Multiple lymphadenopathy – an uncommon presentation of leptospirosis

Izzathunnisa Rahmathullah[1], Sundaresan K Thedchanamoorthy[2], Mayurathan Pakkiyaretnam[2]

(Key words: leptospirosis, lymphadenopathy, outbreak, spirochete, atypical)

Abstract

Leptospirosis is a zoonotic illness with a wide range of organ involvement. We present a case of anicteric leptospirosis in a middle-aged man with numerous cervical lymphadenopathies, which, to our knowledge, has not been reported before in Sri Lanka. Excisional lymph node biopsy revealed reactive lymphadenitis. After ruling out other possible differential diagnoses, concurrently, serology confirmed the leptospiral bacteria as the etiology.

Introduction

One of the fatal zoonotic infections with varying life-threatening consequences is leptospirosis [1]. In 2008, there was a significant epidemic of this infectious disease in Sri Lanka, which is still one of the most widespread infections throughout the entire country [2]. Lymphadenopathy is a recognized manifestation among the uncommon presentation of the disease [3]. Leptospirosis with multiple cervical lymphadenopathies was identified in our case, which remains a rare clinical situation.

Case presentation

A 36-year-old man from Batticaloa district of Sri Lanka was admitted with fever, neck pain, and inability to open his mouth for four days. Before the onset of these symptoms, he was in good health. High fever was associated with significant neck discomfort and bilateral mandibular pain, primarily on the left side. It got worse daily until it eventually prevented him from opening his mouth and caused odynophagia.

He denied having any other systemic illnesses or experiencing constitutional, urinary, or respiratory symptoms. The patient made no mention of any substantial myalgia, arthralgia, bleeding symptoms, headache, or photophobia.

He was a painter, and to fulfill his professional obligations, he frequently traveled to tropical regions and had a recent contact history of mud and flood. He was an alcoholic, not a smoker, but. He denied using illicit drugs or prescription or over-the-counter drugs. No history of suspicious sexual activity or bites from animals or insects existed.

On admission, he looks very ill and febrile. Not pale or icterus. No neck stiffness or sinus tenderness. He had several bilateral cervical diffuse lymphadenopathies. The left submandibular region included a big lymph node that was about 5 cm by 4 cm in size and was warm, painful, and firm to the touch (Figure 1).

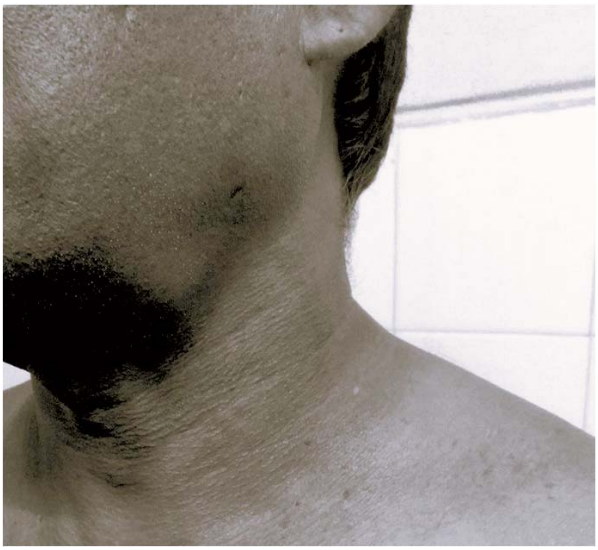

Figure 1. **Multiple cervical lymphadenopathies with a large submandibular node.**

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[1]*Registrar in Medicine,* [2]*Consultant Physicians, University Medical Unit, Teaching Hospital, Batticaloa, Sri Lanka.*

Correspondence: IR, *e-mail: <izzathunnisa1988@gmail.com>.* *Received 26 April 2023 and revised version 04 June 2023 accepted 22 June 2023*

Although oral hygiene was good, the mouth opening was too small to allow a clear view of the throat. Spotty widespread lymph nodes were noted in the left axilla as well. However, he did not exhibit lymphadenopathy in the epitrochlear, or inguinal regions.

His hemodynamic status was stable with a blood pressure of 120/70 mmHg and a pulse rate of 102 beats per minute. He had no organomegaly, and the rest of his examinations were unremarkable.

He underwent several blood investigations listed below (Table 1).

Several reactive lymphadenopathies were identified bilaterally in his neck ultrasound scan, along with an enlarged left submandibular lymph node measuring 5.5 cm by 5 cm.

Using a light microscope, an excisional lymph node biopsy revealed a reactive lymph node structure with an intact fibrous capsule, subcapsular sinuses, trabeculae, and medullary sinuses. There were no appreciable quantities of neutrophils, eosinophils, or plasma cells. There was no necrosis, fibrosis, granulomatous response, or indication of a malignant process (Figure 2).

Table 1.

Parameters	*Reference range*	*Patient value*
White cell count*10^3	(4.0-11.0)	10.96
Neutrophils	(50-70%)	85%
Lymphocytes	(20-40%)	6.8%
Hemoglobin (g/dl)	(12-16)	13.7
Platelets *10^3	(150-450)	80000
ESR (mm in 1st hour)		45
CRP (ng/ml)	(0-10)	318
Alanine transaminase (U/liter)	(12-78)	40
Aspartate transferase (U/liter)	(15-37)	88
Alkaline phosphatase (U/litre)	(46-116)	52
Total bilirubin (µmol/liter)	(3.4-17.1)	46
Direct bilirubin (µmol/liter)	(0-3.4)	28.6
Total protein (g/litre)	(64-82)	57
Albumin (g/litre)	(34-50)	24
INR		0.93
ANA		Negative
SAT for typhoid		Negative
Creatinine (mg/dl)	(0.55-1.03)	1.16
Na (mmol/l)	(136-146)	137
K (mmol/l)	(3.5-5.1)	3.0
Urea (mg/dL)	(15-39)	22
CPK (mcg/L)	10-120	157
Malaria parasite		Negative
Dengue IgM/IgG		Negative
VDRL		Negative
HIV antibodies		Negative
Leptospirosis MAT		Positive

There were no abnormal shadows visible on the chest x-ray. The complete urine report indicated albumin + with 8-10 pus cells and 5-6 red cells.

To rule out syphilis, we requested tests from the Treponema Pallidum Hemagglutination (TPH) and Venereal Disease Research Laboratory (VDRL), both of which came back negative. Moreover, we requested HIV antibodies, which also returned negative. The leptospira micro agglutination test (MAT), performed in light of the patient's epidemiological background and recent history of contact with mud, was reported as positive.

Leptospirosis was diagnosed as a result of these findings, and the patient had an IV ceftriaxone therapy for 14 days. His clinical condition became better with time, and his lymphadenopathy also subsided slowly, which is very firm and well demarcated and restricted his mouth opening later started to discrete gradually and disappeared completely as shown below (Figures 3 and 4).

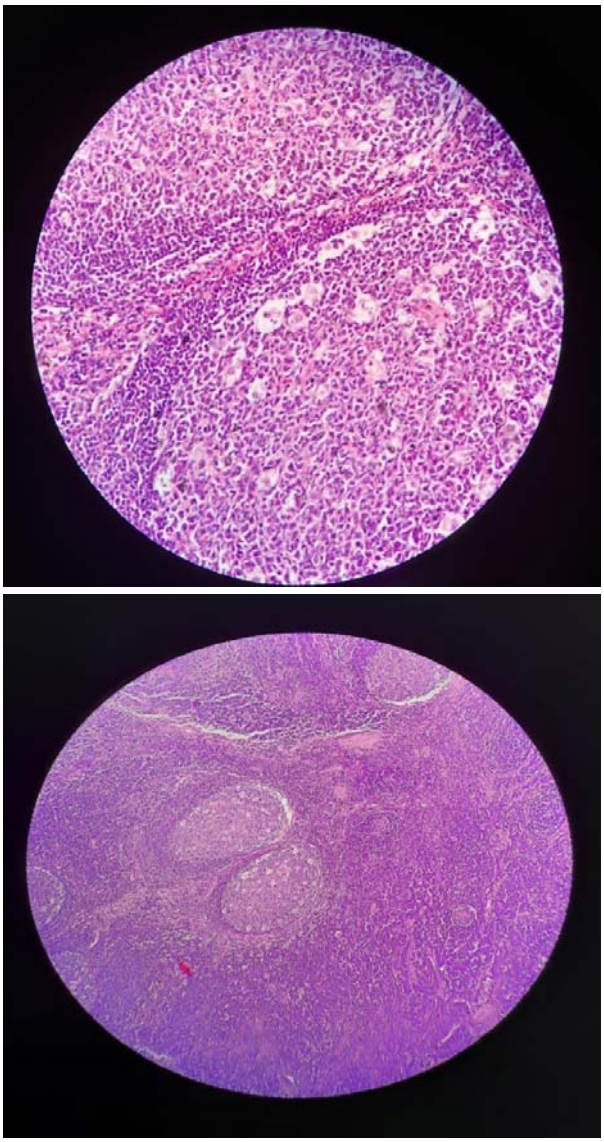

Figure 2. **Excisional lymph node biopsy showed reactive lymphadenitis.**

He fully recovered without experiencing any further relapses, and we were able to discharge him after two weeks. He was evaluated again at the clinic level one month later with repeated blood counts and inflammatory markers, both of which came back normal.

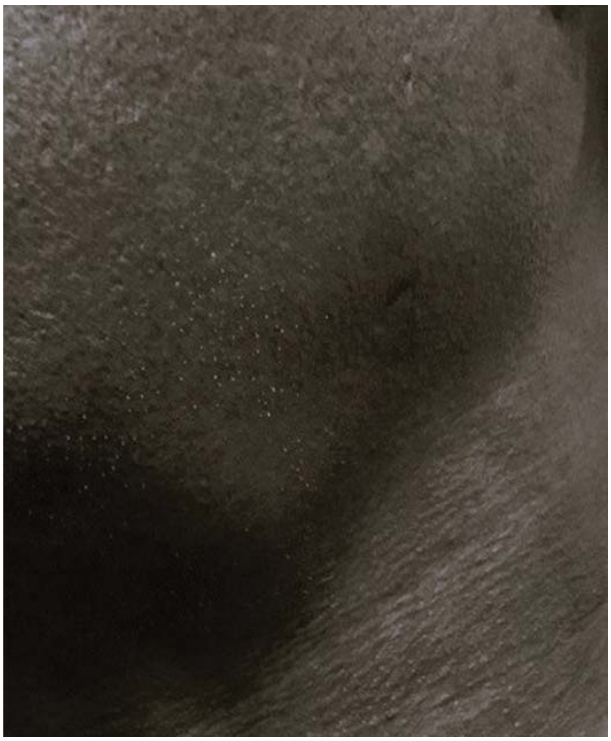

Figure 3. **The initial appearance of a well-demarcated lymph node in the submandibular area.**

Figure 4. **Discrete appearance of lymphnode once treatment initiated.**

Discussion

Leptospirosis is one of the fatal zoonotic diseases, caused by leptospira interrogans, a spirochete belonging to the genus leptospira [1]. The maximum case-death ratio

might be 40% or more because of various organ failures and hemorrhages, and it impacts developing and developed countries. Yet, most infections are either mild or asymptomatic [1].

It became a notifiable disease in Sri Lanka in 1991 and in 2008, an outbreak of leptospirosis caused high mortality in Sri Lanka with high reported cases of 35.7 per 100 000 [1,2].

Leptospirosis manifests in a biphasic phase in symptomatic patients. The initial stage is characterized by symptoms such as fever, headache, and myalgia. Within a few days of the initial immunological phase's resolution, a second immunological phase starts, which may cause life-threatening symptoms such as hepatitis, renal disease, respiratory complications, and electrolyte imbalances as well as multiple organ dysfunction syndrome [3].

In addition to the typical presentation, a number of uncommon and rare clinical manifestations could arise. Acalculous cholecystitis and acute pancreatitis are two unusual GI-related presentations that have been documented in the literature [4,5]. Also described are hematological side effects such as pancytopenia or erythroid hypoplasia, autoimmune hemolytic anemia, thrombotic thrombocytopenic purpura, and hemolytic uremic syndrome. Transverse myelitis and acute disseminated encephalomyelitis have also been documented as diverse neurological manifestations, as have encephalitis-induced coma, and hydrocephalus. Another potentially fatal condition is cardiac problems, including arrhythmias and myocarditis [4].

Lymphadenopathy, pharyngeal injection, hepatosplenomegaly, and skin problems are less frequent and less noticeable signs. According to estimates, 35% of patients will develop lymphadenopathy during the anicteric phase and 12% during the icteric phase [3].

Although generalized or localized lymphadenopathy is a rare manifestation of leptospirosis, only a few cases were reported in the literature. One case of leptospirosis with epitrochlear lymphadenopathy was published in Turkey in 2011 [6]. We could not identify any cases of leptospirosis in Sri Lanka with numerous lymphadenopathy until we reported our case, which may be the first.

The condition could wrongly be diagnosed as dengue, hantavirus, malaria, rickettsioses, or viral sepsis, which may lead to a delayed diagnosis and higher mortality. Pyrexia of unknown etiology is known to have several causes including leptospirosis. Due to this, leptospirosis is frequently misdiagnosed as undifferentiated fevers in unreported cases [7]. Even though there have been many reported complications, the rates have not yet been determined. A lack of understanding of rare complications and atypical presentations will result in a missed diagnosis and poor outcome prediction.

Conclusion

One of the rare clinical manifestations of leptospirosis is localized or generalized lymphadenopathy. Clinicians should be aware of the unique presentation of this zoonotic disease because it is a life-threatening infection. Early diagnosis aids in prompt treatment initiation, prevents unnecessary management and diagnosis delays, and eventually enhances the outcome and prognosis.

Author declaration

Conflict of interest

There are no conflicts of interest.

Acknowledgment

Our sincere thanks to the patient who is aware of this case report and agreed to publish it.

Consent for publication

Written consent was obtained from the patient to publish the case including his photographs.

Author contributions

The idea for the manuscript and its substance were written by the corresponding author. Co-authors have fully contributed to the idea, design, analysis, and drafting of the case report with the help of the corresponding author.

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