



## Plasma Exchange for Lyme Neuroborreliosis delayed diagnosis: A case report

### Diagnostic tardif de la neuroborréliose de Lyme et échange plasmatique

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#### ABSTRACT

Lyme neuroborreliosis (LNB) is a rare infectious disease, caused by *Borrelia burgdorferi* spirochetes and responsible for a variety of neurological manifestations. The most common manifestations of LNB in children are cranial nerve involvement, especially facial nerve palsy often accompanied by lymphocytic meningitis.

In this article, we present a case of a 4-year-old boy presented to our emergency department with abdominal pain evolving for a week and symmetrical ascending progression of weakness responsible for severe respiratory failure. Diagnosis of Guillain-Barré syndrome (GBS) was initially suspected. Although our patient had received 2 courses (each of 5 days) of Intravenous immunoglobulin (IVG) treatment, no clinical improvement was observed. The diagnosis of LNB was confirmed by detection of both IgG and IgM specific antibodies in serum. The patient's muscle weakness got better after a 2-week course of Ceftriaxone but respiratory muscle failure didn't improve with two extubation failures. Consequently, we decided to conduct plasmapheresis procedures. We managed to extubate the child and discharge him after a good recovery of his symptoms.

Pediatricians must consider LNB disease in the differential diagnosis of GBS, especially when the patient didn't recover after IVG treatment. This case shows that plasmapheresis could be effective for pediatric neuroborreliosis cases with severe neurological disorders.

**Key words:** Lyme Disease; Lyme Neuroborreliosis; Guillain-Barre Syndrome; Plasmapheresis.

#### RÉSUMÉ

La neuroborréliose de Lyme (LNB) est une maladie infectieuse rare, causée par les spirochètes *Borrelia burgdorferi* et responsable d'une variété de manifestations neurologiques.

Les manifestations les plus courantes de la LNB chez l'enfant sont l'atteinte des nerfs crâniens, notamment la paralysie du nerf facial souvent accompagnée d'une méningite lymphocytaire.

Dans cet article, nous présentons le cas d'un garçon de 4 ans venu à notre service d'urgence pour des douleurs abdominales évoluant depuis une semaine et une progression symétrique et ascendante de la faiblesse musculaire responsable d'une insuffisance respiratoire sévère. Le diagnostic de syndrome de Guillain-Barré (SGB) a été initialement suspecté. Bien que notre patient ait reçu 2 cures (de 5 jours chacune) d'immunoglobuline intraveineuse (IVG), aucune amélioration clinique n'a été observée.

Le diagnostic de LNB a été confirmé par la détection d'anticorps spécifiques IgG et IgM dans le sérum. La faiblesse musculaire du patient s'est améliorée après un traitement de deux semaines par Ceftriaxone, mais l'insuffisance musculaire respiratoire ne s'est pas améliorée, avec deux échecs d'extubation. Par conséquent, nous avons décidé de procéder à une plasmaphérèse. Nous avons réussi à extuber l'enfant et à le faire sortir après une bonne récupération de ses symptômes.

Les pédiatres doivent considérer la maladie du LNB dans le diagnostic différentiel du SGB, en particulier lorsque le patient ne s'est pas rétabli après le traitement IVG. Ce cas montre que la plasmaphérèse pourrait être efficace pour les cas de neuroborréliose pédiatrique avec des troubles neurologiques sévères.

**Mots clés:** Maladie de Lyme, Neuroborréliose de Lyme, Syndrome de Guillain-Barré, Plasmaphérèse

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## INTRODUCTION

Lyme disease is a tick-borne infectious disease caused by *Borrelia burgdorferi* (Bb) (1). LNB is the manifestation of the spirochetes invasion of the central nervous system. The European Federation of Neurological Societies guidelines defined the diagnostic criteria of definite LNB on the fulfillment of three criteria, and two of them for possible LNB: neurological symptoms, cerebrospinal fluid (CSF) pleocytosis, and Bb-specific antibodies produced intrathecally (2).

We report a case of pediatric LNB in a north African country with an atypical clinical presentation and innovative therapeutic management using plasmapheresis.

## CASE REPORT

This is a 4-year-old boy referred to our intensive care unit for severe respiratory failure. Before ten days, he presented an abdominal pain. Five days later, he developed walking disorder and unsteadiness hence his hospitalization in the pediatric unit. On neurological examination, the patient had severe ataxia and was hyporeflexic at his knees and ankles bilaterally. He subsequently became areflexic. There was a rapidly symmetrical ascending progression of weakness inducing a respiratory distress and requiring invasive ventilation. Infectious meningitis was ruled out due to absence of fever and meningeal signs. Cerebral, posterior fossa and spinal magnetic resonance imaging were normal. Inflammatory markers were normal: the erythrocyte sedimentation rate was 10mm/h., the C-reactive protein level was 5 mg/l and the white cell count was 8400/ ul.

A lumbar puncture was performed 16 days from the onset of the symptoms and did not detect meningitis. There was 20 white cells and the level of protein was 0.4. The patient was diagnosed with GBS. Acute demyelinating neuropathy was observed in nerve conduction studies. Initial treatment with IVG (0.4 g/kg/day) was given for 5 days, since the admission day, but the weakness of the upper and lower extremities didn't make the expective improvement.

Second dose of IVG treatment was started for another 5 days but the patient didn't get better. As part of the differential diagnosis and given the persistence of diffuse polyneuropathy, Lyme disease serology was performed after the first course of IVG. Both IgG and IgM antibodies to *Borrelia* were positive in the blood and the CSF with ELISA and Western blot techniques. He was treated with IV Ceftriaxone with a mild improvement after 15 days. Therefore, we decided to conduct six sessions of plasmapheresis with 200–250 cc per kilogram of weight per patient every 2 days. The outcome was favorable. we successfully weaned the patient from ventilation. From being quadriplegic, the patient regained muscle strength and managed to stand up one week after the last plasmapheresis session and walked with a stick after another 2 weeks of neurorehabilitation. The patient was discharged home and was offered regular physiotherapy to help recuperate full function. After 3years of regular follow-up, the patient regains full resolution of symptoms and signs.

## DISCUSSION

Lyme disease is known to be an infectious pathology that can affect not only adults but also the pediatric population because of the important risk of exposure to tick bites and

low observance of protective measures (3).

In the pediatric population, many clinical manifestations of neurologic involvement in Lyme Borreliosis have been reported (4,8). Facial nerve palsy and Lymphocytic meningitis are the most common neurological symptoms described in LNB (1) but other cranial or peripheral neuropathies or radiculopathies may occur (7). To our knowledge, this is the second case reported of pediatric LNB with painful radiculitis causing isolated abdominal pain as the first manifestation of onset (6). Rare cases of LNB described in the literature were mimicking GBS at initial presentation (5,9). It remains unclear whether we are looking at Lyme disease mimicking GBS, or if it's GBS following an auto-immune response caused by the invasion of CSF by Bp or, indeed, if the two coexisted. In our case, initial symptoms were imitating GBS (rapid ascending paralysis, areflexia and respiratory failure) and had led to misdiagnosis LNB and delay in proper treatment implementation. LNB was explored as a differential diagnosis following a poor response to IVG and confirmed as specific IgG and IgM were positive in both CSF and blood. On balance, we feel that this is a case of Lyme disease mimicking GBS rather than Guillain-Barré caused by Lyme disease.

A systematic review and assessment of the literature conducted by the German Cochrane Centre has defined the diagnosis and treatment guidelines for LNB (10). The Gold standard treatment is antibiotics. Having a good CSF penetration, controlled clinical trials have evaluated IV beta-lactam antibiotics (penicillin G, ceftriaxone and cefotaxime) and oral doxycycline in treating LNB. There was no statistically significant difference with regard to the regression of neurological symptoms after a study period of 4–12 months (11).

In literature, there are rare publications on pediatric LNB cases treated with plasmapheresis. Celik and al reported recently a case of 15-year-old patient diagnosed with Lyme neuroborreliosis, who did not recover after IVG and 4 weeks of Ceftriaxone, however all symptoms relieved following the plasmapheresis (5).

They suggested that the efficiency of plasmapheresis is due to its role in antibodies and inflammatory mediators epuration.

## CONCLUSION

Making the diagnosis of LNB in time is a challenge for pediatricians given the multitude of non-specific symptoms linked to this pathology and leading to confusion with other differential diagnoses. Early recognition of this disease is important to avoid delay in suitable antibiotic treatment. This study also recommends plasmapheresis therapy as a useful alternative treatment for unresponsive LNB cases.

## REFERENCES

- Hengge UR, Tannapfel A, Tying SK, Erbel R, Arendt G, Ruzicka T. Lyme borreliosis. *Lancet Infect Dis*. 2003;3(8):489–500.
- Mygland Å, Ljøstad U, Fingerle V, Rupprecht T, Schmutzhard E, Steiner I. EFNS guidelines on the diagnosis and management of European Lyme neuroborreliosis: Guidelines on neuroborreliosis. *Eur J Neurol*. 2010;17(1):8-e4.
- Vandenesch A, Turbelin C, Couturier E, et al. Incidence and hospitalisation rates of Lyme borreliosis, France, 2004 to 2012. *Eurosurveillance*. 2014;19(34):20883.
- Skogman BH, Croner S, Nordwall M, Eknefelt M, Ernerudh J, Forsberg P. Lyme Neuroborreliosis in Children: A Prospective Study of Clinical features, Prognosis, and Outcome. *Pediatr Infect Dis J*. 2008;27(12):1089-94.
- Çelik T, Çelik Ü, Kömür M, Tolunay O, Dönmezer Ç, Yıldızdas D. Treatment of Lyme neuroborreliosis with plasmapheresis: Plasmapheresis in Pediatric Neuroborreliosis. *J Clin Apheresis*. 2016;31(5):476-8. 6.

6. Savasta S, Fiorito I, Foiadelli T, et al. Abdominal pain as first manifestation of Lyme neuroborreliosis in children, case report and review of literature. *Ital J Pediatr* [Internet]. 2020 [cité 3 déc 2020] ;46(1). Disponible sur: <https://ijponline.biomedcentral.com/articles/10.1186/s13052-020-00936-y>
7. Guet-Revillet H, Levy C, Vallet C, et al. Lyme neuroborreliosis in children: Report of nine cases and a review of the literature. *Arch Pédiatrie*. 2019;26(3):133-7.
8. Kechrid A, Ben Hamida A. La maladie de Lyme: épidémiologie, manifestations cliniques et diagnostic biologique [Lyme disease: epidemiology, clinical manifestations and biological diagnosis]. *Tunis Med*. 1991 Dec;69(12):665-7. French. PMID: 1808778.
9. Garrabe E, Dubois D, Chaix Y, Baudou E, Cheuret E, Brehin C. Lyme neuroborreliosis in pediatrics: A retrospective, descriptive study in southwest France. *Arch Pédiatrie*. 2021;28(7):537-43.
10. Rauer S, Kastenbauer S, Hofmann H, et al. Guidelines for diagnosis and treatment in neurology—Lyme neuroborreliosis. *GMS Ger Med Sci*. 2020;18.
11. Dersch R, Hottenrott T, Schmidt S, et al. Efficacy and safety of pharmacological treatments for Lyme neuroborreliosis in children: a systematic review. *BMC Neurol* [Internet]. 2016 [cité 3 déc 2020];16(1). Disponible sur: <http://bmcneurol.biomedcentral.com/articles/10.1186/s12883-016-0708-y>