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Caso clinico

Case report

Anicteric leptospirosis with pneumonitis, pericarditis and acalculous cholecystitis

Leptospirosi anitterica con polmonite, pericardite e colecistite alitiasica

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INTRODUCTION

Leptospirosis is a spirochetal infection due to pathogenic serovars of the *Leptospira interrogans* species, and this cosmopolitan zoonosis seems to be often underestimated [1-10]. Weil's syndrome is the association of jaundice, hemorrhages and renal failure [1, 3-5, 7]. Arterial hypotension in addition to cardiac and lung injury can herald poor outcomes [3-5,10]. Wild and domestic animals are the natural reservoirs of the spirochetes, and professional, sportive and leisure activities may favor the indirect contact with the infectious agent [1-9].

Worthy of note, concomitant dengue and Hantavirus infection may occur in people with leptospirosis in endemic areas for all these pathogens, like Brasilia-DF periphery region [6, 8]. The incubation period of leptospirosis is variable (from 2 to 30 days) after infection [5].

Diagnostic challenges are enhanced by nonspecific manifestations and late development of serum antibodies, which can establish the diagnosis from the second phase of disease [1-9]. Arrhythmias, myocarditis, endocarditis and pericarditis are described in severe leptospirosis. The exact pathogenesis of the ECG changes should be better cleared by further research [7].

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CASE REPORT

A 19-year-old-man had a left retrosternal pain, which worsened with respiratory efforts, and was associated with cough, yellowish expectoration, and frontal headache during eight days. In addition, he had fever, intense myalgias, arthralgias, abdominal pain, nausea and vomiting. With initial hypothesis of dengue he received intravenous hydration and symptomatic drugs. Five days later, he was admitted with intense asthenia, diarrhea, hypotension and syncope. Previously healthy, he denied tobacco smoking, alcohol abuse and use of any illicit drugs.

There was contact with dogs and, a month previously, he visited a forest region where dengue, yellow fever, and infections caused by Leptospira and Hantavirus had occurred. On physical examination, BMI: 21.85 kg/m^2, heart rate: 102 bpm, and blood pressure: 109/60 mmHg; the lung sounds were reduced on the right lower third, with respiratory rate: 22 rpm. There was mild conjunctival suffusion, and discrete ecchymosis on the left cubital fossa.

Peripheral lymph nodes, liver, and spleen were considered of normal aspect on clinical evaluation. Laboratory tests showed neutrophilia with high band counts (up to 35%), low platelets, high creatine kinase levels, without hyperbilirubinemia or renal failure.

The urinalysis revealed hemoglobin (3+), red cells (213/ HPF) and negative nitrite. Routine blood determinations are shown in Table 1. Echocardiographic studies ruled out hypotheses of myocardiopathy and pericardial effusion.

The tomographic images of chest and abdomen revealed a right basal pneumonia and acalculous cholecystitis, and electrocardiograms showed typical changes of acute pericarditis (Figures 1 and 2).

Blood cultures for microorganisms and tests for Hantaviruses, dengue, infectious mononucleosis, viral hepatitis, cytomegalovirus, HIV, syphilis, and toxoplasmosis were negative.

Positive results of specific serologic tests for leptospirosis (IgM by enzyme immunoassay) were found in the second and third weeks of disease. Arterial gasometry on D4 showed: pH 7.51 (7.35-7.45), $PaCO_2$ 23.6 (35-45 mmHg), PO_2 143 (80-95 mmHg), HCO_3 18.9 (22-26 mEq/L), BE -3.7 (+/- 1), and O_2 saturation 99.5 (95-99%); control findings on D6 were: pH 7.39, $PaCO_2$ 37.2, PO_2 28.7, HCO_3 22.0, BE -2.2, and O_2 saturation 95%. Undergoing supportive care and ceftriaxone 1g IV twice daily, he became asymptomatic.

DISCUSSION

Leptospirosis is worldwide distributed zoonosis, which poses heavy burdens on the public health and on the industries of animal products [9]. It is considered a globally re-emerging condition, with an estimated incidence of approximately 500,000 severe cases per year [9]. Leptospirosis occur in rural as well as in urban en-

Table 1 - Comparative blood determinations in a 19-year-old man with anicteric leptospirosis.

Parameters	*D1*	*D4 1:30 PM*	*D4 9:00 PM*	*D5*	*D6*	*D9*	*D12*
RC (4.7-6.0x10^{12}/L)	5.2	4.7	**3.9**	**3.9**	**3.9**	**4.4**	4.8
Hb (13.5-18 g/dL)	15.6	14.5	**12.1**	**12.0**	**11.9**	**13.3**	14.2
Hematocrit (42-52%)	44.4	**40.2**	**33.5**	**33.4**	**33.2**	**37.8**	**41.1**
WBC (4-11x10^9/L)	7.7	8.6	6.8	9.9	7.4	8.3	7.1
Segmented/bands (%)	75/4	**34/33**	**41/35**	**40/32**	57/**16**	53/1	59/1
Platelets (>150x10^9/L)	**145**	**104**	**84**	**82**	**116**	305	351
TTPa (patient/normal)	ND	0.7	ND	0.8	**1.3**	0.9	ND
INR	ND	1.26	ND	1.24	**1.39**	1.24	ND
Sodium (135-145 mEq/L)	140	139	141	144	143	145	138
Potassium (3.5-5.2 mEq/L)	3.9	4.3	4.1	4.1	4.1	4.2	ND
Urea (10-50 mg/dL)	35.4	33.6	28.5	18.3	18.7	13.5	18.2
Creat (0.7-1.3 mg/dL)	1.5	1.3	1.0	0.9	0.7	0.7	0.8
AST (<39 U/L)	30.8	**86.6**	**84.9**	**97.5**	**68.0**	**62.7**	**56.0**
ALT (<42 U/L)	27.0	35.3	31.1	34.1	40.3	**72.2**	**93.0**
LDH (100-190 U/L)	ND	ND	**613**	**951**	**684**	**606**	ND
Bilirubin (<1.5 mg/dL)	ND	0.53	0.55	0.73	0.53	0.75	ND
CK (38-120 ng/mL)	ND	ND	**654**	**664**	**184**	121	ND
CK-MB (0-3 ng/mL)	ND	ND	**23.1**	**11.6**	ND	1.1	ND
Myoglobin (<90 ng/mL)	ND	ND	**170.6**	**146.0**	ND	ND	ND
Troponin T (<0.1 ng/mL)	ND	ND	**1.64**	**1.93**	ND	**0.89**	ND
CRP (<0.8 mg/dL)	ND	ND	**10,6**	**13,1**	**17,3**	**4,3**	**0.9**

D: days of hospitalization (admitted on May 1 and discharged on May 12). RC: red cells. Hb: hemoglobin. Leukocyte normal ranges (%): segmented (45-70), bands (0-5). Creat: creatinine. CK: creatine kinase. CRP: C-reactive protein. ND: not done.

vironments, more frequently affecting people from poor communities both in industrialized and in developing regions [5, 9].

Infections occur during occupational, sportive and leisure activities, either by direct contact with the infective agent, or indirectly by means of animal sources as pets, rats and mice [5, 9]. Moreover, ticks and other parasitic arthropods may play a role in disease transmission [9]. Outbreaks of disease usually follow periods of intense rainfalls, as occur in Brazil [4-6, 8, 9], and the mortality rate of the more severe infections have ranged from 5% to 50% [9]. Leptospirosis may be anicteric (up to 90%) or with variable jaundice, and evolve in two phases, with a subclinical or symptom-free interval of one to three days between them [9].

The first (septicemic), with blood born distribution of leptospiras for about seven days; and the second (tissue), characterized by diverse signs and symptoms related to organ injury [5, 9]. In this phase, the antibody response develops, acalculous cholecystitis, respiratory and cardiac changes, hemoglobinuria and hematuria can occur, as is described in the present report [5]. The patient herein described had anicteric leptospirosis with some less common features. But, despite of the absence of jaundice or renal failure, the occurrence of fever, headache, hemorrhagic phenomena, myalgia and arthralgia

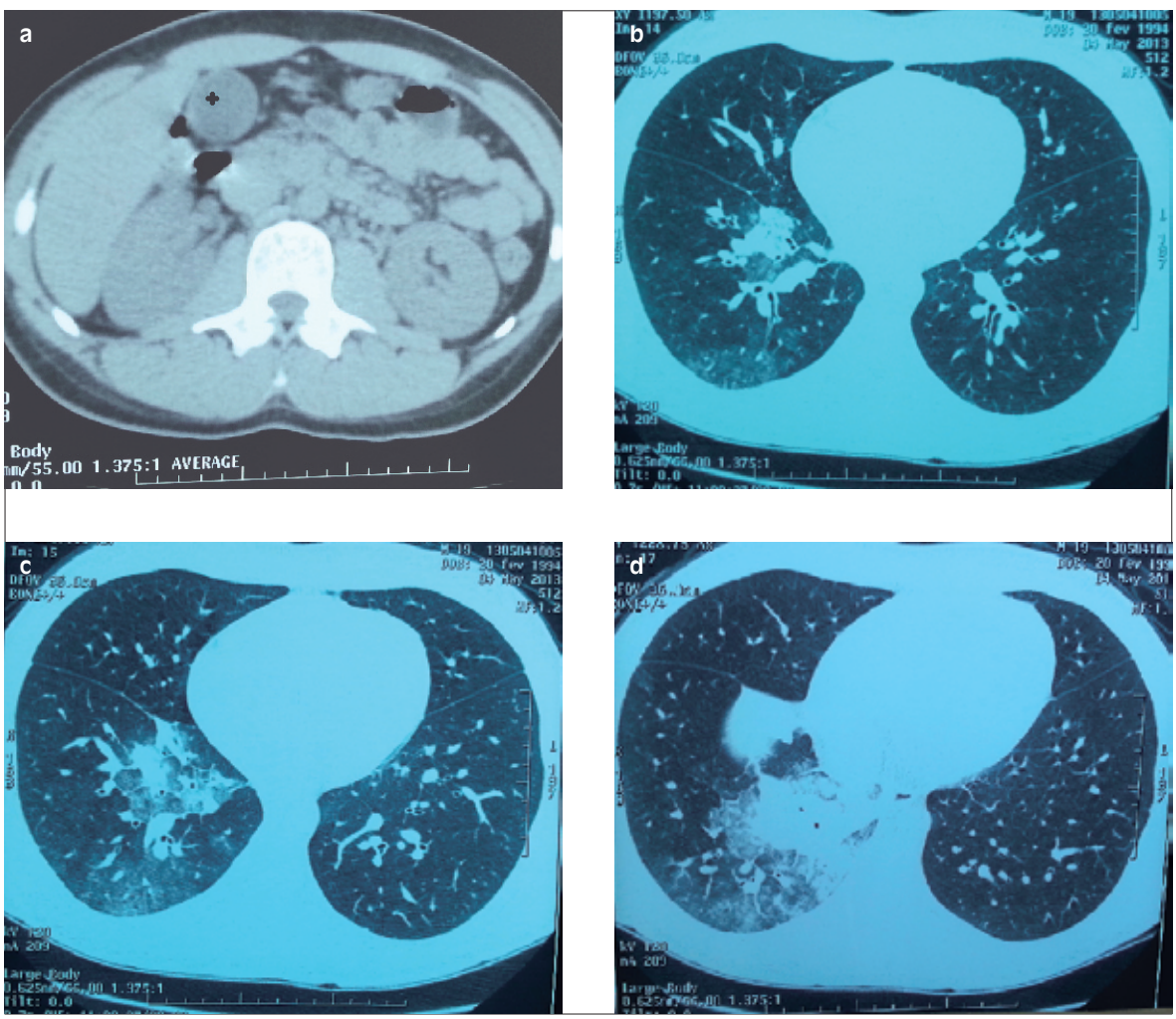

Figure 1 - A: CT of the abdomen showing a distended gallbladder with homogeneous fluid content and inspissated walls (+), consistent features of acalculous cholecystitis; B to D: CT of the thorax revealing images of lung consolidation associated with "ground glass" areas and discrete inspissations of the interlobular septa, in addition to air bronchograms in the right lower lobe, which are indicative of an inflammatory pneumopathy.

after exposure to a rural environment raised the clinical suspicion about leptospirosis.
Dengue and Hantavirus infection were the main differential diagnoses because these pathogens are endemic in the same environment [5, 6, 8]. The initial elevated creatinine level was probably due to pre-renal mechanisms, but the association with lowering platelet counts can be mistaken for Hantavirus hemorrhagic fever with renal syndrome, a condition not yet reported in Brazilian Central Plateau [6, 7]. Imaging studies of chest and abdomen showed normal heart, unilateral lung parenchymal infiltrates, and acalculous cholecystitis. Moreover, the chest pain and typical ECG changes led to diagnosis of acute pericarditis, which is an uncommon manifestation of leptospirosis. Transient ECG changes may be found (up to 68%) in the initial phase, due to the action of Leptospira and metabolic or electrolyte disorders, and are associated with jaundice, high alanine aminotransferase, hypokalemia, low platelets, and abnormal pulmonary images [7, 10]. The patient of this case report had anicteric leptospirosis but presented with precordial pain and ECG abnormalities consistent with acute pericarditis, even in absence of hypokalemia. There was an excess of band forms, moderate anemia, thrombocytopenia, elevated cardiac and muscle injury markers, disorder in coagulation tests, and mild changes in liver enzymes. These findings are usually described in patients with Hantavirus pulmonary syndrome, and coinfections can be under diagnosed because of similar clinical and laboratory data [6, 8]. Concomitant infections were also ruled out, with base on the negative tests for dengue (immunochromatography and MAC-ELISA), and Hantavirus (antibody-capture ELISA) [5, 8]. Yellow fever, malaria and sepsis were other initial concerns as alternative diagnoses, but these entities were ruled out by analysis of clinical features and complementary data [8]. Clinical improvement occurred in spite of antibiotic therapy starting after the first week [2, 4]. In fact, several challenges have played a role in the late diagnosis of leptospirosis [1-4,6]. In addition to the sub-clinical infections, the lack of laboratory resources may also occur [2].

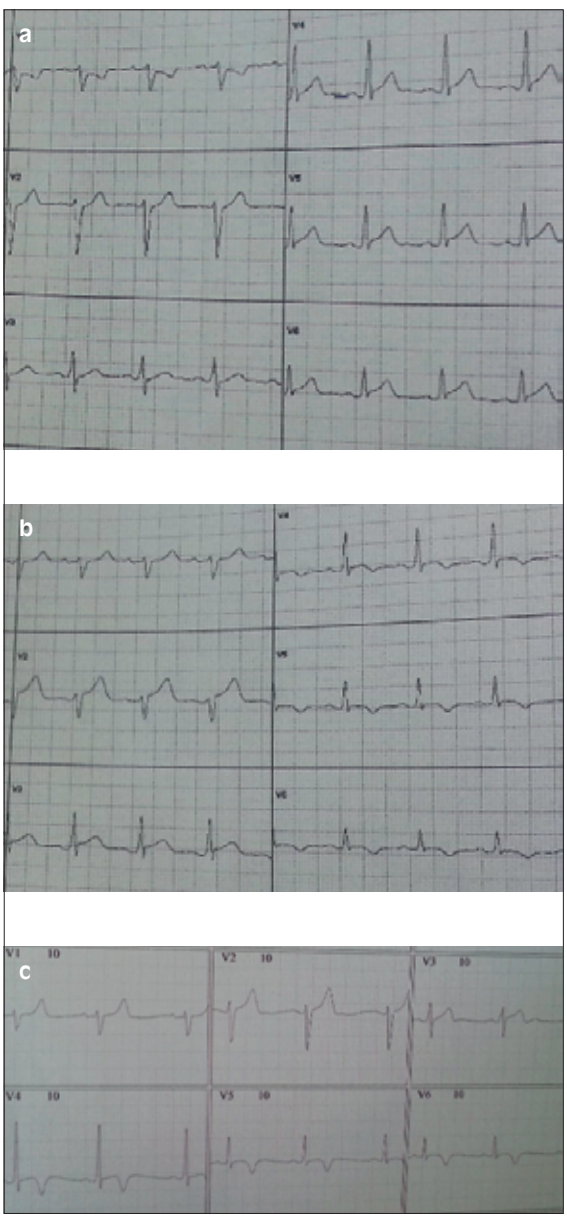

Figure 2 - Control of the ECG changes. A: Normal aspect on D1; B: Ventricular repolarization changes viewed on D2, consistent with acute pericarditis; C: Changes viewed a month later.

CONCLUSION

The role of the suspicion index about leptospirosis should be emphasized, especially in anicteric patients, as well as the possible pulmonary, cardiac and gallbladder involvement in the course of this cosmopolitan zoonosis, which may affect previously healthy travellers.

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Keywords: anicteric leptospirosis, non-lithiasic cholecystitis, pericarditis, pneumonia.

SUMMARY

We report the case of a 19-year-old male patient admitted to hospital with fever, asthenia, vomiting, abdominal and chest pains, cough with yellowish sputum, and hypotension. Laboratory tests showed leukocytosis and high creatine phosphokinase levels, without hyperbilirubinaemia or renal failure. The tomographic images of the chest and abdomen showed a right basal pneumonia and acalculous cholecystitis. The electrocardiograms revealed significant characteristics of acute pericarditis. Specific serology for leptospirosis done in the second and third weeks of disease showed positive results. The use of ceftriaxone 1g intravenously, twice a day for 7 days, resulted in an overall clinic improvement. The role of the suspicion index for diagnosis of leptospirosis is emphasized in anicteric patients, as well as the unsuspected possibility of pulmonary, pericardial and gallbladder involvement.

RIASSUNTO

Riportiamo il caso di un paziente maschio di 19 anni ricoverato in ospedale per febbre, astenia, vomito, dolore addominale e toracico, tosse ed escreato giallastro, e ipotensione arteriosa. Gli esami di laboratorio evidenziavano leucocitosi, aumento della creatinfosfochinasi, senza iperbilirubinemia né insufficienza renale. Le immagini tomografiche di torace e addome evidenziavano una polmonite basale destra e colecistite alitiasica. Gli elettrocardiogrammi mostravano segni caratteristici di pericardite acuta. Le prove sierologiche specifiche per la leptospirosi eseguite nella seconda e terza settimana di malattia hanno mostrato risultati positivi. La terapia con ceftriaxone 1g per via endovenosa, due volte al giorno per un periodo di 7 giorni, ha determinato un miglioramento clinico complessivo. Si sottolinea l'importanza del sospetto diagnostico di leptospirosi nei pazienti senza ittero, con compromissione polmonare e pericardico.

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