Archivos de Cardiología de México

Permanyer

Check for updates

REVIEW ARTICLE

Leishmaniasis and Heart

Leishmaniasis y corazón

*Juan Mª Farina[1], Carlos E. García-Martínez[2], Clara Saldarriaga[3], Gonzalo E. Pérez[1], Marcia Barbosa de Melo[4], Fernando Wyss[5], Alvaro Sosa-Liprandi[6], Hector I. Ortiz-Lopez[7], Shyla Gupta[8], Ricardo López-Santi[9], Ivan Mendoza[10], and Adrian Baranchuk[8]**

[1]Division of Cardiology, Clínica Olivos, Buenos Aires, Argentina; [2]Division of Cardiology, Centro Cardiovascular Avanzado, Guatemala City, Guatemala; [3]Department of Cardiology and Heart Failure Clinic, Cardiovascular Clinic Santa Maria, Universidad de Antioquia, Medellín, Colombia; [4]Division of Cardiology, Hospital Socor, Belo Horizonte, Brazil; [5]Technology and Cardiovascular Service of Guatemala - Cardiosolutions, Guatemala City, Guatemala; [6]Division of Cardiology, Sanatorio Guemes, Buenos Aires, Argentina; [7]Division of Cardiology, Hospital Roosevelt, Guatemala City, Guatemala; [8]Division of Cardiology, Kingston Health Science Center, Queen's University, Kingston, Ontario, Canada; [9]Division of Cardiology, Hospital Italiano de La Plata, Buenos Aires, Argentina; [10]Department of Cardiology, Tropical Medicine Institute, Universidad Central de Venezuela, Caracas, Venezuela

Abstract

As one of the neglected tropical diseases, leishmaniasis is defined as a parasitic communicable disease that is most prevalent in tropical and subtropical regions, affecting especially populations living in poverty. It has a profound negative impact on developing economies. It represents a group of heterogeneous syndromes with a wide spectrum of severity ranging from self-resolving cutaneous injuries to disseminated visceral compromise. Visceral leishmaniasis represents its most severe form, can affect almost all organs, and can have fatal consequences, especially in immunosuppressed patients. Cardiac involvement seems to be rare but has not been deeply studied. Consequently, there are no clear recommendations for the screening of cardiac manifestations in these patients. However, cardiovascular complications could be potentially lethal. In addition, there are valuable reports on the potential cardiotoxicity caused by drugs used in the treatment of this condition, so knowledge of its side effects could have important implications. This article is a part of the "Neglected Tropical Diseases and other Infectious Diseases affecting the Heart" project (the NET-Heart Project); its purpose is to review all the information available regarding cardiac implications of this disease and its treatment and to add knowledge to this field of study, focusing on the barriers for diagnosis and treatment, and how to adopt strategies to overcome them.

Keywords: *Leishmaniasis. Cardiac disease. Neglected diseases.*

Resumen

Como una de las enfermedades tropicales desatendidas (ETD), la leishmaniasis se define como una enfermedad parasitaria transmisible y muy prevalente en regiones tropicales-subtropicales afectando especialmente a poblaciones que viven en la pobreza. Tiene un profundo impacto negativo en las economías en vías de desarrollo. Representa un grupo heterogéneo de síndromes clínicos con un amplio espectro de severidad que va desde lesiones cutáneas que resuelven espontáneamente hasta compromiso visceral diseminado. La leishmaniasis visceral representa su forma más grave, puede afectar a casi todos

Correspondence:
*Adrian Baranchuk
E-mail: Adrian.Baranchuk@kingstonhsc.ca

Date of reception: 08-11-2020
Date of acceptance: 03-04-2021
DOI: 10.24875/ACM.20000508

Available online: 06-07-2021
Arch Cardiol Mex. 2022;92(1):85-93
www.archivoscardiologia.com

los órganos del ser humano y suele tener consecuencias fatales, especialmente en pacientes inmunosuprimidos. La afectación cardíaca parece ser rara, pero nunca se ha estudiado en profundidad. En consecuencia, no existen recomendaciones claras para el cribado de las manifestaciones cardíacas en estos pacientes; sin embargo, las complicaciones cardiovasculares pueden ser potencialmente letales. Además, existen publicaciones sobre la potencial cardiotoxicidad provocada por los fármacos utilizados en el tratamiento de esta afección, por lo que el conocimiento de sus efectos secundarios podría tener importantes implicancias. Como parte del proyecto "Neglected Tropical Diseases and other Infectious Diseases affecting the Heart" (Proyecto NET-Heart), el propósito de este artículo es revisar toda la información disponible sobre el compromiso cardiovascular de esta enfermedad y su tratamiento y agregar conocimientos a este campo de estudio, centrándose en las barreras para el diagnóstico y tratamiento y cómo adoptar estrategias para superarlas.

Palabras clave: *Leishmaniasis. Enfermedad cardiovascular. Enfermedades tropicales desatendidas.*

Introduction

Leishmaniasis is considered a neglected tropical disease (NTD); it is a communicable disease that prevails in tropical and subtropical conditions, costs developing economies significant amounts of money every year, and affects mainly populations living in poverty.[1] The "Neglected Tropical Diseases and other Infectious Diseases affecting the Heart Project" (NET-Heart Project) is an initiative of the "Emerging Leaders" section of the Interamerican Society of Cardiology. Its purpose is to expand knowledge on cardiovascular (CV) involvement of these serious diseases and to help identifying barriers for diagnosis and treatment.[2-4]

Leishmaniasis includes a heterogeneous group of clinical syndromes caused by different parasites of the genus *Leishmania*.[5] Most transmissions occur by phlebotomine sandfly bite and the usual reservoir hosts include humans and domestic or wild animals.[5] Alternative non-vector transmission has also been reported.[6]

Leishmania is an obligate intracellular parasite and the control of this infection involves an effective Th1-dependent cellular immune response.[6] In consequence, the opportunistic character is frequent, particularly in immunosuppressed patients infected with HIV.[6]

Different species of *Leishmania* can cause heterogeneous clinical manifestations with a wide spectrum of severity. Mild forms include usually self-resolving cutaneous lesions but in more advanced forms of the disease, life-threatening visceral involvement may occur.[5] The outcome is determined by the interplay between parasite burden and host factors, specifically their immune response.[6]

The main clinical forms of this parasitic disease are visceral leishmaniasis (VL), cutaneous leishmaniasis (CL), and mucocutaneous leishmaniasis (MCL).[5] VL is the most severe form, it can affect almost all organs, and it is usually fatal unless properly treated. CL is usually limited to ulcers in the skin, but can also lead to more serious physical consequences, such as scarring and disfigurement.[7] Up to 10% of CL cases can progress to more severe manifestations that include involvement of nasal or oral mucosa, and in these cases, the disease is known as MCL.[7]

Although in VL parasites can affect all organs, cardiac involvement is not common and unlike other parasitic diseases, there is limited information regarding CV manifestations. Publications related to direct cardiac involvement are mostly limited to case series/reports of myocardial and/or pericardial complications.[8] However, suspecting cardiac involvement can be challenging, and early detection is paramount to avoid serious complications. In addition, cardiac adverse effects related to drugs used for the treatment of this disease are common and serious.[8] The aim of this systematic review is to provide an overview of cardiac involvement in leishmaniasis and an algorithm for the diagnosis and management of this infrequent but potentially lethal complication.

Methods

A systematic review of the literature was conducted in MEDLINE/PubMed and EMBASE.

The selection of articles of interest was made according to the following criteria: (1) publications issued from 1990 to October 31, 2020; (2) case series, case reports, clinical trials, systematic reviews, and pronouncements of professional associations and scientific societies; (3) human studies and animal models (when deemed to be relevant to the topic); and (4) articles referring to CV involvement in leishmaniasis. Studies were excluded if the full text was not accessible.

The keywords used were chosen according to the MESH terminology: "leishmaniasis," "visceral leishmaniasis," "heart failure," "cardiovascular abnormalities," "cardiovascular disease," "arrhythmia," "myocardial disease," "pericarditis," and "pericardial effusion."

The literature search was conducted independently by two blinded authors (JMF and CEGM). First,

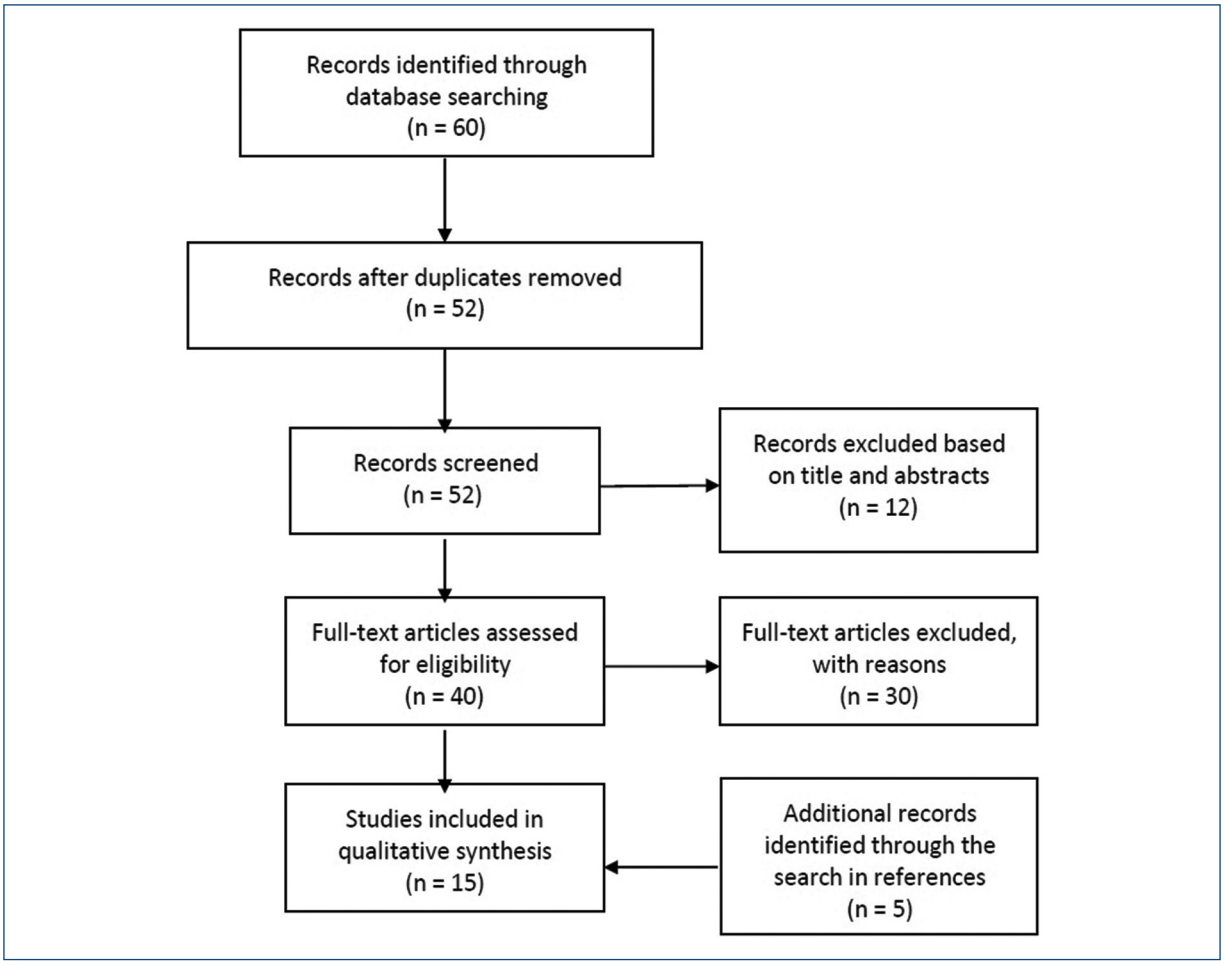

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram for the evidence review selection of the literature.

relevance based on title and abstract was determined. Then, selected publications were further reviewed for relevance using the full text. Kappa interobserver was determined, and disagreement was solved by consensus. A secondary search was conducted by reviewing the reference lists of the included articles. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement in conducting and reporting this systematic review.[9] Two investigators (JMF and CEGM) independently assessed the risk of bias of included studies, according to the National Institutes of Health (NIH) quality assessment tools.[10]

Results

From a total of 60 references obtained in the first search, 15 documents have been considered for this review: eight case reports, one case series, one retrospective study, one cohort study, two reviews, and two animal studies. Kappa interobserver was 0.83. Among these articles, 10 were found directly through the literature search in databases and 5 through the review of references list (Fig. 1). The main characteristics and quality assessment of included studies can be found in Table 1.

Epidemiology

Leishmaniasis is widely distributed around the world and it is considered endemic in the tropical and subtropical regions of more than 90 countries.[1]

Regarding VL, according to the latest estimates of the World Health Organization, the annual incidence is between 0.2 and 0.4 million new cases every year, and more than 90% of new cases occur in seven countries (Ethiopia, Kenya, Somalia, South Sudan, Sudan, India, and Brazil) (Fig. 2).[1] Its epidemiology suffered important

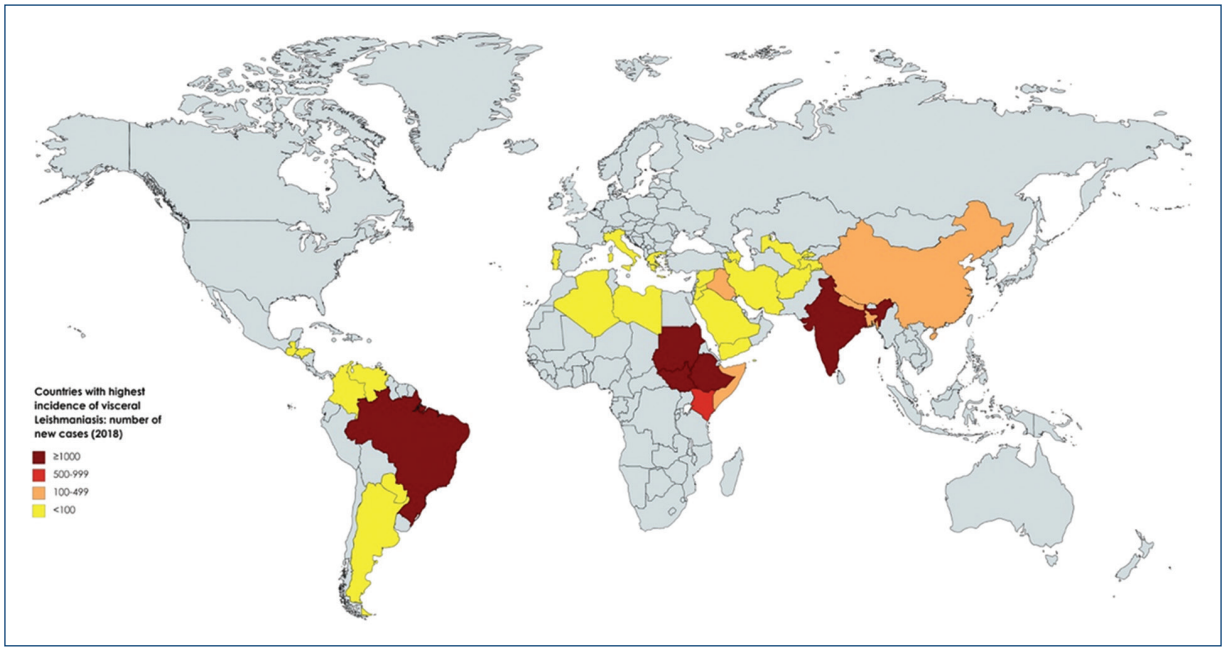

Figure 2. Status of endemicity of visceral leishmaniasis worldwide. Modified from: World Heart Organization, 2020.[1]

changes since the appearance of HIV; in the past, VL was seen more frequently in children, but currently most cases refer to young adults with immunosuppression due to HIV.[6]

Some risk factors related to this infection are worth to mention: (1) living in poverty condition, (2) inadequate sanitation, (3) close contact with vectors and wild/domestic animals, and (4) proximity to forested areas.[7]

Physiopathology and cardiac involvement

Cardiac manifestations in *Leishmania* infection are uncommon and there is not definitive information related to its specific pathophysiology in humans.[8] In general, parasites are transmitted to humans or other mammals by the bite of a sandfly of the genus Phlebotomus in the Old World (Eastern Hemisphere) and Lutzomyia in the New World (Western Hemisphere).[5] Humans are generally considered incidental hosts because the infection is more common in wild or domestic animals (i.e., dogs).[7] Alternative modes of transmission including congenital and person-to-person transmission (through sexual contact, blood transfusion, and organ transplant) have also been described.[5]

After inoculation, the promastigotes initiate the infection through receptor-mediated binding to macrophages.[6] Then, promastigotes transform into and replicate as amastigotes. At this point, the immune system plays a crucial role because the severity of the disease depends on the humoral and cell-mediated immune response of the host and to a lesser extent on the parasite burden.[5] In patients with asymptomatic and mild forms of the infection, Th1 cells predominate, but in cases of VL or other severe forms of the disease, patients usually show a poor response against *Leishmania* organism and have a prominent Th2 cytokine profile.[8,11]

The specific physiopathology of cardiac involvement has not been described in humans.[8] A pathophysiological model has been reported in dogs, describing the presence of an intense inflammatory reaction with large areas of the myocardium being infiltrated with mononuclear immune cells.[12] In this model, this inflammatory reaction leads to muscle atrophy, degeneration, and loss of cardiomyocytes.[12]

The knowledge related to clinical CV manifestations in humans is also considered to be scarce since it comes mostly from case reports or series.[8] Cardiac compromise is estimated to be infrequent, but the real incidence may be underestimated due to underreporting or under diagnosis. Regarding direct myocardial effects of this parasite, this infection is recognized by current guidelines as a cause of myocarditis and inflammatory cardiomyopathy.[13] Severe reversible eosinophilic myocarditis related to MCL and its treatment with

Table 1. Summary of studies mentioning cardiac complications of Leishmaniasis and side effects of its treatment

Study (year)	Type of study	Number of patients	Quality Assessment	Main findings
Dionisio, et al. (2011)*[15]	Retrospective study	51	Good	Retrospective study in VL pediatric population (mean age 27 months; range 7 months – 12 years). A case of sudden myocarditis manifested as acute heart failure was described
Shrivastava, et al. (2007)*[16]	Cohort	14	Good	Echocardiographic evaluation of patients with VL. Pericardial effusion was seen in 4 patients and no changes in systolic function were observed
Armin, et al. (2008)*[17]	Case report	1	Fair	Pericardial effusion in a pediatric patient with VL (3-years-old patient)
Yazdi, et al. (2003)*[18]	Case report	1	Fair	Pericardial effusion in a pediatric patient with VL (3-years-old patient)
Mofredj, et al. (2002)*[19]	Case report	1	Fair	Severe pericardial effusion in a co-infected patient with VL and HIV
Puerto-Alonso, et al. (2006)*[20]	Case report	1	Good	VL with sudden cardiomyopathy and heart failure in a young immuno-competent patient
Frapier, et al. (2001)*[21]	Case report	1	Fair	A case of fatal VL in a heart transplant recipient
Soares, et al. (2015)†	Case report	1	Good	Reversible cardiomyopathy in a patient with VL treated with AmB
Rodriguez-Gonzalez, et al. (2017)†[14]	Case report	1	Good	Severe reversible eosinophilic myocarditis related to MCL and its treatment with meglumine antimoniate
Oliveira, et al. (2011)†[26]	Systematic review (65 articles)	4359	Good	ECG changes (QTc prolongation and ventricular repolarization disturbances) were associated with SbV treatment
Lawn, et al. (2006)†[25]	Retrospective study	65	Good	QTc prolongation was associated with sodium stibogluconate treatment
Maheshwari, et al. (2011)†[28]	Case series	3	Good	Sudden cardiotoxicity in cases of coadministration of SAG and AmB
Nunes, et al. (2017)*†[8]	Review	N/A	Good	Direct cardiac involvement is limited to rare case reports of myocarditis and/or pericarditis. Cardiotoxicity due to treatment with pentavalent antimony (dose-dependent ECG changes, arrhythmias including torsades de pointes and sudden death) or amphotericin B was described
Martínez-Hernández, et al. (2017)[12]	Prospective animal study	48	N/A	Dogs with very severe leishmaniasis exhibit more myocardial injury (higher troponin levels) than dogs with milder forms of the disease or dogs with idiopathic kidney disease
Silvestrini, et al. (2012)[23]	Retrospective animal study	40	N/A	In dogs with leishmaniasis troponin concentration was higher than in controls

*Studies related to direct cardiac complications of leishmaniasis infection.
†Studies related to cardiotoxicity of drugs used for leishmaniasis treatment.
VL: visceral leishmaniasis MCL: mucocutaneous leishmaniasis SbV: Pentavalent antimonials SAG: Sodium antimony gluconate AmB: Amphotericin B N/A: not applicable.

meglumine antimoniate has been also reported.[14] In a retrospective study including pediatric population (mean age 27 months; range 7 months to 12 years) sudden myocarditis manifested as acute heart failure has also been described.[15]

Many case reports have demonstrated the presence of pericarditis and pericardial effusion in patients with VL. In a small cohort, researchers evaluated left ventricular systolic function and presence of pericardial effusion using echocardiography before, during, and at the end of therapy in 14 patients with VL.[16] Pericardial effusion was detected in one patient before treatment, in two more patients during therapy and in one more patient at the end of it. The left ventricular systolic

function remained within normal limits. The four patients with pericardial effusion had a high parasitic burden. Authors postulated that pericardial involvement could represent an exacerbation of the inflammatory reaction, especially in patients with high burden parasitemia. This study showed no clinical or echocardiographic evidence of myocardial damage, but biochemical markers for myocardial injury (such as troponins) were not evaluated. The presence of pericardial effusion as a complication of VL has also been reported in the pediatric population in two case reports (a 3-year-old male patient and a 3-year-old female patient).[17,18]

Coinfection between HIV and *Leishmania* should raise awareness. HIV and leishmaniasis can interact in a vicious cycle of mutual aggravation so that cardiac effects of both conditions could be potentiated.[6] HIV can also generate myocarditis, pericarditis, and pericardial effusion and there are reports of cases of severe pericardial effusion that required urgent pericardiocentesis in coinfected patients.[19] However, immunocompetent young individuals can also be at risk of severe CV manifestations.[20]

VL can lead to severe forms with fatal outcomes in heart transplanted recipients with few cases reported in the literature.[21] The presence of typical symptoms of leishmaniasis in heart recipients who live or have traveled to endemic areas should prompt immediate search for this condition.

Symptoms

CL usually is not a severe disease but can have important cosmetic manifestations that lead in some cases to social stigmatization and complicated psychological consequences.[7] The characteristic skin lesion is often a papule at the sandfly biting site that can rapidly grow and become a nodule with central ulceration.[5] In the cases of concomitant MCL, destructive lesions of the nasal septum, lips, and palate can occur.[7]

For VL, classical clinical manifestations include fever, weight loss, hepatosplenomegaly, and adenopathies.[7] Classic gastrointestinal symptoms include diarrhea, abdominal pain, vomiting, and dysphagia. Without any treatment, the disease is usually fatal within 2-3 years.[7]

Regarding CV involvement, symptoms are variable. In cases of cardiomyopathy linked to VL, symptoms can range from asymptomatic to rapidly impaired ventricular systolic function with decompensated heart failure and cardiogenic shock.[20] If cardiac involvement is limited to the pericardium, symptoms consistent with pericarditis may be present. In cases of pericardial effusion, it usually evolves without symptoms,[16] but in more severe cases, cardiac tamponade may occur, especially in more advanced stages of the disease.[19]

Diagnostic tests

Definitive diagnosis of leishmaniasis can be difficult to achieve because of several reasons: (1) there are different forms of the disease, (2) a variety of parasite species can be involved, (3) there is geographic heterogeneity, and (4) other syndromes with similar symptoms can mask the real diagnoses.[5]

Definitive diagnosis for VL is through direct microscopic observation of the amastigote in tissue specimens (bone marrow aspiration is the preferred, but liver, spleen, and lymph nodes can be considered) or by molecular tests that can detect DNA of *Leishmania* by polymerase chain reaction in blood or biopsy material.[7] Serological diagnosis is based on the presence of specific humoral response and can provide supportive evidence. However, the availability of biological methods may vary by geographic regions and the performance of the tests may be affected by parasite species involved in the infection and by host factors such as HIV-coinfection.[22] Sensitivity and specificity of proposed serological techniques are described in Table 2.[22]

At present, there is no single gold standard test for CL, but the observation of amastigotes in a clinical specimen confirms the diagnosis.[5]

Considering the low prevalence of CV involvement, there is no precise indication for using diagnostic tests as screening for cardiac complications. However, there are some situations that deserve to be mentioned. In the event of symptoms compatible with heart failure and/or pericarditis with or without pericardial effusion, an echocardiogram to assess both myocardial function and the presence of pericardial effusion should be indicated.[16] Clinical suspicion and the indication of complementary CV tests may be performed earlier in patients with HIV coinfection or with suspected high parasitemia.[16,19] An algorithm to guide the suspicion of CV involvement in VL is shown in figure 3.

Few reports on elevation of cardiac biomarkers as evidence of myocardial damage in domestic animals with asymptomatic forms of leishmaniasis have been published.[23] The role of biomarkers as part of the screening for myocardial injury in humans with VL should be investigated in the future. Given the presence of VL in poorly developed areas, costly imaging (i.e., cardiac magnetic resonance imaging) and its value in

Table 2. Performance of proposed serological tests for visceral leishmaniasis diagnosis

Test	Sensitivity (range)	Specificity (range)
Enzyme-Linked Immunosorbent Assay (ELISA)	77.5-93.8%	77.2-96.2%
Immunofluorescence Antibody Test (IFAT)	78.8-100%	82.3-96.2%
Direct Agglutination Test (DATs)	70.5-99.0%	89.2-100%
Immunochromatic Tests (Antigen-based ICTs)	42.0-80.0%	88.0-100%
Western Blot (WB)	80.0-100%	98.0-100%

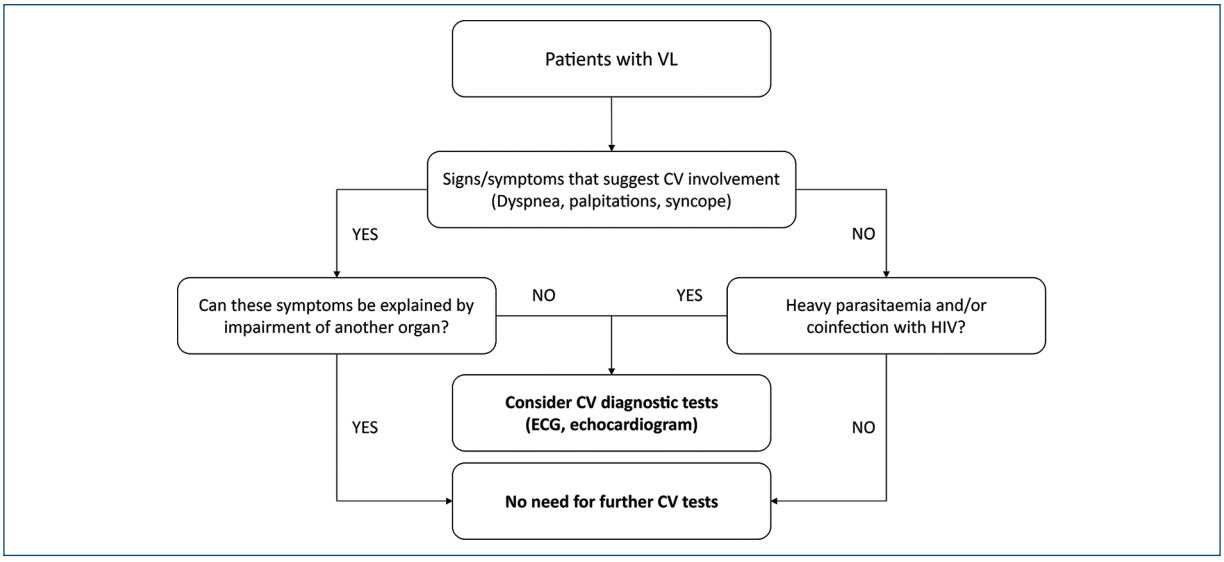

Figure 3. Algorithm to guide diagnosis and management of cardiac involvement in visceral leishmaniasis. VL: visceral leishmaniasis; CV: cardiovascular.

the diagnosis, has not yet been explored. Future directions on the use of more sophisticated imaging may help in the early diagnosis of CV involvement.

Treatment

The main objective of treatment for leishmaniasis is to eliminate the parasite, since related cardiac dysfunction often resolves spontaneously with adequate hemodynamic support, if needed.[8] There is no specific treatment for direct CV complications of leishmaniasis other than regular measures for cases of myocarditis or complicated pericarditis. In the case of myocarditis with impaired left ventricular function, treatment should be directed toward the hemodynamic support until full recovery.[20] If there is significant pericardial effusion, drainage and treatment with anti-inflammatories should be indicated.[19] Monitoring for the potential adverse effects of these drugs, especially if there is already an advanced visceral compromise established by VL, is suggested.

The main options for the medical treatment of leishmaniasis are pentavalent antimonials (SbV) and amphotericin B (AmB).[5] The treatment can vary considerably depending on the geographic area and the specific species of parasite to be targeted. Some drugs used for the treatment of arrhythmias in other clinical scenarios, such as amiodarone, have been tested for the treatment of CL in mice, demonstrating a reduction in the parasitic burden and a reduction of the ulcer surface area.[24]

Most used medications for this disease can present adverse effects impacting the CV system. Regarding SbV cardiotoxicity, the main manifestation is represented by dose-dependent ECG changes.[25,26] In a retrospective study evaluating adverse effects of sodium stibogluconate,

almost half of the patients developed some ECG alteration including T-wave inversion and QTc prolongation.[25] Almost 50% of patients presented some degree of progressive QTc prolongation, while 10% developed a potentially serious prolongation with risk of ventricular arrhythmias.[25] In a systematic review, cardiac complications were reported in 17% of patients treated with meglumine antimoniate and in 9% of those who received sodium stibogluconate.[26] Most frequent ECG alterations in this study were T-wave inversion and prolonged QTc interval.[26] More severe arrhythmias, such as premature ventricular contraction and *torsades de pointes,* occur more often with doses higher than 20 mg/kg/day. These abnormalities usually disappear after discontinuation of the drug. Sudden death has also been reported, but particularly with high doses of SbV (30-60 mg/Kg/day).[26]

Treatment with AmB can also generate ECG changes, mainly in the context of hypokalemia. Direct toxic cardiac damage is a rare adverse event, but reversible dilated cardiomyopathy associated with AmB treatment has been reported, especially in patients with a certain predisposing factor for heart failure.[27]

Cumulative cardiotoxicity of SbV such as sodium antimony gluconate (SAG) and AmB has been reported, causing potential severe complications including sudden death.[28] The mechanism of this cardiotoxicity is not well-defined. It has been postulated that SAG possibly increases the susceptibility of the myocardium to damage by AmB.[28] Therefore, it would be advisable to take a rest period of at least 14 days (or longer if ECG abnormalities persist) before starting AmB treatment in patients who have previously received SAG.[28]

If specific medical treatment for leishmaniasis is to be started with antimonials or AmB, a baseline ECG, serum creatinine, electrolytes, and echocardiogram could be of vital importance for the detection of possible pre-existing abnormalities. Then, twice weekly ECG monitoring could be a helpful strategy to identify potential QTc prolongation.[25] If cotreatment with at least two drugs is planned, extended cardiac monitoring could be advisable. The presence of cardiotoxicity (cardiomyopathy and/or ECG abnormalities) may lead to discontinuation of the therapy (but maintaining hemodynamic support) since the interruption of treatment has demonstrated the reversibility of drug-related adverse effects.[26]

Discussion

Unlike other NTDs, knowledge about CV involvement of leishmaniasis is limited. The available information can be divided into two groups: case reports/small studies related to direct effects of the parasitic disease on the heart (both due to direct aggression or autoimmune reaction) and cardiotoxicity mediated by the drugs routinely used for the medical treatment of this condition (Table 1).

The potential pathophysiology of CV involvement requires further exploration, and it seems to be related to an intense inflammatory reaction.[12] Acute (or fulminant) myocarditis and severe pericardial involvement have been occasionally reported.[19,20] Even when the reported incidence of CV implications of leishmaniasis seems to be low, the real global prevalence is unknown, probably due to under reporting or under diagnosis barriers. Health-care providers working in endemic regions should be aware of these potential lethal complications and aim for early recognition.

It is also important to highlight that CV complications could be more frequent and more severe in some special situations such as high parasitemia and immunosuppression (mainly coinfection with HIV and cardiac transplant recipients).[16,19] In these situations and also when CV symptoms are suspected, despite the fact that currently there is no precise indication for performing screening diagnostic tests for CV involvement, this group considers that ECG and echocardiogram should be considered as part of the initial monitoring strategy as proposed in the algorithm of figure 3.

Animal studies in which high levels of cardiac biomarkers have been detected suggest a possible silent cardiac injury.[23] The use of troponins or other molecules for the early detection of cardiac injury in humans should be an area of further studies.

It is of utmost importance to monitor for potential CV side effects when treatment for leishmaniasis includes either SbV or AmB. In both cases, routine ECG follow-up and early echocardiography are mandatory when CV involvement is suspected. On detection of these adverse events, interruption of antiparasitic treatment has demonstrated full reversibility.[26]

Conclusions

Leishmaniasis continues to be a serious health problem in endemic regions. Cardiac involvement seems to be rare, however, it could be potentially lethal. Early detection of cardiac involvement could be crucial to improve prognosis. Affordable strategies (ECG/echocardiogram) should be considered to facilitate early diagnosis and for guiding effective treatment.

Funding

This research has not received any specific grant from agencies in the public, commercial, or non-profit sectors.

Conflicts of interest

The authors declare that does not exist conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

References

1. World Heart Organization. Neglected Tropical Diseases. Geneva: World Heart Organization; c2020. Available from: https://www.who.int/neglected_diseases/diseases/en. [Last accessed on 2020 May 28].
2. Burgos LM, Farina J, Liendro MC, Saldarriaga C, Liprandi AS, Wyss F, et al. Neglected tropical diseases and other infectious diseases affecting the heart. The NET-heart project: rationale and design. Global Heart. 2020;15:60.
3. Ortiz HI, Farina JM, Saldarriaga C, Mendoza I, Liprandi AS, Wyss F, et al. Human African trypanosomiasis and heart. Expert Rev Cardiovasc Ther. 2020;18:859-65.
4. Zhou Z, Lopez HI, Pérez GE, Burgos LM, Farina JM, Saldarriaga C, et al. Toxoplasmosis and the heart. Curr Probl Cardiol. 2021; 46:100741.
5. Burza S, Croft SL, Boelaert M. Leishmaniasis. Lancet 2018; 392(10151): 951-70.
6. Ferreira MS, Borges AS. Some aspects of protozoan infections in immunocompromised patients: a review. Mem Inst Oswaldo Cruz. 2002; 97:443-57.
7. Abdoli A, Maspi N, Ghaffarifar F, Nasiri V. Viscerotropic leishmaniasis: a systematic review of the case reports to highlight spectrum of the infection in endemic countries. Parasitol Open. 2018;4:1-14.
8. Nunes MC, Júnior MH, Diamantino AC, Gelape CL, Abreu Ferrari TC. Cardiac manifestations of parasitic diseases. Heart. 2017;103:651-8.
9. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009;62:1006-12.
10. National Institutes of Health (NIH) [Internet]. Study Quality Assessment Tools; c2021 [cited March 26, 2021]. Available from: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools
11. Castellano LR, Filho DC, Argiro L, Dessein H, Prata A, Dessein A, et al. Th1/Th2 immune responses are associated with active cutaneous leishmaniasis and clinical cure is associated with strong interferon-gamma production. Hum Immunol. 2009;70:383-90.
12. Martínez-Hernández L, Casamian-Sorrosal D, Barrera-Chacón R, Cuesta-Gerveno JM, Belinchón-Lorenzo S, Gómez Nieto LC, et al. Comparison of myocardial damage among dogs at different stages of clinical leishmaniasis and dogs with idiopathic chronic kidney disease. Vet J. 2017;221:1-5.
13. Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, et al. Current state of knowledge on etiology, diagnosis, management, and therapy of myocarditis: a position statement of the European society of cardiology working group on myocardial and pericardial diseases. Eur Heart J. 2013;34:2636-48.
14. Rodríguez-González MJ, Wadnipar-Gutiérrez MI, Calvo-Betancourt LS. Eosinophilic myocarditis as a cause of reversible left ventricular dysfunction. RCC. 2017;24:56.e1-5.
15. Dionisio MT, Dias A, Rodrigues F, Felix M, Estevao MH. Paediatric visceral leishmaniasis: experience of a paediatric referral center: 1990-2009. Acta Med Port. 2011;24:399-404.
16. Shrivastava R, Sinha PR, Singh VP, Sundar S. Echocardiographic evaluation of cardiac status in Indian visceral leishmaniasis patients. Trans R Soc Trop Med Hyg. 2007;101:429-32.
17. Armin S, Gharib A, Khalaj E. Heart involvement in Kala Azar. Pak J Med Sci. 2008;24:879-82.
18. Yazdi C, Narmani M. Visceral leishmaniasis with cardiac involvement in a three years old boy. Internet J Infect Dis. 2003;2:1-4.
19. Mofredj A, Guerin JM, Leibinger F, Masmoudi R. Visceral leishmaniasis with pericarditis in an HIV-infected patient. Scand J Infect Dis. 2002;34:151-3.
20. Puerto-Alonso JL, Molina-Ruano FJ, Gómez-Soto F, Gómez-Rodríguez F. Visceral leishmaniasis with cardiac affectation in an immunocompetent patient. Med Clin (Barc). 2006;127:519.
21. Frapier JM, Abraham B, Dereure J, Albat B. Fatal visceral leishmaniasis in a heart transplant recipient. J Heart Lung Transplant. 2001;20:912-3.
22. Lévêque MF, Lachaud L, Simon L, Battery E, Marty P, Pomares C. Place of Serology in the Diagnosis of Zoonotic Leishmaniases With a Focus on Visceral Leishmaniasis due to Leishmania infantum. Front Cell Infect Microbiol. 2020;10:67.
23. Silvestrini P, Piviani M, Alberola J, Rodríguez-Cortés A, Planellas M, Roura X, et al. Serum cardiac troponin I concentrations in dogs with leishmaniasis: correlation with age and clinicopathologic abnormalities. Vet Clin Pathol. 2012;41:568-74.
24. Bemani E, Oryan A, Bahrami S. Effectiveness of amiodarone in treatment of cutaneous leishmaniasis caused by leishmania major. Exp Parasitol. 2019;205:107747.
25. Lawn SD, Armstrong M, Chilton D, Whitty CJ. Electrocardiographic and biochemical adverse effects of sodium stibogluconate during treatment of cutaneous and mucosal leishmaniasis among returned travellers. Trans R Soc Trop Med Hyg. 2006;100:264-9.
26. Oliveira LF, Schubach AO, Martins MM, Passos SL, Oliveira RV, Marzochi MC, et al. Systematic review of the adverse effects of cutaneous leishmaniasis treatment in the New World. Acta Trop. 2011;118:87-96.
27. Soares JR, Nunes MC, Leite AF, Falqueto EB, Lacerda BE, Ferrari TC. Reversible dilated cardiomyopathy associated with amphotericin B therapy. J Clin Pharm Ther. 2015;40:333-5.
28. Maheshwari A, Seth A, Kaur S, Aneja S, Rath B, Basu S, et al. Cumulative cardiac toxicity of sodium stibogluconate and amphotericin B in treatment of kala-azar. Pediatr Infect Dis J. 2011;30:180-1.