

## Brief Reports

### ENTEROVIRAL TESTING AND LENGTH OF HOSPITAL STAY FOR CHILDREN EVALUATED FOR LYME MENINGITIS

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**Abstract—Background:** In Lyme disease–endemic areas, many children with aseptic meningitis are hospitalized while awaiting Lyme serology results. Although Lyme serology takes several days, an enteroviral polymerase chain reaction (EV PCR) test takes only a few hours to return results. **Objective:** Our aim was to measure the impact of EV PCR testing on duration of stay for children evaluated for Lyme meningitis. **Methods:** A retrospective cohort study was performed with children evaluated for Lyme meningitis at 3 Emergency Departments located in Lyme disease–endemic areas. We defined Lyme meningitis using the Centers for Disease Control and Prevention criteria (either positive Lyme serology test result or an erythema migrans rash). The duration of stay was compared by EV PCR test result (positive, negative, and not obtained). **Results:** There were 423 study patients identified, 117 (28%) of whom had Lyme meningitis and 209 (49%) had an EV PCR test performed. Median length of stay varied by the EV PCR test status: children with a positive EV PCR test ( $n = 103$ ; 28 h; interquartile range 17–48 h), those with a negative EV PCR test ( $n = 106$ ; 72 h; interquartile range 48–120 h), and those who did not have an EV PCR test obtained ( $n = 214$ ; 48 h; interquartile range 24–96 h;  $p \leq 0.001$ ). **Conclusions:** Rapid EV PCR testing could assist clinical decision making by Emergency Physicians, avoiding

potentially unnecessary hospitalization and parenteral antibiotics for children at low risk of Lyme meningitis. © 2013 Elsevier Inc.

**Keywords—**enterovirus; polymerase chain reaction test; Lyme disease; meningitis

#### INTRODUCTION

Enteroviral meningitis, the most commonly identified cause of aseptic meningitis, and Lyme meningitis have many overlapping clinical features (1–4). While children with enteroviral meningitis require only supportive care, those with Lyme meningitis are treated with parenteral antibiotics.

In Lyme disease–endemic areas, some children with cerebrospinal fluid (CSF) pleocytosis will have Lyme rather than enteroviral meningitis (5). Many children in whom the diagnosis of Lyme meningitis is considered are hospitalized and receive empiric parenteral antibiotics, even when the risk of bacterial meningitis is very low (6,7). While Lyme serology tests take an average of 3 to 4 days, newer enteroviral polymerase chain

reaction (EV PCR) tests of the CSF can confirm the presence of the viral genome within hours, potentially while the patient is still in the Emergency Department (ED). Lyme CSF PCR tests, however, have very low sensitivity and are not generally helpful (8).

To determine the impact of the EV PCR test on the care of children evaluated for Lyme meningitis, we assembled a multicenter cohort of children with CSF pleocytosis presenting to the ED. In our study population, we compared length of stay and duration of parenteral antibiotics based on EV PCR testing status.

## METHODS

We performed a retrospective cohort study of children 1 to 18 years of age with CSF pleocytosis (CSF white blood cells [WBC]  $\geq 10$  cells/mm<sup>3</sup>) who presented to one of three EDs located in Lyme disease–endemic areas between 1996 and 2010 (study period varied by study site). All study patients also had peripheral Lyme serology obtained with results available in the hospital medical record. We excluded patients who had any of the following: a positive CSF Gram stain, critical illness, presence of a ventricular shunt or recent neurosurgery, immunosuppressive conditions, or focal bacterial infections requiring parenteral antibiotics and antibiotic pretreatment within 72 h of diagnostic lumbar puncture. Details of the study protocol have been described previously (9). The Institutional Review Board of each participating center approved the study protocol with a waiver of informed consent.

CSF EV PCR test results were categorized as positive or negative. We defined a case of Lyme meningitis as a child with CSF pleocytosis and either physician-documented erythema migrans rash or a positive Lyme serology (IgM or IgG antibodies) (10). Patients with a rise between acute and convalescent Lyme titers were also considered to have Lyme meningitis.

We defined the length of stay as the time from ED triage to discharge from either the ED or the hospital. For admitted patients, we used the time the discharge order was written. To reflect actual antibiotic coverage, we defined the duration of parenteral antibiotics as the time from first to last dose of parenteral antibiotics plus the standard antibiotic dosing interval. The timing of antibiotic administration was determined by review of the hospital medication administration record.

Our primary goal was to determine the impact of the EV PCR test on the clinical management of study patients. First, we compared the clinical characteristics of patients who were tested with those who were not tested. Next, we compared the length of stay for the following three groups of patients by EV PCR test status: no EV PCR test performed, negative EV PCR test, and positive EV PCR test.

As duration of stay might also vary based on a patient's risk of Lyme meningitis, we used a previously validated Lyme meningitis clinical prediction rule that calculates the risk of Lyme meningitis based on the duration of headache, presence of cranial nerve palsy, and percent CSF mononuclear cells (9,11,12). We used a Poisson regression model to compare duration of stay after adjusting for risk of Lyme meningitis as well as hospital center. Lastly, for those patients without Lyme meningitis, we compared the duration of parenteral antibiotics for children with a negative vs. positive EV PCR test result.

We compared medians with Mann-Whitney test and proportions using the  $\chi^2$  test. Confidence intervals for proportions were calculated using the exact binomial method. All analyses were conducted with SPSS Statistical Software, version 19 (SPSS Corporation, Chicago, IL).

## RESULTS

We identified 546 patients, of these, 423 (77%) met inclusion criteria. Of these, 117 (28%) had Lyme meningitis and none had bacterial meningitis. All of the children with Lyme meningitis had positive Lyme serology. Ninety-three percent of the children were admitted to the hospital and 59% presented between June and October (peak enteroviral season).

EV PCR tests were performed in 209 (49%) patients. The proportion of children who had an EV PCR test obtained varied by hospital center (39%, 46%, and 65% of study patients at hospitals 1, 2, and 3, respectively). Patients who had an EV PCR test performed were more likely to present during peak season and had slightly higher triage temperatures, CSF WBC counts, and CSF absolute neutrophil counts. Clinicians were less likely to obtain an EV PCR test in children who were ultimately diagnosed with Lyme meningitis (Table 1).

The EV PCR test was positive in 103 (49%) of the 209 children tested. Median length of stay (LOS) varied by the EV PCR test status: children who did not have an EV PCR test performed ( $n = 214$ ; LOS 48 h; interquartile range [IQR] 24–96 h); those with a negative EV PCR test ( $n = 106$ ; LOS 72 h; IQR 48–120 h); and those with a positive EV PCR test ( $n = 103$ ; LOS 28 h; IQR 17–48 h;  $p < 0.001$ ). After adjustment for risk of Lyme meningitis using a previously validated Lyme meningitis prediction rule (8), as well as hospital center, children with a positive EV PCR test had a shorter duration of stay than those with a negative test (LOS 26 h; 95% CI 17–33 h).

Children with Lyme meningitis were treated with parenteral antibiotics for a median duration of 21 days (IQR 14–28 days). For the 176 children without Lyme meningitis who had an EV PCR test performed, the median

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