CASE REPORT

Case Report: Bilateral diaphragmatic dysfunction due to *Borrelia Burgdorferi* [v1; ref status: indexed, http://f1000r.es/4fe]

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Abstract

Summary:
In this case report we describe a rare case of bilateral diaphragmatic dysfunction due to Lyme disease.

Case report:
A 62-years-old male presented to the hospital because of flu-like symptoms. During initial evaluation a bilateral diaphragmatic weakness with orthopnea and nocturnal hypoventilation was observed, without a known aetiology. Bilateral diaphragmatic paralysis was confirmed by fluoroscopy with a positive sniff test. The patient was referred to our centre for chronic non-invasive nocturnal ventilation (cNPPV). Subsequent investigations revealed evidence of anti-*Borrelia* seroactivity in EIA-IgG and IgG-blot, suggesting a recent infection with Lyme disease, and resulted in a 4-week treatment with oral doxycycline. The symptoms of nocturnal hypoventilation were successfully improved with cNPPV. However, our patient still shows impaired diaphragmatic function but he is no longer fully dependent on nocturnal ventilatory support.

Conclusion:
Lyme disease should be considered in the differential diagnosis of diaphragmatic dysfunction. It is a tick-borne illness caused by one of the three pathogenic species of the spirochete *Borrelia burgdorferi*, present in Europe. A delay in recognizing the symptoms can negatively affect the success of treatment. Non-invasive mechanical ventilation (NIV) is considered a treatment option for patients with diaphragmatic paralysis.

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**Introduction**

Patients with bilateral diaphragmatic paralysis may initially present with dyspnea, orthopnea, and as the disease progresses respiratory failure. Bilateral diaphragmatic paralysis is a severe generalized muscle weakness, however in few cases it has been observed that the diaphragm can be the only involved organ. The most common causes of bilateral diaphragmatic paralysis are damage to the phrenic nerves and generalized muscle diseases. Nocturnal ventilatory assistance may have a significant beneficial effect. These patients show reduced ventilatory muscle strength, as measured by maximal inspiratory and trans-diaphragmatic pressures. These symptoms could improve in association with an improved functional score and decreased dyspnea under ventilatory assistance. Non-invasive positive pressure ventilation (NPPV) is the therapeutic tool of choice for symptomatic patients with bilateral diaphragmatic paralysis.

This case report describes the development of diaphragmatic paralysis in a patient with Lyme disease with the need for ventilatory support.

Lyme disease is a tick-borne illness caused by the spirochete *Borrelia burgdorferi*. There are three species of the *Borrelia*, all of them appear in Europe, and two appear in Asia. Lyme disease has a broad spectrum of clinical manifestations and varies in severity. Regarding the clinical manifestations of Lyme disease, three phases have been described: early localized, early disseminated and late disease. Early localized disease is characterized by the appearance of the erythema migrans, with or without constitutional symptoms. The early-disseminated disease is characterized by multiple lesions, and the late disease is typically associated with intermittent or persistent arthritis involving one or a few large joints, especially the knee. Late Lyme disease may develop months to a few years after the initial infection.

**Case report**

A 62-year-old male was referred to our hospital as a second opinion for further analysis of respiratory failure due to bilateral diaphragm dysfunction. He presented initially with flu-like symptoms. These consisted of low-grade fever, arthralgia in the neck and shoulders and symptoms of nocturnal hypventilation. The symptoms started months before the actual clinical presentation and led to deterioration of the patient’s general condition. Initially there was also a skin rash at the back of his right leg due to an unnoticed tick-bite. The rash started in the form of a ring, later progressed to a size of 10 cm in diameter. At that time the patient had also developed a numbness of the left-side of his face. This gradually resolved during the next days. He complained of dyspnoea that was worse on supine position. There was no evidence of motor/sensory abnormality in the extremities. He had no headache, but he was complaining of neck and shoulder stiffness. He developed a low-grade fever (38.7°C) without shivering. Gradually, fatigue and inactivity evolved.

The patient is an otherwise healthy Caucasian carpenter. He is married and has two healthy kids. He took no medication, had stopped smoking 32 years earlier and drank 2 units alcohol per day. History of allergy developed later when he started ceftriaxone as a second choice for peripheral neuroborreliosis. He works as a volunteer for a forest preservation fund. As a hobby he liked to walk in the woods and he was not aware of any tick-bite.

Initially on physical examination, the patient was hemodynamically stable and not febrile. The fundoscopic exam was normal. The neck was supple and there was no evidence of positive meningeal signs. On percussion the left lung base was higher situated than the right lung base. In upright position our patient had a breathing rate of 24 per minute and SpO2 of 97%. Lying down for 45 second caused severe shortness of breath and an increase in respiratory rate to 40 per minute. Paradoxical breathing was observed and the saturation dropped to 91%.

The chest radiographs (Figure 1a and 1b) demonstrated an elevated left hemi-diaphragm. Screening of diaphragmatic movement during fluoroscopy with sniff manoeuvres revealed a paradoxical movement of both hemi-diaphragms (Figure 2). A pulmonary function test revealed a decrease in supine vital capacity of more than 20% of predicted (Table 2). Arterial blood gases showed pH 7.40, PaCO₂ 4.9kPa, PaO₂ 7.8kPa, HCO₃ 24.6 mmol/l, base excess -0.2 mmol/l. Antibodies to extractable nuclear antigens SSA, SSB, RNP, Sm, SCL-70, Jo-1 and serology of Q-fever were negative. IgG antibodies to *B. burgdorferi* were detectable in serum.

Ultrasomography showed lack of thickening of the diaphragm with inspiration indicating a non-functioning diaphragm. Polysomnography without ventilatory support showed periods of nocturnal hypoventilation.

![Figure 1a](image1.png)  ![Figure 1b](image2.png)

**Figure 1.** (a) Frontal chest radiograph during initial presentation. (b) Lateral chest radiograph during initial presentation.
Figure 2. Fluoroscopy with sniff test.

desaturations together with out-of-phase thoracic and abdominal movement (Figure 3 and Figure 4).

There was no clinical evidence of central neurological abnormalities. The electromyogram (EMG) of the diaphragm revealed a normal distal motor latency with normal CMAP-amplitude of phrenic nerve on both sides. Needle EMG revealed good recruitment without spontaneous muscle activity in the right hemi-diaphragm. Technically measurement of the hemi-diaphragm was less reproducible. In conclusion there was no evidence for traumatic phrenic nerve palsy.

Table 1. Extended differential diagnosis of bilateral diaphragmatic paralysis.

| Neurologic causes                      | Myopathic causes                        |
|---------------------------------------|-----------------------------------------|
| Spinal cord transaction               | Limb-girdle dystrophy                   |
| Multiple sclerosis                     | Hyperthyroidism                         |
| Amyotrophic lateral sclerosis          | Malnutrition                            |
| Neuralgic amyotrophy                   | Acid maltase deficiency                 |
| Poliomyelitis                          | Connective tissues diseases             |
| Guillain-Barre syndrome                | Systemic lupus erythematosus            |
| Phrenic nerve dysfunction              | Dermatomyositis                         |
| Compression by tumor                   | Mixed connective tissues disease        |
| Cardiac surgery cold injury            | Amyloidosis                             |
| Blunt trauma                           | Idiopathic myopathy                     |
| Idiopathic phrenic neuropathy          |                                         |
| Post-viral phrenic neuropathy          |                                         |
| Radiation therapy                      |                                         |
| Cervical chiropractic manipulation     |                                         |

Table 2. Pulmonary function test.

| Substance      | Pred | Upright | % of pred. value | LLN | ULN | Supine | % of pred. value | % change |
|----------------|------|---------|------------------|-----|-----|--------|------------------|----------|
| FEV1 (L)       | 3.37 | 1.79    | 53.2             | 75.2| 124.8| 0.53   | 15.9             | 29.8     |
| FVC1IN (L)     | 4.47 | 1.84    | 41.2             | 79.5| 120.5| 0.58   | 12.9             | 31.5     |
| FEV1%VCmax (%) | 76.1 | 79.12   | 104.0            | 84.5| 115.5| 77.67  | 102.1            | 98.2     |
| FVC (L)        | 4.30 | 2.26    | 52.6             | 76.7| 123.3| 0.69   | 16.0             | 30.4     |
| PEF (L/s)      | 8.41 | 8.53    | 101.4            | 76.4| 123.6| 1.28   | 15.2             | 15.0     |
| PIF (L/s)      | 5.38 |         |                  |     |      | 1.34   |                 |          |
| FRC (L)        | 3.63 | 2.57    | 70.7             | 72.9| 127.1|        |                 |          |
| RV (L)         | 2.47 | 2.32    | 94.1             | 72.7| 127.3|        |                 |          |
| TLC (L)        | 7.14 | 4.80    | 67.1             | 83.9| 116.1|        |                 |          |
| RV%TLC (%)     | 38.1 | 48.40   | 126.9            | 76.5| 123.5|        |                 |          |
| FRC%TLC (%)    | 56.8 | 53.58   | 94.3             | 80.5| 119.5|        |                 |          |

FEV1: Forced expiratory volume in 1 second
FVC: Forced vital capacity
PEF: Expiratory peak flow
PIF: Peak inspiratory flow
FRC: Functional residual capacity
RV: Residual volume
TLC: Total lung capacity
Figure 3. Polysomnographic tracing without ventilatory support showing paradoxical movements of thorax and abdomen (traces 3 and 4, respiratory inductive plethysmography). From the nasal pressure signal (trace 5) it can be seen that breathing movements follow the inspiration.

Figure 4. Polysomnography with ventilatory support (Bilevel PAP, IPAP=14, EPAP=6, see trace 5). Abdominal and thoracic movements are not completely in-phase because the ventilatory support is not triggered before there is inspiratory flow.
The diagnosis of Lyme disease was made on the basis of serological tests demonstrating recent infection with *B. burgdorferi*. The diagnosis of bilateral diaphragmatic weakness was made on the basis of fluoroscopy with a sniff test (Figure 2) and ultrasonography of the diaphragm. The patient received oral doxycycline (200 mg q.d. for 4 weeks) and nocturnal support with NIV/BiPAP was started. Following therapy, our patient showed a dramatic improvement. He stopped using the nocturnal support of mechanical ventilation. He can now lie down in supine position without being orthopneic. The Epworth Sleepiness Scale (ESS) is obviously improved, and he has no other complaints. The repeated pulmonary function test showed improvement in the forced vital capacity (FVC) in supine position (from 31.5% to 65% predicted), however the difference between supine and upright position remain above the 20%. The pressure of the main inspiratory muscle is also improved in the follow-up. In the repeated polysomnography without ventilator support there was still dominant out-phase motion between abdomen and chest, which indicate persistent diaphragm dysfunction.

**Discussion**

In our case the diagnosis was based on the clinical signs and symptoms, chest radiographs and serology indicating recent infection by *B. burgdorferi*. Our patient was not aware of a tick-bite one year before the initial presentation, but the numbness in the left side of his face and the skin erythema spontaneously resolved within a couple of weeks, put us on track. By definition, the nervous system involvement only occurs in the disseminated phase of the infection.1

The symptoms of neurologic involvement may occur weeks to several months after tick bite and may be the first manifestation of Lyme disease.1 Neurological evaluation revealed no abnormalities in our patient. Although the facial nerve is the most commonly affected cranial nerve, the classic manifestations of acute neurologic abnormalities due to Lyme disease are meningitis, cranial neuropathy, and motor or sensory radiculoneuropathy. Each of these findings may also occur individually2. Ventilatory support is very useful in acute respiratory impairment due to diaphragmatic weakness in a patient with Lyme disease.

In conclusion, Lyme disease is an important differential diagnosis in patients with diaphragmatic paralysis. There can be an important delay between the tick bite and the development of symptoms, which has to be taken into account when dealing with these patients.

**Consent**

Written informed consent for publication of clinical details and clinical images was obtained from the patient.

**Author contributions**

Suhail Basunaid: corresponding author, literature search and data collection. Chris van der Grinten: physiologist, head of pulmonary function department. Nicole Cobben: Chest physician, Director of the Centre for Home Mechanical Ventilation. Astrid Otte: Chest physician. Roy Sprooten: Chest Physician. Follow-up data collection. Gernot Rohde: Chest Physician, data control.

**Competing interests**

The abstract describing this work has been presented at the European Respiratory Society Annual Congress 2013.

**Grant information**

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Current Referee Status:  

Version 1

Referee Report 27 January 2015

W.N. Welvaart
Department of Surgery, Riverland Hospital Tiel, Tiel, Netherlands

The authors report a patient with bilateral diaphragmatic dysfunction due to Borrelia.

I enjoyed reading this interesting and well written manuscript.

I think it would be nice to point out more details about the etiology of functional disorders of the diaphragm and acquired paralysis to explain why Lyme disease should be considered in the differential diagnosis of functional disorders of the diaphragm beside the mentioned extended differential diagnosis in table 1.

Despite my comments, I think that in its current form it can be accepted for indexing.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.

Referee Report 05 January 2015

Sezai Celik
Thoracic Surgery Department, Siyami Ersek Cardiothoracic Training Hospital, Istanbul, Turkey

The authors report a patient with bilateral diaphragmatic paralysis due to Borrelia, which improved with antibiotic therapy and non-invasive ventilation. The manuscript is quite well written and sufficiently well documented. The duration of NIV/BiPAP should be clearly pointed out.

It can be accepted for indexing in its current form.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.