

Visceral Leishmaniasis at the National Reference University Hospital Center of N'Djamena (Chad): Epidemiological, Clinical, Diagnostic, Therapeutic and Prognostic Aspects

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Abstract

Introduction: leishmaniasis is a group of parasitic diseases caused by a parasite of the genus *Leishmania* transmitted by the bite of an infected vector called a sandfly. There are four forms. Visceral leishmaniasis is the most severe form. The aim of our work is to study the epidemiological, clinical, diagnostic, therapeutic and prognostic aspects of the disease in the Infectious Diseases Department of the Centre Hospitalier Universitaire de Référence Nationale in N'Djaména. **Methodology:** Patients were recruited on the basis of clinical signs suggestive of visceral leishmaniasis, *i.e.* prolonged fever, splenomegaly and altered general condition. Biological confirmation was performed with a rapid diagnostic test using recombinant K39 parasite antigen, which is known to have good specificity and sensitivity. Epidata version 3.1 software was used to process patient data. **Results:** From 05/04/21 to 15/12/23, 153 positive cases were managed. The mean age of patients was 18 years, with a sex ratio of 9.2. Of these patients, 103 (67.3%) had recently stayed at gold mining sites. Patients testing positive were treated with sodium stibogluconate combined with paromomycin for 17 days. The mortality rate was 13.2%. **Conclusion:** Leishmaniasis is a serious and little-known disease in Chad. In order to respond to the disease, it is necessary to reinforce the capacities of health structures and to carry out appropriate actions in the out-breaks.

Keywords

Visceral Leishmaniasis, Gold Mining Sites, Chad

1. Introduction

Leishmaniasis are parasitic diseases caused by protozoa of the leishmania genus which are transmitted through a dipteran, the sand fly. They affect humans and certain animals including dogs, horses and cats [1].

There are three main forms in humans: visceral, cutaneous and mucocutaneous leishmaniasis. The cutaneous form has been known since antiquity.

They are classified by the WHO among the neglected tropical diseases.

Visceral leishmaniasis is distributed in 5 foci across the world: Indian, Mediterranean, Chinese, American and African.

Each year, the number of people affected by visceral leishmaniasis is estimated at 700,000 to 1,000,000 new cases, including 20,000 to 30,000 deaths [1].

In Chad, leishmaniasis was not among the diseases described in the health statistics directory nor on the list of diseases mentioned in the epidemiological surveillance system [2]. An upsurge in visceral leishmaniasis has appeared over the last five years to the point of leading the Ministry of Public Health to bring together the fight against leishmaniasis and leprosy within the same program [3]. Visceral leishmaniasis occurs mainly in the northern part of the country, particularly in gold mining sites. The promiscuity and difficult living conditions of gold miners would favor the spread of the disease [1].

The Infectious Diseases Department of the National Reference University Hospital Center has been welcoming an increasing number of cases of the disease since 2021.

The objective of this work is to study the epidemiological, clinical, diagnostic, therapeutic and prognostic aspects of the disease in our context.

2. Patients and Methods

This is a retrospective, descriptive and analytical study carried out at the Infectious Diseases Department. Patients were recruited from the first cases diagnosed on April 5, 2021 until December 15, 2023 in an exhaustive manner. Patients were received in the department through the usual consultation or after referral by another health structure.

The diagnostic presumption was based on the existence of one or more clinical signs suggestive of visceral leishmaniasis, namely: persistent fever, weight loss, clinical anemia, splenomegaly, hepatomegaly. Staying on a gold site was also sought after.

Suspected cases were subjected to the specific IT LEISH[®] test. The test is carried out using capillary blood and the result appears after 20 minutes.

IT LEISH[®] is a rapid test recommended by the WHO. This is an immuno-

romatographic test using the recombinant K39 antigen to detect antibodies against *Leishmania* spp. According to the manufacturer, the specificity is estimated at 99% and its sensitivity at 100% [4].

The variables retained were: age, sex, origin, clinical signs, results of additional examinations, treatment received, duration and outcome of hospitalization.

Patients testing positive carried out a basic pre-therapeutic assessment consisting of the following additional examinations: CBC, blood sugar, blood creatinine measurement, transaminases, HIV, hepatitis B and C serology as well as the malaria test. Other examinations could be proposed depending on the clinical context.

All patients who tested positive were hospitalized and received a standard treatment protocol that combined 20 mg per kilogram of weight of sodium stibogluconate per day and 11 mg per kilogram of weight of paromomycin per day. Both products are administered intramuscularly for 17 days according to national guidelines.

Blood transfusion was prescribed in cases of severe anemia. Vitamin therapy (B group vitamins and multiple vitamins) is regularly associated with different treatments as well as iron, folic acid and antipyretics.

The variables cited above were used to develop a questionnaire using Epidata version 3.1 software where patient data was collected and used.

3. Results

From April 4, 2021 to December 15, 2023, *i.e.* in 33 months, 153 patients with visceral leishmaniasis were treated in the disease department of the National Reference University Hospital Center of N'Djamena. During the year 2022, the service hospitalized a total of 1896 patients. Thus, cases of visceral leishmaniasis represented 3.3% of admissions. (**Table 1**)

Table 1. Distribution of cases by year.

Year	2021	2022	2023
Number of cases	25	62	66

The monthly number of visceral leishmaniasis cases increased from 2.8 cases in 2021 to 5.2 cases in 2022 and 5.5 cases in 2023.

The disease mainly affected males with a sex ratio of 9.2.

The ages of the patients ranged from 12 to 77 years with an average of 18 years. The median age was 23 years old. For females, the extreme ages were 18 and 53 years.

The cases came from several provinces as illustrated in **Figure 1** (map of Chad).

The majority of reported cases have a notion of a recent stay in a gold mining site: 67.3% (103/153). However, only one female case came from one of these sites (Miski).

The other 14 female cases came from urban areas: N'Djamena (4 cases), Abéché (2 cases), Mongo (2 cases), Mao (2 cases), Massakory (1 case), Man-

galmé (1 case), Gounougaya (1 case) and Bédaya (1 case).

Of all the patients, only 10 cases came from the southern part of the country while more than a quarter of the cases came from the locality of Mangalmé in the province of Guéra.

Concerning clinical manifestations, the following symptoms were more often observed: fever, deterioration of the general condition, splenomegaly and hepatomegaly. (**Table 2**)

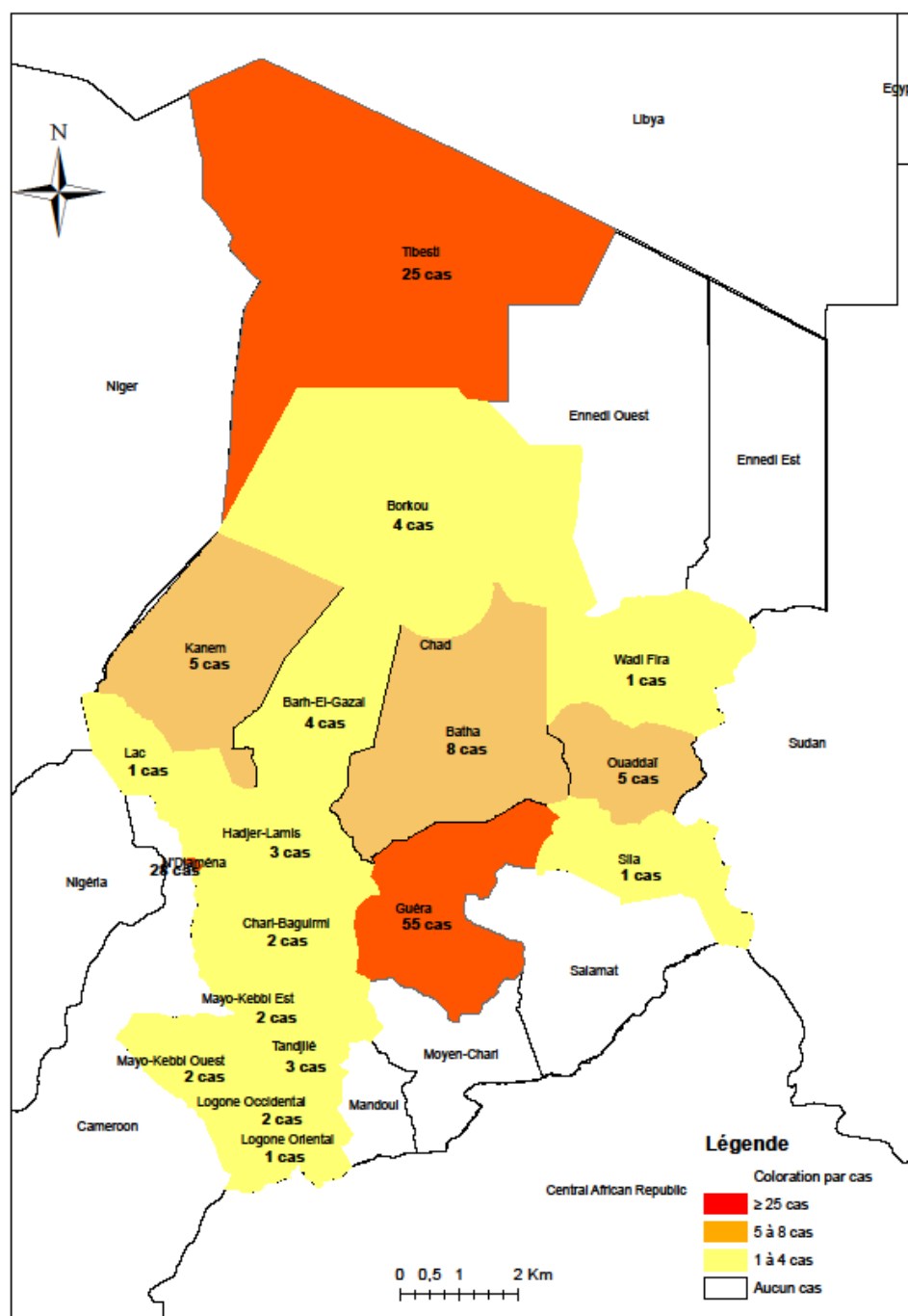


Figure 1. Distribution of cases of visceral leishmaniasis according to province of origin.

Table 2. Sociodemographic and clinical characteristics of cases.

Features	Number	Percentage
Sex:		
• Male	138	90.2%
• Female	15	9.8%
Age groups		
• Under 18 years old	9	5.9%
• 18 to 27 years old	90	64%
• 28 to 37 years old	28	19.3%
• 38 to 47 years old	6	3.9%
• Over 47 years old	12	7.8%
Concept of stay on a gold site		
• Yes	103	67.3%
• No	50	32.7%
Symptoms		
• Fever	153	100%
• Splenomegaly	152	99.3%
• Hepatomegaly	139	90.8%
Length of hospitalization		
• Less than 17 days	34	22.7%
• 17 to 20 days	80	53.3%
• More than 21 days	36	24%

All patients who tested positive were febrile on admission. It is a variable fever but generally plateaus during the first days of hospitalization. Apyrexia occurred no later than one week after the start of treatment.

Splenomegaly and hepatomegaly were homogeneous on abdominal ultrasound.

A deterioration in general condition was observed in 148 patients (96.7%). It was often associated with a state of weight loss.

Superficial lymphadenopathy was found in 20% of cases.

Epistaxis occurred in 4 patients.

Biologically, it was found that 83% of patients had anemia (127/153). Leukopenia and thrombocytopenia affected 120 (78.4%) and 98 patients (64%) respectively. Pancytopenia was found in 95 patients or 62.1%.

Out of 148 patients who took the malaria test, it turned out to be positive for 79 patients or 53.4%.

Antimalarial treatment based on injectable artesunate was immediately started. Then the relay was done with a therapeutic combination based on artemisinin (CTA).

HIV serology was positive for 6 patients or 3.9% of cases. Antiretroviral treatment was deferred until the end of specific treatment for visceral leishmaniasis.

Of the 137 patients who performed a blood creatinine test, 12 had significantly elevated values (at least twice normal), *i.e.* 8.7%. These were referred to the nephrology department for further treatment.

Concerning the other examinations, 8 patients carried out the proteinemia and gammaglobulinemia, 11 patients the blood ionogram. Compared to normal values, serum protein was lowered for 7 patients, gammaglobulinemia was increased for 8 patients. Furthermore, 8 patients had hypokalemia, 6 hypomagnesemia, 5 hyponatremia, 5 hyponatremia, 4 hypochloremia and 4 hypocalcemia.

Regarding treatment, all patients screened positive in the IT LEISH[®] test received the standard treatment currently recommended by national guidelines. These were sodium stibogluconate and paromomycin.

Patients suffering from severe anemia, *i.e.* having a hemoglobin level below 6 g/dl, received a blood transfusion. There were 14 patients or 9.2%.

Antibiotic therapy was prescribed to 63 patients (39.6%) for a bronchitis-type respiratory tract infection.

Evolutionarily, two cases of persistent splenomegaly accompanied by anemia were referred for visceral surgery after specific treatment of leishmaniasis and were subjected to splenectomy.

Overall mortality was 13.2%. All 18 patients who died had fever, splenomegaly, hepatomegaly, and anemia. Only one case of death was female, giving a mortality rate of 15.9% for men and 8.3% for women.

4. Discussion

The first cases of visceral leishmaniasis were recorded in the Infectious Diseases Department of the National Reference University Hospital at the beginning of the second quarter of 2021. However, the occurrence or resurgence of the disease was observed on gold mining sites as early as 2020 [5]. Cutaneous forms were observed sporadically in hospitals [2] but the visceral form was not reported by health services in recent decades before the development of gold prospecting activities. Indeed, the discovery of gold deposits sparked a rush to the far north of the country. This research is carried out in an artisanal manner and results in significant displacement of populations from surrounding provinces, distant provinces as well as neighboring countries, especially Sudan. Hygienic conditions are dismal and promiscuity is very marked. Entomological studies have reported the presence of sandflies in the sites.

Visceral leishmaniasis is little known in Chad while in Sudan, a neighboring country, this disease is endemic [1]. It caused 100,000 deaths between 1989 and 1994 in this country [3].

Concerning age, the average was 18 years in our study. These are generally young adult males. This profile is compatible with gold panning activity. Conversely, according to data from countries around the Mediterranean, particularly in Tunisia, Algeria and Morocco, the disease mainly affects children and young adolescents in rural areas [6] [7] [8]. In Europe on the other hand (France and

Spain) the disease mainly affects adults who are immunocompromised, particularly by HIV [9]. Other causes of immunosuppression are also identified as risk factors, namely situations of malnutrition and organ transplants.

The context in which the disease occurred in Chad does not allow certain domestic animals such as dogs to be directly included in the chain of transmission as in other countries [9].

The clinical picture observed includes fever, splenomegaly and hepatomegaly as in other countries [1] [6] [7]. In our series, fever was constant in all patients. Splenomegaly and hepatomegaly are very common.

The disturbances in the blood count are similar to those reported in the literature, namely anemia, leukopenia and thrombocytopenia [5] [10]. This would be a normocytic and a regenerative anemia [10].

Concerning the biological diagnosis, we used IT LEISH[®] which is a rapid serological test whose sensitivity and specificity offer a satisfactory level of reliability and which is also easy to perform [4].

At the start of the epidemic, the parasitological diagnosis was carried out on the first cases revealing *Leishmania donovani* [5].

Other diagnostic means such as immunofluorescence, ELISA, Wester Blott are not available in Chad [3].

The occurrence of the disease in young subjects led to the systematic proposal of HIV serology which rarely proved positive unlike in European countries where HIV infection is often associated with leishmaniasis in this category of patients [3]. A study carried out in Morocco did not find HIV serology in a group of adults suffering from visceral leishmaniasis [11] [12].

Certain paid biological examinations could only be carried out by a portion of patients with the necessary resources. These include blood ionogram, protein levels, blood gamma globulin [3].

Chain Reaction would have greater sensitivity than direct examination for the diagnosis of childhood visceral leishmaniasis. This technique could be used in some hospitals.

Therapeutically, the standard treatment for visceral leishmaniasis was liposomal amphotericin B. This drug has been used in the first line since 1994 and has reduced the number of days of hospitalization compared to traditional treatment based on meglumine antimoniate [3]. In Chad, meglumine antimoniate was used mainly to treat cases of cutaneous leishmaniasis. The experience of using the combination of sodium stibogluconate and paromomycin is recent and we do not have enough experience to assess its effectiveness compared to other drugs previously used. However, this protocol is recommended by the World Health Organization for the treatment of visceral leishmaniasis caused by *Leishmania donovani* in Africa [13] [14].

Symptomatic visceral leishmaniasis is known to be fatal if left untreated and the low mortality rate (13.2%) obtained using this combination encourages its continued use.

The short-term tolerance of the treatment is also encouraging. It is necessary to monitor patients after hospitalization to ensure recovery and assess the long-term tolerance of the treatment. This follow-up is made difficult because patients generally come from remote locations and, after a fairly long hospitalization, their only concern is finding their loved ones.

Apart from visceral leishmaniasis, it cannot be ruled out that other serious health problems linked to artisanal gold mining described in sites in other countries may also be observed in Chad. This concerns in particular mercury poisoning used for the aggregation of gold particles and silicosis due to dust from rock fragments in gold prospecting sites [15].

5. Conclusions

Leishmaniasis is a serious and little-known disease in Chad. The occurrence of cases in the country has overwhelmed a health system already weakened by other endemics and epidemics.

The mobilization of national actors and partners helped to ensure prompt treatment for patients and to limit hospital mortality.

In order to carry out an adequate response, it seems useful to strengthen the capacities of health structures located close to the main focus to ensure local care and prevent patients from traveling long distances to receive adequate care. It is also necessary to carry out investigations in order to determine the contributing factors and provide an appropriate response to the situation.

Conflicts of Interest

The authors declare the absence of a conflict of interest.

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