Long-Term Neuropsychologic and Health Outcomes of Children With Facial Nerve Palsy Attributable to Lyme Disease

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ABSTRACT. Background. There is little information about the long-term outcomes of children with facial nerve palsy attributable to Lyme disease, a group putatively at high risk for poor neurologic outcomes.

Objective. The purpose of this study is to assess the long-term neuropsychologic and health outcomes of children with facial nerve palsy attributable to Lyme disease.

Methods. We conducted a matched cross-sectional study of children with facial nerve palsy in Connecticut who met the Centers for Disease Control and Prevention national surveillance case definition for Lyme disease. We identified children with facial nerve palsy attributable to Lyme disease from population-based data for the state of Connecticut from 1984 to 1991 as well as from selected clinical practices from 1984 to 1998. For each case, 2 controls without Lyme disease, matched by age, were selected by sequential digit dialing technique. Both patients and controls (or their parents) were interviewed using structured questionnaires. Outcomes included self/parents’ reports both of symptoms and of abilities to perform normal daily activities since the diagnosis was made (or for an equivalent period of time for controls). In addition, the patients with facial nerve palsy attributable to Lyme disease were evaluated with a battery of neuropsychologic tests.

Results. Of the 43 patients, 30% were female and 93% were white. Median age at diagnosis was 8 years (range: 2–18 years). Mean time to follow-up was 49 months (range: 7–161 months). Of the patients, 16% had been treated parenterally with ceftriaxone and 84% had been treated orally with either doxycycline or amoxicillin. Overall, 79% believed they were cured of Lyme disease, 9% believed they were not cured, and 12% did not know. The proportions of patients and of matched controls that reported increased problems with normal daily activities (eg, exercise, academic performance, word recall, sleeping) were similar. Patients with facial nerve palsy attributable to Lyme disease were more likely than matched controls to report symptoms of neck pain, changes in behavior, pains in joints or muscles, numbness or funny sensations in nerves, and problems with memory, but three quarters of them did not attribute these problems to Lyme disease. Twenty patients agreed to undergo neuropsychologic testing; all had average to above average scores on tests of IQ (eg, mean IQ was 110.2), memory, learning, attention, concentration, math, reading and spelling performance, executive functioning, abstract thinking, sequential processing, visuospatial scanning, and motor speed. There were no apparent differences in outcomes between children who received oral versus parenteral treatment.

Conclusions. The neuropsychologic and health outcomes of children with facial nerve palsy attributable to Lyme disease 7 to 161 months earlier are comparable to those who did not have Lyme disease. Pediatrics 2003;112:e93–e97. URL: http://www.pediatrics.org/cgi/content/full/112/2/e93; Lyme disease, facial nerve palsy, long-term outcomes, and neuropsychologic outcomes.

Lyme disease is caused by the spirochete Borrelia burgdorferi that is transmitted to humans by Ixodes ticks. First described in Connecticut in the late 1970s by Steere et al, Lyme disease is a multisystem disorder with 3 clinical stages that include dermatologic (erythema migrans), cardiac (heart block, carditis), neurologic (facial nerve palsy, meningitis, meningoencephalitis), and rheumatologic (arthritis) symptoms. Peripheral cranioptaxy or facial nerve palsy is the single most common neurologic manifestation of Lyme disease in children. In many cases, it may be the only neurologic abnormality present and it can develop without an antecedent erythema migrans rash. Lyme disease is identified as the causative agent in up to 25% of all cases of facial nerve palsy in children who reside in endemic areas. Although more common in Europe, facial nerve palsy is found in ~3% to 5% of all children with Lyme disease in the Unites States. We are particularly interested in children with facial nerve palsy attributable to Lyme disease because they are a group that may be at particularly high risk for adverse neuropsychologic sequelae, because a high proportion have pleocytosis of the cerebrospinal fluid.

The pathophysiology of facial nerve palsy involvement in Lyme disease is poorly understood. For example, it is not well known whether the infection affects the facial nerve by direct invasion of the organism or via indirect immune mechanisms, nor whether the palsy is primarily attributable to an effect solely on the peripheral nerve or to an effect on the central nervous system. These uncertainties may explain why the clinical management of these patients, particularly with respect to diagnostic testing and treatment, vary widely among practitioners.

The inclusion of a lumbar puncture as part of the diagnostic evaluation in children with facial nerve palsy when Lyme disease is suspected is controversial, especially since studies have found a high fre-
frequency of abnormalities of the cerebrospinal fluid (pleocytosis, elevated protein concentration, and/or intrathecal production of antibodies) even in children without signs of central nervous system involvement. Furthermore, some patients with facial nerve palsy attributable to Lyme disease are treated with oral antimicrobials, whereas others are treated with parenterally administered antibiotics.

Despite the generally favorable outcomes of children with facial nerve palsy attributable to Lyme disease reported in previous studies, some of which included children who never received treatment for the disease, there is widespread concern about possible long-term neurologic sequelae. Several reports in adults have suggested that there may be adverse cognitive effects from Lyme disease, particularly in memory processes (short-term and long-term memory), intelligence, information processing speed, fine-motor dexterity, problem solving, and new learning. No studies have specifically evaluated the long-term outcomes of children with facial nerve palsy attributable to Lyme disease. The aim of this study is to assess the long-term neuropsychologic and health outcomes of children with facial nerve palsy attributable to Lyme disease.

METHODS

Study Population

The study population consisted of children and adolescents between the ages of 2 and 18 years who resided in Connecticut and developed facial nerve palsy attributable to Lyme disease. Patients were identified from 2 separate sources: from all reports of patients with Lyme disease to the State of Connecticut Department of Public Health from 1984 to 1991 and from all patients from 11 clinical practices from 1984 to 1996, which included 6 general pediatric practices, 2 pediatric neurologists, and 3 pediatric infectious diseases specialists. These practices were chosen because they are among the largest pediatric practices in the state of Connecticut. Ten of the case subjects participated in a prior study of Lyme disease, but they did not previously undergo neuropsychologic testing.

Enrollment Criteria

Children 2 to 18 years of age at the time of diagnosis with facial nerve palsy attributable to Lyme disease that was diagnosed at least 6 months before enrollment were eligible for the study. We defined cases of Lyme disease according to the Centers for Disease Control and Prevention national surveillance case definition; thus, all cases had facial nerve palsy and either erythema migrans or positive serology.

For each case, 2 controls without a previous history of Lyme disease were matched by age (±1 year for those <2 years of age, ±2 years for those 2 to 10 years of age, ±3 years for those 11 to 18 years of age). Controls were selected by sequential digit dialing, a technique in which telephone numbers are dialed sequentially.

Questionnaires

Cases and matched controls (or their parents for subjects under 16 years of age or if unavailable for the interview) were interviewed by telephone using structured questionnaires. The questionnaires included data on demographics, comorbidity, education, review of systems, medications, memory, and cognitive function. For patients only, we asked whether they thought they were cured of Lyme disease. For both patients and controls, we asked whether they noticed any changes in the frequency of certain symptoms since the diagnosis, or for a comparable time interval for controls. We also asked about any difficulties in their abilities to perform normal daily activities. Socioeconomic status was assessed with the Hollingshead index.

Medical Records

The medical records of all case subjects were reviewed.

Neuropsychologic Testing

To assess possible abnormalities that were not apparent to either the patient or the parent, we invited patients who had Lyme disease to undergo age-appropriate standardized neuropsychologic tests. The following are the tests that were administered: 1) the Stanford Binet 4th edition for intelligence (IQ) and overall cognitive functioning has a well-standardized memory domain and is appropriate for the entire range of ages of the participants in the study; 2) the Children’s Memory Scale for memory and for both auditory/verbal and visual/non verbal learning as well as for attention/concentration is a comprehensive learning and memory test for children ages 5 through 16 years; 3) for persons aged 16 years or older, the Wechsler Memory Scale was used to assess general, verbal, and visual memory, as well as attention, concentration, and delayed recall; 4) the Kaufman Test of Educational Achievement was used to assess math, reading, and spelling competence; 5) the Wisconsin Card Sorting Test: Computer Version was used to assess executive functioning, abstract thinking, and perseveration; 6) the Trail Making Test was used to assess sequential processing, visuospatial scanning, motor speed, mental flexibility, and sustained concentration. The latter 2 tests require the ability to perform strategic planning, to use feedback, to shift cognitive sets, and to concentrate. In addition, they require visuospatial scanning, motor speed, and impulse control. All tests were administered by child psychologists and trained research assistants at the Yale Child Study Center and took from 2 to 5 hours to complete.

Statistical Analysis

The data were analyzed using standard statistical techniques. All analyses were 2-tailed; values of <0.05 were considered statistically significant. Mean values were compared using the 2-sample t test for equality of means. For the matched analysis, relative risks, their associated 95% confidence intervals, and the statistical significance of differences were calculated with the use of True Epistat.

This study was approved by the Yale University School of Medicine Human Investigations Committee. Informed consent was obtained from all study subjects and/or from their guardians.

RESULTS

Characteristics of the Patients With Facial Nerve Palsy Attributable to Lyme Disease

We identified 58 children with facial nerve palsy attributable to Lyme disease that met our criteria for enrollment. Thirteen of the children could not be located and 4 declined to participate in the study. Of the 43 children enrolled in the study, age at the time of diagnosis ranged from 2 to 18 years (median: 8 years). A mean of 49 months had elapsed from the time of diagnosis to the time of the interview (median: 44; range: 7–161 months). All of the case subjects met the Centers for Disease Control and Prevention surveillance case definition for Lyme disease. Thirteen (30%) of the patients were female and 40 (93%) were white. Thirteen (30%) had erythema migrans at the onset of facial nerve palsy attributable to Lyme disease. The majority of the interviews were completed by either a parent or a guardian (79% of the cases and 80% of the controls).

As is the case with most patients with facial nerve palsy attributable to Lyme disease, all case subjects in the study had peripheral facial nerve palsy with both the forehead and the eye affected, indicating a
TABLE 1. Are You Cured of Lyme Disease?

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
<th>Relative Risk</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes*</td>
<td>34 (79%)</td>
<td></td>
<td>2.9 (2.0–4.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>No†</td>
<td>4 (9%)</td>
<td></td>
<td>2.6 (1.7–4.0)</td>
<td>0.006</td>
</tr>
<tr>
<td>Don’t know‡</td>
<td>5 (12%)</td>
<td></td>
<td>2.5 (1.5–4.2)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

* Five (12%) answered Yes, except for the palsy. However, 1 patient had significant residual facial nerve palsy documented in the medical record—a child born with congenital ptosis.
† 1. Occasional headaches and fatigue.
2. Heard the disease could remain dormant in one’s body.
3. Parent sees occasional red rings around joints.
4. Occasionally hears popping sounds at joints, especially if moving.
‡ 1. Frequent body aches and headaches.
2. Last time test, the Lyme disease blood test was still positive.
3. Occasional knee pain.
4. Overweight since the diagnosis.
5. Headaches.

Outcomes

Of the patients, 34 (79%) reported that they believed they were cured of Lyme disease, 4 (9%) believed they were not cured, and 5 (12%) did not know or were unsure if they were cured. Reasons for their answers are shown in Table 1. Although the number of patients who received parenteral therapy for Lyme disease was small, their outcomes were similar to those who were treated orally: 71% (5 of 7) believed they were cured and 29% (2 of 7) did not know. Depending on the specific question, from 0% to 21% of patients reported either increases in symptoms or difficulties performing normal daily activities since the diagnosis (Table 2); however, these rarely were attributed to Lyme disease.

Neuropsychologic Testing

Twenty patients agreed to undergo standardized neuropsychologic testing. The characteristics of these 20 were similar to those of the entire cohort. Median age at the time of diagnosis was 8 years (range: 3–17 years). A mean of 48 months had elapsed from the time of diagnosis to the time of the interview (range: 7–161 months). On all measures, subjects scored either average or above average (Table 3). Results of the tests of executive functioning ability, such as strategic planning, concentration, and use of feedback were all normal.

Twenty percent underwent lumbar puncture and 80% believed they were cured of Lyme disease. The subjects who underwent lumbar puncture had similar scores to those who did not undergo lumbar puncture.
There is concern that unfavorable long-term neuropsychologic sequelae may develop in patients after facial nerve palsy attributable to Lyme disease—regardless of whether patients had signs or symptoms of central nervous system involvement at presentation. This is the first study to evaluate the long-term outcomes, including possible neuropsychologic sequelae, specifically of children with facial nerve palsy attributable to Lyme disease. We assessed the health and neuropsychologic long-term outcomes of 43 children with facial nerve palsy attributable to Lyme disease obtained from various sources of data-surveillance reports to a state department of public health, offices of general pediatricians, pediatric neurologists, and infectious diseases specialists. We believe that having chosen subjects with facial nerve palsy attributable to Lyme disease from these varied sources of data allowed us to cover the wide spectrum of the disease.

Overall, results of recovery from facial palsy in our study are in agreement with previous reports showing that the recovery in patients with facial nerve palsy attributable to Lyme disease is very good and is similar to that of patients with idiopathic or Bell’s palsy. Four subjects in our study thought they were not cured of Lyme disease and 5 were unsure; however, their reported persisting symptoms appear to be nonspecific and do not suggest continuing infection as a cause. Although the number of children who received parenteral therapy in our study was small, there did not appear to be any differences in the outcomes of children treated parenterally compared with those who received oral therapy.

Patients who had facial nerve palsy attributable to Lyme disease occasionally reported increases in symptoms or difficulties with normal daily activities since their diagnosis; however, few attributed them to Lyme disease. Compared with age-matched controls, children with facial nerve palsy attributable to Lyme disease were more likely to report symptoms of occasional neck pain, changes in their behavior, pains in the joints and muscles, numbness or funny sensations in the nerves, and problems with memory. This may be explained, in part, by reporting bias (ie, a patient may be more likely to report minor pain if they are labeled as having Lyme disease). Moreover, there were no significant differences in reported problems in normal daily activities between the 2 groups.

We assessed the possibility of long-term cognitive sequelae by administering well-accepted neuropsychologic tests, as objective measures of outcomes, and found that the results were well within the normal range. Furthermore, by self or parent’s reports, children with a previous history of facial nerve palsy attributable to Lyme disease were not more likely to report difficulties in academic performance, doing schoolwork, or attendance of school than were controls, which supports the results of the cognitive tests.

Previously, Adams et al27 had examined possible cognitive sequelae of Lyme disease in 41 children and found no deficits 2 years after disease onset, but only a small proportion of the children in their study had facial nerve palsy. The differences in neuropsychologic outcomes between our results and occasional reports of cognitive difficulties in adult patients with Lyme disease may be attributable, in part, to intrinsic differences between the 2 age groups—including the occurrence of senile dementia, normal aging, etc. Another plausible explanation is that these reported cognitive difficulties are unrelated to Lyme disease because, even in adults, reports of poor outcomes are rare. Recently, Kalish et al28 conducted a follow-up evaluation of adult patients with Lyme disease and found no deficits 2 years after disease onset, but over, there were no significant differences in reported problems in normal daily activities between the 2 groups.
impressions of the children and of the parents of children who had had facial nerve palsy attributable to Lyme disease. This may, in part, explain some of the differences in reports of symptoms between cases and controls, because persons labeled as having had Lyme disease may be more likely either to notice or to report a given symptom than those never diagnosed with Lyme disease. It is also possible that the parental perceptions may have been influenced by their concerns and anxieties about the disease and may have affected their responses. We did not examine the patients; however, we carefully reviewed the medical records to confirm self or parental reports in the interview forms. The fact that patients did not attribute their reported symptoms to Lyme disease does not exclude the possibility that they were attributable to Lyme disease.

CONCLUSIONS

Our results indicate that the long-term neuropsychologic and health outcomes of children with facial nerve palsy attributable to Lyme disease 7 to 161 months earlier are comparable to those of children who did not have Lyme disease.

ACKNOWLEDGMENTS

This work was supported by a Robert Wood Johnson Foundation Minority Medical Faculty Development Award (to Dr Vázquez), a grant from the National Institutes of Health (K24-A101703), and a grant to the Yale Children’s Clinical Research Center from the General Clinical Research Centers, Program of the National Center for Research Resources (MO1-RR06022).

We thank Diane Goudreau, Amy Catalano, Julie Klunk, Stephanie Davis, and Nancy Holabird for their participation in data collection. We also thank the following for their invaluable contribution: David Goudreau, Amy Catalano, Julie Klunk, Stephanie Davis, and Nancy Holabird.

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