

Acute Chagas disease

Diagnostic experience through an outbreak

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Abstract

Chagas disease is a public health problem in Latin America, with a tendency to globalize due to migration phenomena. The acute phase of the disease tends to be indolent, but a low percentage of patients have an ominous course, especially when the route of transmission is oral, presenting as a prolonged febrile syndrome in the form of an epidemic outbreak. Early detection of the disease will probably avoid morbid outcomes and, in some cases, death. In this case report we summarize a diagnostic approach by describing the index case in an epidemic outbreak. (*Acta Med Colomb* 2022; 48. DOI: <https://doi.org/10.36104/amc.2023.2727>).

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Introduction

Chagas disease (CD) is caused by *Trypanosoma cruzi* (Tc), a blood flagellate parasite transmitted by various species of hematophagous insects, mainly in endemic areas (1). Although the disease was first described by Carlos Chagas in 1909, Tc DNA has been found in Latin American mummies dating to more than 9,000 B.C. (2). In Latin America, it is one of the main causes of heart failure and is a public health problem tending toward urbanization and globalization, due to migration patterns (3).

The acute phase of the disease may occur as an outbreak, especially when an oral transmission source is presumed. These outbreaks have been reported sporadically in Colombia, with increasing frequency (4). This is a report of the index case in an outbreak in Puerto Triunfo, Antioquia, in 2019. We use a question and answer format to summarize the most relevant data in the clinical approach.

Clinical case

A 22-year-old woman lived in rural Magdalena Medio (Antioquia, Colombia) with her two children (two and six years old) and her husband. They engaged in agriculture and had a farm with horses and rabbits.

She had no other remarkable history. She consulted with a complaint of one month of fever, asthenia, myalgias, large joint migratory polyarthralgia and mechanical lumbago. Over the last two weeks, self-limiting erythematous morbilliform skin lesions had appeared. On hospital admission, the physical exam was only remarkable for erythematous-violaceous plaques on her thighs and legs, suggestive of panniculitis.

Is this a nonspecific febrile syndrome?

When faced with a febrile patient in Colombia, we must include clinical patterns framed within syndromes: jaundice, hemorrhagic, exanthematous, adenopathy, traveler's, outbreak or nonspecific. Likewise, the duration of the fever, defined as acute or prolonged depending on whether it lasts less than or more than seven days, respectively, can help guide the diagnosis. In this case, despite the presence of a rash, there were no specific data to orient toward the most representative causes (rickettsiosis, arbovirus infection, syphilis, measles, rubella, leptospirosis, salmonellosis and human immunodeficiency virus [HIV]) (5). For lesions suggestive of erythema nodosum, several agents should be considered, including *Mycobacterium tuberculosis*, *Histoplasma capsulatum*, *Brucella sp.*, and *Treponema pallidum*, along with some noninfectious conditions (lymphoma, inflammatory bowel disease, Behçet's disease, sarcoidosis and polyarteritis nodosa) (6).

Is it important to inquire about contact with animals?

This epidemiological factor in the context of a fever of unknown origin should lead to a suspicion of zoonosis (7). However, no sacroiliitis, osteomyelitis or endocarditis (*Coxiella burnetii*); ulcerated, ocular or regional lymph node lesions (*Francisella tularensis*); or inoculation papules or hepatocellular lesions (*Bartonella sp.*) were detected (7).

Complementary tests showed elevated acute phase reactants (C-reactive protein, 11 mg/dL, and erythrocyte sedimentation rate, 65 mm/h) and mild lymphopenia (990 cells per mm³). The microbiology tests were negative (Tables 1 and 2).

When the history was broadened, the patient mentioned similar symptoms in her two-year-old child, who was hospitalized at another institution with a diagnosis of prolonged febrile syndrome with hepatosplenomegaly and cytopenia (anemia and thrombocytopenia), with no clear cause despite multiple tests, and with the same timing of the onset of symptoms.

Is it essential to inquire about similar and simultaneous cases in the approach to a prolonged fever?

Repeating the history and physical in fever of unknown origin (FUO) is key (8). This information allowed us to deduce that we were probably facing an outbreak. The appearance of concomitant cases in the same geographical area or in patients with a common source of exposure can lead us to suspect mainly rickettsiosis, leptospirosis, salmonellosis or acute CD (4,5).

We decided to perform immunoglobulin G (IgG) serology for Tc, which was positive. An echocardiogram reported scant pericardial effusion, with no structural involvement. Hepatosplenomegaly or adenopathy syndrome with cytopenia are common in some systemic infections (9) like the mononucleosis syndrome (10) caused by HIV, Epstein-Barr virus, cytomegalovirus or *Toxoplasma gondii*, but has this been reported in acute CD? Hepatosplenomegaly (documented in the patient's son) and adenopathy and cytopenia (anemia and thrombocytopenia) have been reported in the acute phase of CD (11-13).

Although it is assumed that infections are the main cause of FUO (26-55%) (14), parasites are uncommon (0.59%) (15), and mostly leishmaniasis and malaria; in our patient, the epidemiological nexus was key.

So, how are panniculitis and pericardial effusion involved in acute CD?

The skin lesions described in this phase include inoculation edema (chagoma), conjunctivitis with eyelid edema (sometimes as Romaña's sign or bilateral bipalpebral edema with an unclear mechanism) (16) and a generalized maculopapular rash (schizotripanides). Panniculitis has been reported associated with reactivation during immunosuppression (17). Pericardial effusion is more common in the severe forms of acute CD (42%) and may be moderate or severe (18). In the mild forms, it is uncommon and scant.

Despite the negative serial thick smears, we contacted the biology and control of infectious diseases (BEIC) laboratory at Universidad de Antioquia, who performed a polymerase chain reaction (PCR) test for Tc, which was positive. The samples were sent on to the departmental public health laboratory in Antioquia, where an IgG test for Tc was also positive. The direct tests (fresh whole blood) were negative. Serology tests on the rest of the relatives were positive.

Table 1. Blood tests.

Variable	Reference range	Result
Hematocrit (%)	38-48	37
Hemoglobin (g/dL)	12-16	12.2
MCV (fl)	86-96	85
RDW (%)	11-15	14
MCHC (g/dL)	32-38	31
Leukocytes (per mm ³)	4,500-11,000	7,620
Neutrophils (per mm ³)	1,500-8,000	5,800
Lymphocytes (per mm ³)	1,500-4,000	990
Monocytes (per mm ³)	30-900	210
Eosinophils (per mm ³)	40-500	260
Basophils (per mm ³)	0-50	30
Erythrocytes (per mm ³)	4,200,000-5,400,000	4,300,000
Platelets (per mm ³)	150,000-450,000	380,000
ESR (mm/h)	0-20	65
CRP (mg/dL)	0-1	11
PT (sec)	11-14	11
PTT (sec)	22-35	32
Albumin (gr/dL)	3.4-4.8	4
ALT (U/l)	10-49	34
AST (U/l)	0-34	50
ALP (U/l)	45-116	74
TB (mg/dL)	0.3-1.2	0.45
DB (mg/dL)	0-0.2	0.15
LDH (U/l)	120-246	300
Calcium (mg/dL)	8.5-10	8.8
Potassium (mmol/L)	3.5-5.5	3.5
Sodium (mmol/L)	135-145	140
Glucose (mg/dL)	70-100	79
CPK (U/l)	0-145	28
Creatinine (mg/dL)	0.5-0.8	0.4
BUN (mg/dL)	9-23	10
BNP (pg/mL)	0.5-30	20

MCV: mean corpuscular volume; RDW: red cell distribution width; MCHC: mean corpuscular hemoglobin concentration ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PT: prothrombin time; PTT: partial thromboplastin time; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; TB: total bilirubin; DB: direct bilirubin; LDH: lactate dehydrogenase; CPK: creatine phosphokinase; BUN: blood urea nitrogen; BNP: B-type natriuretic peptide.

Table 2. Initial microbiology tests.

Variable	Result
HIV ELISA	Negative
VDRL	Negative
HBsAg	Negative
Anti-HBc	Negative
Anti-HVC	Negative
Blood cultures (6): prolonged incubation	Negative
<i>Rickettsia typhi/R. mooseri</i> IgM	Negative
<i>Brucella</i> (hemagglutination)	Negative
Thick drop(s)/ direct parasitic tests	Negative

HIV: human immunodeficiency virus; **VDRL:** non-treponemal test (Venereal Disease Research Laboratory); **HBsAg:** hepatitis B surface antigen; **Anti-HBc:** antibodies to hepatitis B core antigen; **Anti-HVC:** total antibodies to hepatitis C virus; **IgM:** immunoglobulin M.

Is acute CD ruled out in the absence of parasites on the direct tests?

Direct parasitology tests, while very specific, are operator dependent, and therefore their sensitivity varies. The definition of an acute case also includes serology and indirect tests (blood cultures and PCR) (3, 19). For the two hospitalized patients, the BEIC laboratory reported positive blood cultures, and triatomines were found in their home during the site visit.

The weekly epidemiological bulletin (Week 23, August 11-17, 2019) and the event report by the Instituto Nacional de Salud [National Health Institute] confirmed the outbreak in this region of Antioquia months later, coinciding with probable oral transmission. There was no clearly implicated food (19, 21).

The patient and her relatives began treatment with nifurtimox; during the first month of follow up, their symptoms improved, with no drug toxicity. It was concluded, then, that this was an acute outbreak of CD (two or more confirmed acute cases with an epidemiological nexus) (19), with no fatalities.

Discussion

Oral CD transmission has ceased to be a myth and has become an ever-closer reality, associated with contaminated food sources. This is probably secondary to environmental changes due to disruptions in the parasitic reservoir and vector niches. It is thought to be transmitted through foods contaminated with triatomine feces, like fruit pulp, water or vegetables, as well as poorly cooked or raw meat from infected animals, or armadillo blood (4, 22).

Outbreaks have been reported in different areas of Colombia, mainly in Santander and Norte de Santander. The first recorded outbreak was in 1992, in the town of Tibú (Norte de Santander), among a group of soldiers in a jungle area;

six Tc positive cases with acute myocarditis were confirmed. Since then, simultaneous cases have been recorded which suggest a common transmission source (4), presumably oral rather than vector. In 2019, in addition to the outbreak described, there were another five outbreaks (51 people) with different suspect foods (21).

The acute phase of CD has a shorter incubation period in the oral transmission form, due to the high burden of parasites, which may last up to a couple of months (22). It is often a mild disease or even asymptomatic, with no entry point signs (which are classic in vector transmission), and although the relationship with systemic symptoms is rare, prolonged fever is more likely (the most common symptom), with a higher fatality rate, possibly due to the higher burden of parasites and susceptibility caused by gastrointestinal mucosal permeability (23). Acute CD is ideally diagnosed by microscopy using a direct test (in fresh blood with an anticoagulant or in the affected tissues), followed by a Strout concentration method (22). The role of PCR, blood cultures and serology in some cases should not be overlooked (22). The acute phase may be followed by an asymptomatic period (indeterminate phase) and close to 30% develop a chronic phase several years later, with parasitic damage to target organs, especially the heart and gastrointestinal system (23), which may be prevented with antiparasitic treatment (3, 22).

Benznidazole and nifurtimox are the recommended drugs for the etiological treatment of CD in acute cases, reactivations, congenital infections, pregnancy, laboratory accidents and early chronic forms. They can be given to patients over the age of 18 who are in the indeterminate phase and for chronic CD with non-advanced heart disease (3). In addition, support should be provided for complications, comorbidities and post-transplantation or HIV states in which the risk of reactivation may be up to one third of the cases with latent infection (24).

Conclusions

In Colombia, and for travelers to endemic areas of other countries, the approach to a prolonged febrile syndrome should include CD, especially when it occurs as an outbreak, keeping in mind that oral transmission is the most likely mechanism. The importance of this lies in detecting cases which may be treated in the acute phase, despite their severity, with the presumable goal of preventing the unfortunate third of cases which develop chronic morbid and lethal forms.

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