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Lyme Disease and Papilledema: A Retrospective Study on Clinical Characteristics and Outcomes

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Abstract

Objective: Describe the clinical characteristics, treatment strategies, and outcome data of children with papilledema associated with Lyme Disease at a large tertiary care pediatric hospital.

Methods: Retrospective cohort study of children 1–18 years-old who received care at our institution between 1995–2019 with concurrent diagnoses of papilledema and Lyme disease. Data were abstracted from records and prospective family surveys.

Results: Among 44 children included (median age 9.7 years), 66% (29/44) had additional cranial neuropathies, and 78% (32/41) had CSF pleocytosis. All children were treated with antibiotics (39% oral, 55% intravenous, 7% both); 61% (27/44) were also treated with oral acetazolamide. Symptoms fully resolved in 86% (30/35) of children with follow-up data. Proportion recovered did not significantly differ by antibiotic administration route or presence/absence of CSF pleocytosis.

Conclusions: Papilledema in Lyme disease may occur with or without CSF pleocytosis. Most children recover without residual deficits following treatment, though exceptions exist.

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Keywords

intracranial hypertension; neuroophthalmology; pediatric

INTRODUCTION

Lyme disease is a multistage, multisystem, tick-borne illness most often caused by the spirochete *Borrelia burgdorferi*. It is the most common vector-borne disease in the United States, where about 300,000 people are diagnosed annually, about a quarter of whom are children.[1–3] In its disseminated stages, 10–15% of people with Lyme disease have a neurologic manifestation, such as lymphocytic meningitis, cranial neuropathies, radiculoneuritis, and less commonly encephalomyelitis and mononeuritis multiplex.[4–7]

Papilledema (optic disc swelling) secondary to intracranial hypertension (IH) has been reported in 6–7% of children with neurologic manifestations of Lyme disease [8–18]; the associated clinical features, optimal treatment strategies, and long-term neurologic and visual outcomes of these children has not been systematically described. While most cases are reported in association with concurrent cerebrospinal fluid (CSF) pleocytosis, isolated papilledema without pleocytosis may also occur, the pathophysiology of which is not understood. We aimed to describe the clinical characteristics, laboratory, treatment, and outcome data of a cohort of 44 children with concurrent diagnoses of papilledema and Lyme disease, with and without pleocytosis, who received care at our tertiary care pediatric hospital over a 25-year time period.

METHODS

Study Design and Setting

We performed a retrospective cohort study of children with concurrent papilledema and Lyme disease who received care at Children's Hospital of Philadelphia (CHOP), a large academic tertiary care children's hospital. In addition to data documented in the electronic medical record (EMR), we also collected outcome data from prospective family telephone surveys. Contact information for the patients, patients' parent(s), and/or guardian(s) in the EMR was used to telephone the patient (if ≥18 years-old), parents(s), and /or guardians(s). Informed consent for enrollment in the study was obtained from all patients and their parents/guardians who were able to be reached by telephone. A waiver of informed consent was obtained from the CHOP institutional review board for eligible study candidates who could not be reached by telephone after three consecutive attempt. In those cases, pertinent information was obtained from their medical records for the retrospective component of the study only.

Data Collection

We queried the EMR and a local Neuro-Ophthalmology registry (created and managed by author GTL) for any child 1.0–18.0 years-old that received inpatient or outpatient care at CHOP between 1/1/95 – 12/31/19 with concurrent diagnoses of papilledema (ICD-10 H47.11) and Lyme disease (ICD-10 A69.20). Data were abstracted from the

EMR onto a standardized data collection form. Children were excluded if records did not demonstrate positive serum Lyme testing by United States Centers for Disease Control (CDC) criteria (immunoassay followed by confirmatory Western Blot- see below), if an alternative diagnosis was identified, or if patients/families were able to be contacted by telephone but declined to be part of the study.

Study Definitions

Papilledema was diagnosed by EMR documentation of clinical exam by a staff ophthalmologist or neuro-ophthalmologist. The neuro-ophthalmologists at our institution characterize papilledema and optic disc elevation using descriptive terms and typically do not use formal grading scales (i.e. Frisen), so formal grading criteria for papilledema were not available for this retrospective study. *Lyme disease* was defined by standard CDC criteria,[19] including the presence of a positive serum enzyme immunoassay with positive confirmatory Western Blot (≥2/3 IgM and/or ≥5/10 IgG bands). If screening immunoassay was positive but Western Blot was negative, the test was considered negative. If Western blot data was unavailable for direct review but EMR specifically reported these results as positive, Lyme testing was considered positive. *Month of presentation* was defined by numeric calendar year (e.g. January = 1, December = 12). *Pleocytosis* was defined as CSF white blood cells (WBC) ≥5 cells/μL.[20] *Elevated opening pressure* on lumbar puncture (LP) was defined as an opening pressure ≥ 28cm H_2O.[21] Opening pressure on LP that was greater than the upper limit of the manometer was recorded as 36cm H_2O, the upper limit of standard manometers. *CSF Lyme testing* included CSF Lyme total antibody levels and Western Blot, both of which were performed by Associated Regional and University Pathologist (ARUP) Laboratories. *Intravenous (IV) antibiotics* were recorded as received if the child received any doses of IV antibiotics. However, because many children received IV antibiotics for 24–48 hours only while awaiting CSF culture results, we further defined a *complete course of IV antibiotics* as ≥10 days of IV therapy. *Ophthalmologic outcomes,* including visual acuity, presence or absence of diplopia, and resolution of papilledema, were defined by EMR documentation during follow-up visits with neuro-ophthalmology. Visual field data was not routinely collected as part of clinical care, unless the visual acuity deficit was severe. *Recovery* was defined as complete if all symptoms and papilledema had resolved, partial if there were residual symptoms or papilledema and no recovery if symptoms worsened or failed to improve. Residual deficits were considered to be related to Lyme infection if they occurred within six months of presentation with Lyme disease. New visual symptoms that developed after treatment were not considered to be related to Lyme infection. If follow-up data were not available, these data were recorded as missing.

Statistical Analysis

All data were analyzed using STATA 14.2 (College Station, TX) and R (R Core Team 2021)[22] with two-sided tests and a p-value <0.05 as the criteria for statistical significance. We used non-parametric analyses given small sample size. We described continuous variables (such as age) using median with interquartile range (IQR) or range, and compared them using the unpaired Mann-Whitney test (Wilcoxon rank-sum test). We described categorical variables (such as gender) using counts, frequencies, and proportions, and compared them using the chi-squared or Fisher exact test.

RESULTS

Demographics of the study population

We identified 44 children with concurrent papilledema and Lyme disease during the study time period (Figure 1). Demographic and clinical characteristics of the overall cohort, as well as broken down by those with and without CSF pleocytosis, are presented in Table 1. Overall, the median age at presentation was 9.8 years (range of 4.2–17.7 years). While most children presented during summer months, all children presented between June through January, consistent with known Lyme epidemiology.[1]

Clinical Features: Signs, symptoms, and exam findings

Common symptoms at the time of clinical presentation included headache (68%), diplopia (57%), and nausea/vomiting (48%) (Table 1). Papilledema, present in all children based on inclusion criteria, was bilateral in 42/44 (95%). Among those with objective measurements of optic nerve head elevation, elevation ranged from 115–350μm. Twenty-nine children (66%) had at least one additional cranial nerve neuropathy, the most common of which was an abducens (sixth) nerve palsy in 24 (55%), nearly half of which were bilateral. Other focal neurologic signs and signs/symptoms of meningitis were rare. The median time from symptom onset to presentation was 20 days (range 0–73 days), though nine children did not have available information on symptom onset).

Diagnostic features

Blood serologic testing for Lyme disease was completed in 43 patients (one patient had serologic testing in CSF only). Forty-two children underwent LP in the course of their clinical evaluation. LP was not performed in one child because of a Chiari malformation on screening neuroimaging. The reason for lack of LP in the other patient was not identified on record review. There was limited documentation on leg position during opening pressure measurements so this variable was not evaluated. Median opening pressure among those measured was elevated (36cm H_2O, range 10–60, n=29). Seven of these patients had pressures above the upper limit of the manometer, so the true median opening pressure was likely higher.

Conversely, ten children had normal opening pressures. Seven of these ten patients underwent magnetic resonance imaging (MRI) of the brain, four of whom had neuroimaging findings believed to be associated with IH (Table 2). Of these four patients, one had ≥3 typical radiologic findings (flattening of globe, optic nerve sheath dilation, optic nerve, and/or pituitary sella appearance), consistent with published criteria for diagnosing IH in patients without papilledema.[23,24] Notably, this patient had an opening pressure of 10cm H2O, which was the lowest opening pressure of all the subjects in this study. A second patient had only two of these typical findings, and the two other patients had only one typical finding. Four children with normal opening pressures also had sixth nerve palsies (three of whom had MRI findings believed to be associated with IH). Fifteen patients did not have opening pressures documented, but eight of these 15 had MRIs: three patients had two of the typical radiographic findings of IH described above, two others had cranial nerve enhancement.

Pleocytosis was present in 32 of 41 children with cell counts available (range 5–630 cells/μL). Most pleocytosis was lymphocyte or monocyte predominant (96%), consistent with prior studies of Lyme meningitis.[15,25,26] More males than females had pleocytosis, but there was no significant difference in age, CSF glucose, or opening pressure between those with and without pleocytosis. Median CSF protein was higher among those with pleocytosis as expected with intrathecal inflammation (Table 1). There was no statistically significant correlation between degree of pleocytosis and opening pressure (Spearman correlation coefficient = −0.14, p=0.48).

CSF Lyme antibody testing was performed in 13 children, and were positive in 9/13. Two of these nine were positive for IgG only, three were positive for both IgG and IgM, and four had reports of an unspecified positive antibody.

MRI of the brain was obtained for 34 children. Findings believed to be associated with IH (see Table 2) were found in 20 (59%). In addition, 24% (8/34 that had gadolinium-enhanced MRI) of children also had associated enhancement of multiple cranial nerves that did not consistently correlate with clinical neuropathies. Notably, of the 9 children without pleocytosis, 3 had facial nerve palsies (1 of these patients had multiple cranial nerves enhance on MRI) and a different subject had positive CSF Lyme serology.

Treatment

All 44 children received antibiotics to treat Lyme disease. Oral antibiotics were prescribed in 39% of patients for a median of 14 days (range 13–18 days), and a full IV antibiotic course was prescribed in 55% of patients for a median of 18 days (range 13–21 days). There were three patients (7%) that received a complete oral course of antibiotics and then received a subsequent full IV course due to ongoing symptoms. Oral antibiotic courses were shorter than the standard 14-day course because many patients presented to the emergency department and received a 24–48 hour course of IV antibiotics while their CSF cultures were pending, and then completed the remainder of their 14-day antibiotic course with oral therapy. Of the patients treated with oral antibiotics, fourteen received doxycycline, two received amoxicillin, and two received cefuroxime (one patient had amoxicillin for 7 days and then switched to doxycycline for 7 days). Almost all patients treated with IV antibiotics received ceftriaxone, although penicillin was used in one patient instead. Children that received IV antibiotics (compared to those that did not) had a higher median CSF WBC (Table 3). This was likely due to previous Lyme treatment guidelines that recommended IV antibiotics for patients with meningitis; RedBook guidelines were updated in 2007 to include oral doxycycline as a treatment option for Lyme meningitis.[27,28] Twenty-seven patients were treated with acetazolamide for IH for a median duration of 62 days (range 10–191 days), which was then tapered after papilledema resolved. Two children required optic nerve fenestration to preserve vision, in one case the procedure was bilateral.

Outcomes

Thirty-five of the 44 children were seen in clinical follow-up after their initial presentation (median total follow-up duration 121 days, range 6–1479). Among these 35 children with documented follow-up, 30 (86%) had complete recovery. Thirty-two children had follow-up

within 3 months of presentation and 47% of those had completely recovered within this time frame. Overall, the median time to recovery was 94 days (range 12–426 days). Papilledema was generally the last sign to recover; about a third of patients had residual papilledema at follow-up evaluation within 3 months of presentation. There was no difference in follow-up duration or proportion of ultimate symptom resolution between those receiving oral versus IV antibiotics or between those with and without pleocytosis, although resolution of symptoms was significantly faster in the patients with pleocytosis (median 77 days versus 134 days, p=0.004).

There were five children who had EMR documentation of residual symptoms at last follow-up. There was no difference in age, sex, opening pressure, or median CSF WBC count (three did not have pleocytosis) between those with complete resolution and those with residual symptoms (Table 4). Among the five with residual symptoms, two children had severe vision loss (20/200 bilaterally) at presentation, requiring optic nerve sheath fenestration with subsequent partial improvement in visual acuity, but with residual restricted visual fields and optic disc pallor. Two children presented with papilledema and facial palsy, one of whom had persistence of mild facial weakness at last documented follow-up, the other of whom had mild residual optic disc elevation that was stable over four years and possibly the baseline appearance of her optic nerves prior to infection. Finally, one child had papilledema and a sixth nerve palsy with esotropia at presentation. Interestingly, his sixth nerve palsy resolved after one month, but the child had persistent esotropia and amblyopia that was present a year later and ultimately required strabismus surgery.

Telephone Interviews

Seventeen patient families participated in the prospective telephone survey. Three of the children who did not have follow-up in the retrospective analysis participated in the prospective survey. Four families reported that their child had residual symptoms, two of whom had already been identified on chart review above (patients with optic nerve fenestration). Two families reported changes in visual acuity following Lyme infection that corrected with glasses suggesting a refractive error. It is uncertain if this concern is definitively attributable to Lyme infection. In these patients, all their other presenting symptoms resolved after treatment. Notably, of the five children with residual symptoms on retrospective chart review, the family of the child with mild residual optic disc elevation (which may have been her baseline prior to infection) reported complete symptom resolution.

DISCUSSION

We present a cohort of 44 children with Lyme disease and papilledema. While most (86%) affected children ultimately fully recovered without residual neuro-ophthalmic deficits regardless of antibiotic administration route, acetazolamide therapy, or presence/absence of pleocytosis, a small proportion had residual deficits.

While there have been multiple large studies examining Lyme meningitis in the children, previous data on papilledema and Lyme disease are limited.[29,30] Kan et al. reviewed 12 cases of Lyme disease and papilledema in 1998, of whom half had pleocytosis, and half

had an abducens nerve palsy.[31] Ramgopal et al. reported seven pediatric patients with Lyme disease and papilledema in 2016, all of whom had elevated CSF opening pressure and pleocytosis on LP.[16] Available literature examining papilledema in pediatric Lyme disease is otherwise largely limited to case reports, or small numbers of pediatric patients reported in larger adult case series.[18] It is important to note that some prior studies globally refer to papilledema from Lyme disease as pseudotumor cerebri syndrome.[9,17,32] However, the diagnosis of pseudotumor cerebri syndrome requires a normal CSF profile, and is thus not applicable to the majority of children with papilledema and Lyme disease that have pleocytosis.

The proportion of children without pleocytosis (22%) in this cohort is consistent with prior reports.[31] Papilledema in the presence of pleocytosis is a well described occurrence in the context of meningeal inflammation leading to impaired CSF flow. However, the pathophysiology of papilledema without pleocytosis in Lyme disease is not well understood. One possibility is that this phenomenon still represents a central nervous system infection. If there is a specific period following infection when pleocytosis peaks, it is possible that transient pleocytosis was missed if a child undergoes only one LP. A 2006 report described a child without pleocytosis on initial LP that developed a lymphocytic predominant pleocytosis on repeat LP the next day.[33] Or, perhaps Lyme disease should be considered to be one cause of secondary pseudotumor cerebri syndrome. Alternatively, optic disc swelling without pleocytosis in Lyme disease may result from a localized non-infectious inflammatory process such as papillitis, similar to that suspected to occur in Lyme-related facial nerve palsies.[34,35] Papillitis is typically not associated with vision loss or optic nerve enhancement on MRI. Finally, our hospital is situated in a Lyme endemic area; it is possible that papilledema occurred independently of Lyme infection in some children. The latter two considerations may explain why three children without pleocytosis had residual symptoms. In addition, it is possible that the patients without pleocytosis did not have active Lyme disease and their positive serologic testing was from a prior exposure, but 4/9 of these children had facial palsies or positive CSF serology which would be more suggestive of active Lyme infection.

While papilledema is by definition associated with intracranial hypertension, ten children in this cohort had normal opening pressures on LP, and 15 children did not have an opening pressure documented in their records. There are several possible explanations for the finding of optic nerve head elevation in these patients. First, depending on the timing of LP, peak IH may have been missed, similar to missed transient pleocytosis as discussed above. Second, individual children may each have unique ICP set points. For children with relatively low set points, an elevation in opening pressure over their baseline that is still < 28cm H_2O may lead to papilledema. Secondary findings associated with IH seen on brain MRIs in this study and the presence of abducens palsies (particularly those that were bilateral) support this hypothesis, which is why we elected to include these patients in our study. Finally, it is possible that these patients with normal opening pressure did not have papilledema, but rather an alternative process causing optic nerve head elevation (i.e., papillitis or alternative optic neuropathy). In this case, the optic nerve edema may be akin to a facial nerve palsy where diffuse CNS neuroborreliosis is not typically observed.

Acetazolamide is a carbonic anhydrase inhibitor that reduces ion (and subsequently water) transport across choroid plexus epithelial cells and thus can significantly decrease CSF secretion and reduce ICP.[36,37] It was used in 61% of children in this cohort, but was not associated with differences in time to recovery. While there are no clear guidelines on its use in Lyme-related papilledema, it likely reduces symptoms related to IH. However, treatment of the underlying infection per published guidelines is likely more important for recovery.[3,7]

Overall, the majority of children make complete recovery. While we did see a difference in the time to recovery between patients with pleocytosis and those without, this could have been skewed by the timing of their follow-up. Alternatively, this could also suggest that the disease process underlying the papilledema in patients with pleocytosis and those without is slightly different; thus, the recovery process is more prolonged in patients without pleocytosis.

Our study had several limitations. First, because this was a retrospective study, there were missing data for some children that may have been available to the treating team in real time (e.g. opening pressure from LP not documented in the EMR), and details of specific childrens' clinical courses may have been lost. The prospective survey helped to address this limitation in outcome ascertainment. Second, the sample size was small, so subtle differences in outcomes between patients treated with IV antibiotics or oral antibiotics, or with/without pleocytosis may have been missed. Furthermore, given the small sample size, this study is not powered to statistically compare outcomes between IV and oral antibiotic administration. Third, time to resolution data may have been confounded by severity of illness; children with less severe symptoms may have had longer time until follow-up. However, total proportion resolved data should still be valid. Finally, our goal was to focus on those patients with neuro-ophthalmologic complications, as such, we did not focus on the larger population of patients with Lyme disease. This limits the ability to make conclusions on the relative incidence of papilledema in patients with Lyme meningitis.

CONCLUSION

In conclusion, papilledema in Lyme disease may occur with or without pleocytosis. It is critical for clinicians to remain vigilant to this neurologic manifestation of Lyme disease, so it can be promptly identified and treated. While we were unable to quantify the prevalence of papilledema in all Lyme disease with our study design, future prospective work could further examine this question, and in the interim, all affected children should be screened for vision loss with consideration of a fundoscopic exam. While the pathophysiology of this phenomenon is not completely understood, most affected children recover, regardless of route of antibiotic administration or the presence of pleocytosis. However, a small proportion do have residual neuro-ophthalmic deficits.

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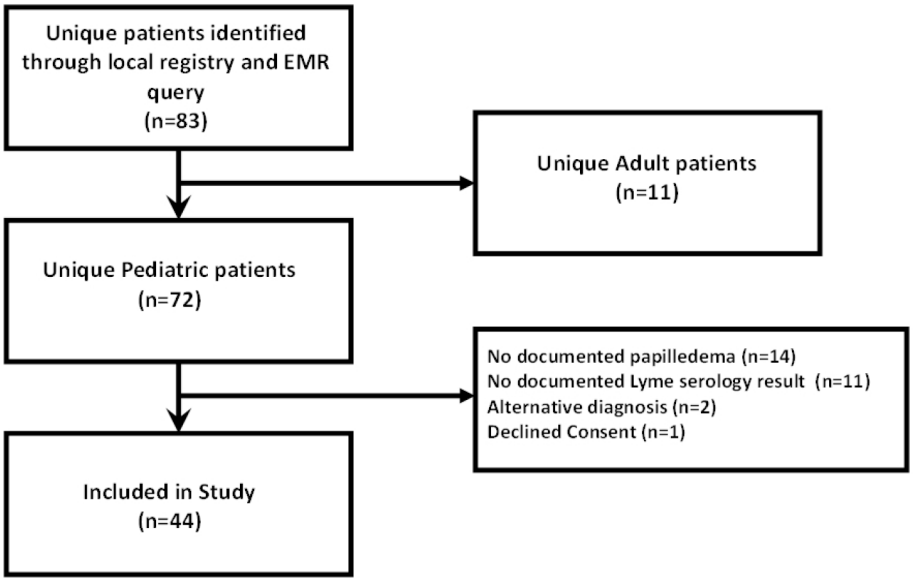

Figure 1.
Flowchart of subjects identified for retrospective study

Table 1:

Demographics and clinical features of patients with papilledema and systemic Lyme disease, 1995–2019.

Characteristic[a]	All (n=44)	By Pleocytosis [b,c] CSF WBC ≥ 5 (n=32)	CSF WBC < 5 (n=9)	p-value[b]
Male sex (%)	25 (57)	22 (69)	2 (22)	**0.021**
Median age in years (IQR)	9.8 (7.4–12.0)	9.5 (7.4–11.8)	10.8 (9.6–11.1)	0.45
Median month at presentation (IQR)	8 (7–9.5)	8 (7–8)	8 (7–9)	0.40
History of tick bite in preceding 6 months (%)	6 (14)	5 (16)	1 (11)	1
Symptoms in 6 months prior to presentation				
Headache (%)	30 (68)	20 (63)	9 (100)	0.29
Diplopia (%)	25 (57)	16 (50)	6 (67)	1.0
Nausea/Vomiting (%)	21 (48)	16 (50)	5 (56)	0.69
Fever, >38.0 (%)	9 (20)	8 (25)	1 (11)	0.39
Erythema Migrains (%)	7 (16)	4 (13)	3 (33)	0.36
Nuchal Rigidity (%)	7 (16)	3 (9)	4 (44)	0.08
Blurry Vision (%)	7 (16)	3 (13)	2 (22)	1.0
Facial Droop (%)	6 (14)	3 (9)	3 (33)	0.16
Tinnitus (%)	2 (5)	0 (0)	2 (22)	0.07
Neuro-ophthalmologic exam findings				
Decreased visual acuity (%)	3 (7)	2 (6)	2 (11)	1.0
Bilateral papilledema (%)	42 (95)	31 (97)	8 (89)	0.40
Other cranial nerve impairment (%)	29 (66)	20 (63)	7 (78)	0.69
Cranial nerve 3, 4, and/or 7 palsy (%)	9 (20)	5 (16)	3 (33)	0.34
Cranial nerve 3 palsy (%)	1 (2)	1 (3)	0 (0)	1.0
Cranial nerve 4 palsy (%)	2 (5)	1 (3)	0 (0)	1.0
Cranial nerve 7 palsy (%)	6 (14)	3 (9)	3 (33)	0.052
Cranial nerve 6 palsy (%)	24 (55)	16 (50)	6 (67)	0.51
Labwork: blood				
Lyme WB Serology (n=43)[d]				0.87
IgG and IgM positive (%)	25 (57)	19 (59)	5 (56)	-
IgM only positive (%)	5 (11)	4 (13)	1 (11)	-
Positive WB, but unknown bands (%)	13 (30)	8 (25)	3 (33)	-
Labwork: CSF				
CSF opening pressure (mm H2O, IQR; n=29)	36 (25–36)	36 (23.5–36)	35.5 (31.5–53.5)	0.49
Opening pressure >28cm H_2O (%; n=29)	19/29 (66)	12/20 (60)	7/8 (88)	0.21
Median CSF WBC (IQR; n=41)	18 (6–58)	34 (15–68)	2 (1–2)	**<0.001**
CSF glucose (interquartile range)	49 (44–54)	47 (44–52)	54 (50–56)	0.08
CSF protein (interquartile range)	34 (21–58)	38 (24–65)	20 (19–28)	**0.007**
Positive Oligoclonal Bands (%, n=8)	2/8 (25)	2/7 (29)	0 (0)	0.75
CSF Lyme testing sent	23 (52)	16 (50)	6 (67)	0.59
Positive CSF Lyme total antibody levels (%, n=13)	9/13 (69)	7/10 (70)	1/2 (50)	1.0

Characteristic[a]	All (n=44)	By Pleocytosis [b,c] CSF WBC ≥ 5 (n=32)	CSF WBC < 5 (n=9)	p-value[b]
Positive CSF Lyme PCR (%, n=15)	0/15 (0)	0/9 (0)	0/6 (0)	n/a
Treatment				
Oral antibiotics (%)	17 (39)	10 (31)	7 (78)	**0.021**
Intravenous antibiotics (%)	24 (55)	20 (63)	1 (11)	-
Both Oral and IV antibiotics (%)	3 (7)	2 (6)	1 (11)	-
Acetazolamide (%)	27 (61)	18 (56)	8 (89)	0.12
Median duration in days (interquartile range)	62 (42–108)	54.5 (29.5–84.5)	116 (53–163)	**0.050**
Outcome				
Complete resolution (%, n=35)	30/35 (86)	20/23 (87)	7/9 (78)	0.60
Complete resolution within 3 months (%)	15/32 (47)	12/23 (52)	1/9 (11)	**p=0.050**
Median days to resolution (interquartile range)	94 (57–124)	77 (38–105)	134 (105–387)	**p=0.004**
Median follow-up duration in days (interquartile range)	120.5 (43–226)	108 (19–253)	134 (105–213)	p=0.26

[a] Categorical variables are described using n (%). Continuous variables are described using median (intraquartile range)

[b] p-values comparing characteristics between children with CSF pleocytosis and children without CSF pleocytosis were calculated using chi-square (if each sample ≥10) or Fisher's exact (if any sample <10) tests for categorical variables and Wilcoxan rank-sum tests for continuous variables.

[c] Three children in the overall cohort did not have CSF data (2 did not have LPs and 1 did not have CSF cell counts recorded in the chart)

[d] One subject did not have serum testing; Lyme diagnosis was made based on positive CSF Lyme Western blot. None of the patients had IgG only bands

Abbreviations: CSF, cerebrospinal fluid; WBC, white blood cells; WB, western blot; PCR, polymerase chain reaction;

Table 2:

MRI findings in patients with papilledema and systemic Lyme disease.

MRI finding[a]	All n=34	By Pleocytosis[b] CSF WBC ≥ 5 (n=25)	CSF WBC < 5 (n=7)	p-value[c]
Secondary signs of increased intracranial pressure	20 (59)	14 (56)	5 (71)	0.75
Optic disc protrusion	16 (47)	11 (44)	5 (71)	0.53
Dilated optic nerve sheath	9 (26)	6 (24)	2 (29)	1.0
Flattened globes	8 (24)	5 (20)	2 (29)	1.0
Optic nerve restricted diffusion	8 (24)	5 (20)	3 (43)	0.60
Empty or patially empty sella	6 (18)	4 (16)	2 (29)	0.45
Narrowing of transverse sinus	4 (12)	1 (4)	3 (43)	**0.037**
Cranial nerve enhancement	8 (24)	7 (28)	1 (14)	0.65

[a] Categorical variables are described using n (%). Continuous variables are described using median (intraquartile range)

[b] Two children with MRI imaging did not have lumbar punctures with documented CSF cell counts.

[c] p-values comparing characteristics between children with CSF pleocytosis and children without CSF pleocytosis were calculated using chi-square tests for categorical variables and Wilcoxan rank-sum tests for continuous variables.

Abbreviatons: CSF, cerebrospinal fluid; WBC, white blood cells

Table 3:

Characteristics of patients treated with oral or intravenous (IV) antibiotics.

Characteristic[a]	Oral Antibiotics (n=17)	IV Antibiotics (n=24)	Both Oral and IV Antibiotics (n=3)	p-value[b]
Percent of Total (n=44)	39	55	7	n/a
Age (median, interquartile range)	9.6 (7.4–11)	9.8 (7.5–12)	11.1 (9.5–13.4)	p=0.78
Male (n, %)	9 (53)	15 (63)	1 (33)	p=0.54
CSF WBC (median, IQR)	9 (2–19)	39 (15–85)	5 (2–43)	**p=0.003**
Opening Pressure (median, IQR)	35 (24–36)	36 (24–47)	44 (36–52)	p=0.44
Acetazolamide treatment (n, %)	10 (59)	14 (58)	3 (100)	p=0.98
Acetazolamide duration in days (median, IQR)	59 (36–133)	65 (50–99)	92 (20–176)	p=1
Oral Antibiotic duration in days (median, IQR)	14 (13–18)	n/a	12 (12–18)	n/a
IV antibiotic duration in days (median, IQR)	0 (0–1)	18 (13–21)	15 (14–21)	**p=<0.001**
Complete resolution (n, %)	11/14 (79)	17/18 (94)	2/3 (67)	p=0.18
Time to Complete resolution in days (median, IQR)	104 (77–134)	79 (43–112)	245 (63–426)	p=0.29
Follow-up duration in days (median, IQR)	105 (49–162)	130 (23–259)	154 (92–426)	p= 0.84

[a] Categorical variables are described using n (%). Continuous variables are described using median (intraquartile range)

[b] p-values comparing characteristics between children that received only oral or only IV antibiotics (not both) were calculated using chi-square tests for categorical variables and Wilcoxan rank-sum tests for continuous variables.

Table 4:

Characteristics of patients with complete resolution or with residual symptoms.

Characteristic[a]	Complete Resolution (n=30)	Residual Symptoms (n=5)	p-value[b]
Age (median, interquartile range)	9.8 (7.4–11.8)	13.4 (10.8–16.2)	0.19
Male (n, %)	14 (47)	3 (60)	0.66
Median duration of symptoms prior to presentation in days (interquartile range)	20 (9–31)	18 (4–30)	0.49
CSF WBC (median, interquartile range)	18 (2–58)	5 (4–6)	0.29
Opening Pressure (median, interquartile range)	33.5 (23.5–36)	36 (25–36)	0.86
Intravenous antibiotics (n, %)	19 (63)	2 (40)	0.37
Acetazolamide treatment (n, %)	20 (67)	4 (80)	1
Acetazolamide duration in days (median, interquartile range)	63.5 (44.5–129)	41 (21.5–79)	0.31
Resolution at 3 months (n, %)	15 (50)	-	-
Time to Complete resolution in days (median, interquartile range)	94 (57–124)	-	-
Follow-up duration in days (median, interquartile range)	139.5 (94–239)	469 (92–635)	0.32

[a]Categorical variables are described using n (%). Continuous variables are described using median (intraquartile range). 9 patients did not have documented follow-up data.

[b]p-values comparing characteristics between children with complete resolution and children with residual symptoms were calculated using chi-square tests for categorical variables and Wilcoxan rank-sum tests for continuous variables.