Approval

Ethical approval of the case report is not required as per local guidelines.

## Consent

The patient was informed to the full extent of the use of their information and provided affirmative written consent for the publication of this case report and accompanying images.

## Authors' Contributions

Glenda Velasquez, Boris Caballero, Gladys Colombia and Leyther Llanga, were involved in drafting of the manuscript. Adriana Sarango, was responsible for checking and reviewing the test data. Glenda Velasquez was responsible for the quality of the test data and the intercepted images. All authors approved the final draft for publication. Diana Berzina and Adriana Sarango, equally contributed to this work.

## Recommendations

- Strengthen Active Surveillance of suspected cases of Carrion disease at all levels of care of the Ministry of Public Health of Ecuador.
- Undertake an active search for cases in the territory, focusing mainly on areas with a history of disease transmission.

- Sensitize operational personnel to detect suspicious cases that meet the operational definition.
- Conduct more exhaustive Entomological Research in coordination with the National Institute of Public Health Research (INSPI).
- Establish communication with the Ministries of Health of Peru and Colombia, in order to hold discussions about Carrion's Disease, based on the historical experiences in localities of these neighboring countries.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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