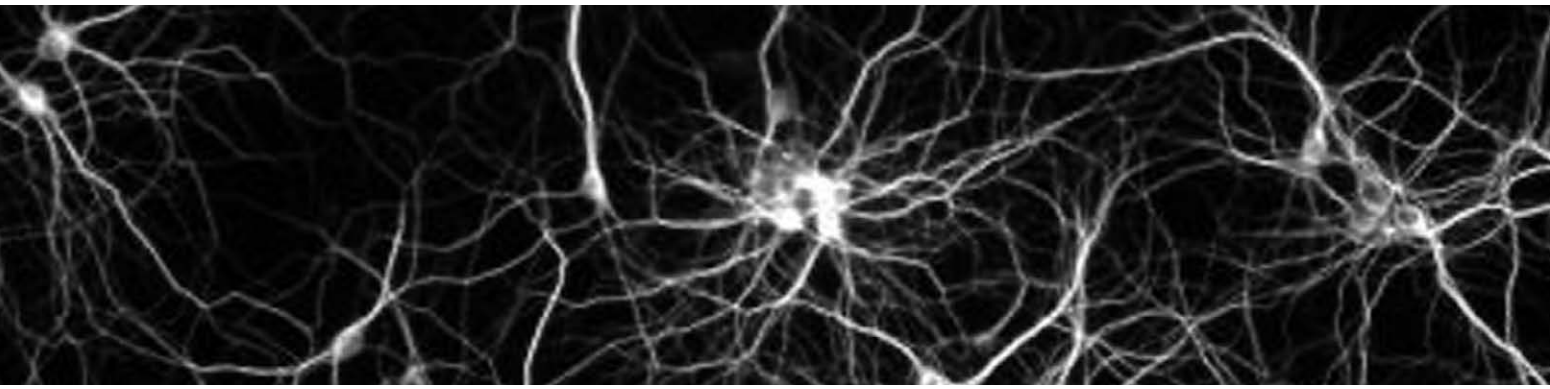

Bilateral facial palsy and left abducens palsy in a patient with neuroborreliosis

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ABSTRACT – *Objectives: Borrelia burgdorferi* (BB) is causing Lyme disease (LD) which acutely manifests as erythema migrans (EM). If the infection is unrecognized and untreated it can progress to carditis, arthritis, or neurological disorders presented as meningitis, encephalitis, or cranial nerve palsies (CNPs). Most frequently affected are seventh and sixth cranial nerves (CNs) individually. *Case description:* In this case report we present a patient with sudden onset of bilateral peripheral facial palsy and left side abducens palsy who was hospitalised in the Department of Neurology, University Hospital Centre Zagreb. Results of wide diagnostics have shown polyclonal hypergammaglobulinemia and positive serology on BB. The patient was treated with ceftriaxone and acyclovir which resulted in improved neurological status. *Results:* Based on clinical presentation, positive serology on BB and good response to ceftriaxone treatment working, diagnosis of neuroborreliosis was confirmed. *Conclusion:* Simultaneous bilateral facial palsy and unilateral abducens palsy without EM is a rare manifestation of LD. Polyclonal hypergammaglobulinemia is proven to occur in acute infectious diseases but the specific relation between the condition and BB infection has not yet been investigated. Early diagnosis and treatment of LD are of immense importance because they prevent dissemination of infection and complications.

Keywords: abducens nerve palsy, *Borrelia burgdorferi,* neuroborreliosis, facial palsy, Lyme disease

OBJECTIVES

Lyme borreliosis or Lyme disease (LD) is a zoonosis affecting multiple organ systems (1). Spirochete *Borrelia burgdorferi* (BB) causes the infection and is transmitted through the bite of the tick (1, 2). Clinical manifestations are grouped into three stages: early localized stage, early disseminated stage, and late disseminated stage (3). The most frequent manifestation of LD is erythema migrans (EM) (89%) (1). If EM is unrecognised and untreated, 10%-15% of infections will progress to neuroborreliosis (3). The most common manifestation of acute Lyme neuroborreliosis in adults in Europe is meningoradiculoneuritis, also known as Garin-Bujadoux-

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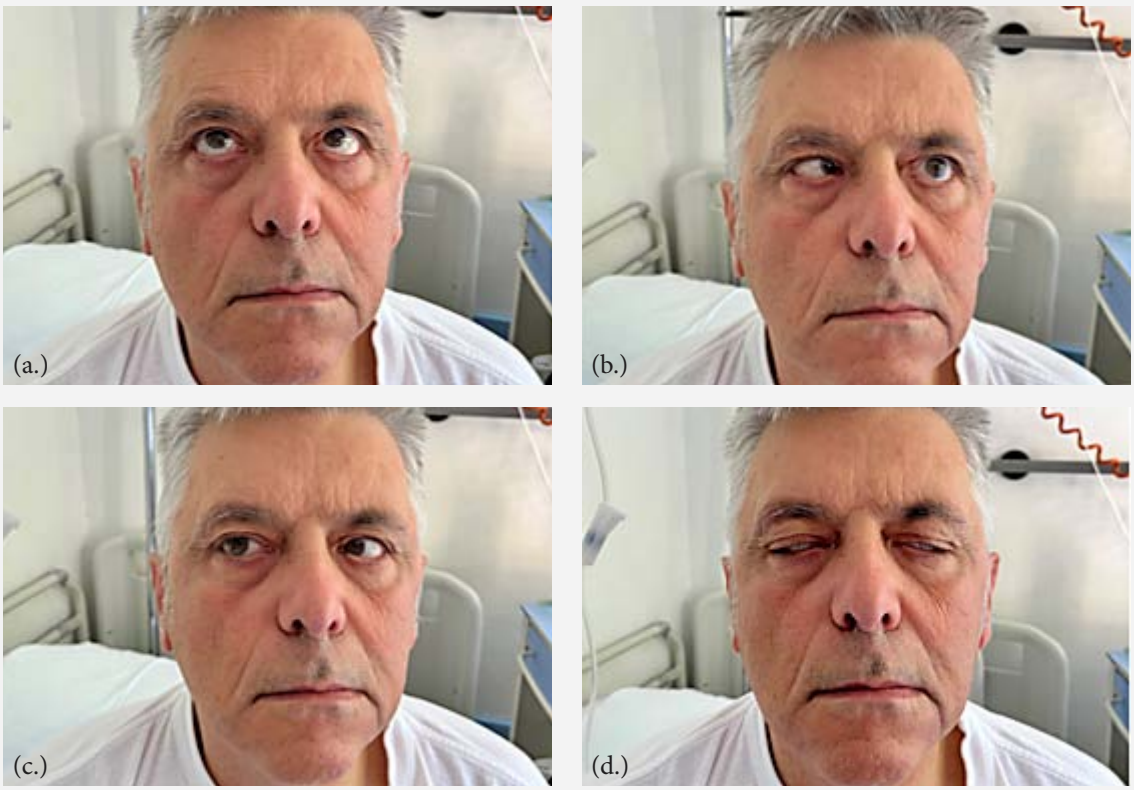

Fig. 1. *Photos taken during the neurological examination of CN innervation while the patient was hospitalised at the Department of Neurology, University Hospital Centre Zagreb: (a.) left abducens palsy presented as slightly adducted left eye when the patient is asked to look up due to tonic action of the medial rectus muscle; (b.) left abducens palsy presented as the inability to abduct left eyeball when looking left; (c.) presentation of eyeballs position when the patient is asked to look right; (d.) bilateral facial palsy presented as the inability to close both eyes and bilateral lowered mouth angle.*

Bannwarth syndrome, and the predominant symptom in about 60% of them is cranial nerve palsy (CNP) (1). The seventh cranial nerve (CN) is affected in 80% of cases and in about 30% of them it is bilateral (5). Other CN deficit is rarely described in the available literature. The second most often damaged nerve is the abducens nerve, occurring in about 5% of patients with Lyme neuroborreliosis (5). In this case report we present a 66-year-old man with an acute onset of neuroborreliosis symptoms and rare clinical manifestation of bilateral facial palsy and left side abducens palsy.

CASE DESCRIPTION

A 66-year-old patient was examined in the emergency room (ER) because of double vision in all directions and left abducens palsy. Besides double vision, he reported bilateral oropharyngeal tingling, headache, difficulty speaking, and lowered left mouth angle. The patient negated nausea, vomiting, fever, and allergies. A week and a half before the onset of symptoms, he was bitten by the thick. The patient did not notice erythema on the thick bite side. In neurological status, he was dysarthric, had left abducens palsy with double vision in all directions, and no nystagmus (Figure 1a-b), bilateral facial palsy (Figure 1d), and his tongue was left positioned in protrusion. From other diseases, he has had inguinal hernia surgery in 1996.

In ER standard laboratory tests, electrocardiogram, computed tomography (CT) of the brain with angiography of the head and neck vessels, polymerase chain reaction (PCR) for COVID-19, and cerebrospinal fluid (CSF) analysis were done. The results of all tests were without deviation from normal. The ophthalmologist examined the patient and did not find ophthalmological reasons for the patient's symptoms. He underwent carotid and vertebral ultrasound imaging with no findings of arterial stenosis. The patient was cardiopulmonary compensated, afebrile, and eupnoeic with blood pressure 140/80 mmHg and was hospitalized.

The literature describes a wide range of causes and differential diagnoses that are linked to cranial neuropathies. Some of them were considered in

Table 1. *Results of serology testing for BB in serum interpreted as Lyme borreliosis of undefined duration. Arbitrary units per millilitre (AU/ml).*

Search	Finding	Result	Unit	Method	Referent range
B. burgdorferi IgM	POSITIVE	>=190	AU/ml	CLIA	Pos. > 22 Neg. < 18
B. burgdorferi IgG	POSITIVE	186.9	AU/ml	CLIA	Pos. > 15 Neg. <10
B. burgdorferi IgM WB	POSITIVE			WB	Neg.
B. burgdorferi IgG WB	POSITIVE			WB	Neg.

Table 2. *Results of serology testing for BB in CSF. Arbitrary units per millilitre (AU/ml).*

Search	Finding	Result	Unit	Method	Referent range
B. burgdorferi IgM	negative			CLIA	Pos. > 3.5 Neg. < 2.5
B. burgdorferi IgG	REACTIVE	38.3	AU/ml	CLIA	Pos. > 5.5 Neg. < 4.5
Neuroborreliosis IgM	negative			EIA	Pos. > 0.3
Neuroborreliosis IgG	negative			EIA	Pos. > 0.3

this particular case: inflammatory and infectious (BB, *Treponema pallidum* (TP), *Varicella-zoster* virus (VZV), *Herpes simplex* virus (HSV), Cytomegalovirus (CMV), Epstein-Barr virus (EBV), *Mycobacterium tuberculosis* (TB), Toxoplasma gondii (TG)), autoimmune diseases (Guillain-Barré syndrome, multiple sclerosis, neurosarcoidosis, autoimmune encephalitis), stroke, tumor, head trauma, and anomalies of blood vessels. Therefore, a wide range of targeted neurological tests were done immediately upon hospitalisation. Magnetic resonance imaging (MRI) of the brain with contrast did not show pathological processes. Electroneurography of the upper and lower extremities did not show signs of polyneuropathy. Besides standard laboratory tests (haematology, biochemistry, and urine analysis), special biochemistry (proteins, IgG, IgA, IgM), electrophoresis of proteins in serum, coagulation tests, a broad spectrum of immunological markers including panel of antibodies for autoimmune encephalitis, proteins and specific proteins in serum (alfa-1-antitrypsin, ceruloplasmin, ferritin, haptoglobin, beta-2- microglobulin) and tumor markers values (AFP, CEA, CA19-9, PSA, NSE and CYFRA) were measured. Vitamin B12, folic acid, copper in serum and in 24-hour urine native and stimulated with penicillamine, iron, and UIBC were measured.

All laboratory findings were normal with the exception of polyclonal hypergammaglobulinemia which raises suspicion of autoimmune disease or infection. Immunology, Gastroenterology, and Haematology specialists were consulted, and further diagnostics were suggested. CT of the thorax, abdomen, and pelvis did not show any abnormalities.

Serum and CSF were tested for CMV, EBV, TG, VZV, HSV 1, and HSV 2. Methods that were used are enzyme-linked fluorescence assay (ELFA) and enzyme-linked immunosorbent assay (ELISA). Also, PCR for HSV and Interferon Gamma Release Assay (IGRA) known as QuantiFERON-TB-Gold ELISA for detection of TB and serologic tests for Syphilis (Venereal Disease Research Laboratory / Rapid Plasma Reagin (VDRL/RPR), Treponema pallidum hemagglutination (TPHA) test and IgM and IgG- Fluorescent Treponemal Antibody Absorption (FTA-ABS)). Chemiluminescence immunoassay (CLIA), Western blot (WB), and Enzyme immunoassay (EIA) were used to detect BB in serum and CSF. Positive serology results of BB were the key for making a final diagnosis which was neuroborreliosis with reactive polyclonal hypergammaglobulinemia (Table 1. and Table 2.).

The patient was treated with 2 grams of ceftriaxone intravenously once daily and 750 milligrams of acyclovir intravenously three times a day for 14 days which resulted in reduction of neurological deficit. The patient underwent logopaedic treat-

ment. He was discharged from the hospital and recommended to take doxycycline 100 milligrams orally twice daily for the next 14 days. Neurological, gastroenterological, and logopaedic follow-up examinations were foreseen.

RESULTS

LD is diagnosed based on three criteria: positive epidemiological history, presence of signs and symptoms associated with BB infection, and typical finding with a predictive value of the diagnosis such as EM or by laboratory confirmation (2). Considering facial and abducens palsy, MRI is used to exclude differential diagnosis such as compressing lesion, brainstem infarct, perineural tumour spread or focal lesion, inflammatory aetiologies, multiple sclerosis, and sarcoidosis (6). CSF typically shows lymphocytic pleocytosis with plasma cells, activated lymphocytes, and a significant increase in total protein or albumin ratio with lactate levels slightly above normal values (1), and in this case CSF was normal. Laboratory diagnosis is based on the demonstration of an antibody that reacts with BB and the established approach is so-called 2-tiered testing: ELISA followed by WB if the ELISA is either positive or borderline (2). In our case, positive BB antibodies in serum and CSF were definitive findings that supported a working diagnosis of Lyme disease neuroborreliosis.

Blood test results have also shown polyclonal hypergammaglobulinemia. In a review published in 2021, polyclonal hypergammaglobulinemia was related to 114 aetiologies classified in 15 nosology groups, of which infectious diseases were among the most frequent causes (18%) and followed by non-malignant haematological conditions (16%), autoimmune diseases (15%), and hematologic malignancies (14%) (7). Despite a detailed list of the most common infectious diseases with polyclonal hypergammaglobulinemia, searching available literature, we did not find a report that specifically linked BB to this laboratory finding.

Literature was searched for similar cases that would include negative anamnestic data of EM and multiple CNPs. One American case report published in June 2021 was found. The patient described in a report was a young female from a Lyme endemic region who presented with bilateral sixth CNP and a dilated right pupil, a partial third CNP and facial nerve palsy. MRI of her brain showed enhancement of CN III, V, VI, VII, VIII, IX, and X symmetrically. MRI of the spine also showed diffuse enhancement of the cauda equina nerve roots and enhancement of nerve roots throughout the cervical spine. Her CSF analysis revealed a lymphocytic pleocytosis and detection of Lyme IgM and IgG bands by WB (8).

CONCLUSION

To conclude, bilateral facial palsy and unilateral abducens palsy with normal CSF and MRI findings, as described in our case presentation, have not yet been described in the literature. Besides the rare presentation, CNP with normal CSF and MRI findings should be differentially diagnostic considered as neuroborreliosis. Relations and underlying pathophysiology between polyclonal hypergammaglobulinemia and BB infection should be further investigated. Early diagnosis and treatment of the acute onset of LD is important for preventing dissemination of the infection and further complications.

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