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Accuracy of physical signs for detecting meningitis: A hospital-based diagnostic accuracy study

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ABSTRACT

Objectives: To evaluate accuracy of physical signs for detecting meningitis.
Patients and methods: We enrolled patients aged 12 years or more, admitted with acute encephalitis syndrome (fever, headache, altered mental status, vomiting, seizures, neurodeficit) to a rural teaching hospital. The design was a double-blind, cross-sectional analysis of consecutive patients, independently comparing signs of meningeal inflammation (nuchal rigidity, head jolt accentuation of headache, Kernig's sign and Brudzinski's sign) elicited by internal medicine residents against an established reference standard (cerebrospinal fluid white cell count >5 white cells/μL). Diagnostic accuracy was measured by computing sensitivity, specificity and likelihood ratios (LRs) and their 95% confidence interval (CI) values.
Results: Of 190 patients (119 men, 71 women; ages 13–81 years; mean 38(SD 18) years) CSF analysis identified meningitis in 99 (52%; 95% CI 44, 59%) patients. No physical sign of meningeal irritation could accurately distinguish those with and without meningitis: nuchal rigidity (LR+ 1.33 (0.89, 1.98) and LR− 0.86 (0.70, 1.06)), head jolt accentuation of headache (LR+ 5.52 (0.67, 44.9) and LR− 0.95(0.89, 1.00)), Kernig's sign (LR+ 1.84 (0.77, 4.35) and LR− 0.93(0.84, 1.03)) and Brudzinski's sign (LR+ 1.69 (0.65, 4.37) and LR− 0.95 (0.87, 1.04)).
Conclusion: Physical signs of meningeal inflammation do not help clinicians rule in or rule out meningitis accurately. Patients suspected to have meningitis should undergo a lumbar puncture regardless of the presence or absence of physical signs.

1. Introduction

Meningitis is an important cause of morbidity and mortality, worldwide. Bacterial meningitis is among the 10 most common infectious causes of death and kills estimated 135,000 people throughout the world each year [1]. It is estimated that about a quarter of adults with bacterial meningitis [2,3], and a third of all patients with tuberculous meningitis die [4]. Another one-fourth of survivors develop transient or permanent neurologic morbidity [2,3]. Early recognition of this serious infection in primary care settings is important; so as to initiate timely life saving treatments and appropriate referrals. This in turn can reduce mortality and morbidity in meningitis.

For over 100 years, clinicians have used three physical signs – nuchal rigidity, Kernig's and Brudzinski's signs – to help diagnose meningitis at bedside and to decide need for lumbar puncture, or more intensive care. Although Verghese and Gallemore [5] argued that "the physical signs of meningeal irritation may aid in early diagnosis and treatment of meningitis and are excellent demonstrations for medical students and house staff of the art of the bedside examination", there is limited information about the accuracy of these signs for detection of meningitis. A prospective cross-sectional study [6] has concluded that physical signs do not accurately discriminate between patients with and without meningitis (Kernig's sign (sensitivity, 5%; likelihood ratio for a positive test result (LR+), 0.97)), Brudzinski's sign (sensitivity, 5%; LR+, 0.97), and nuchal rigidity (sensitivity, 30%; LR+, 0.94). Another study [7] that evaluated 54 patients with fever and new headaches reported that jolt accentuation of headache may be the best sign for meningitis (sensitivity, 97%; LR+, 2.4).

Despite poor accuracy, the physical signs of meningeal irritation continue to be part of bedside clinical teaching and practice. In resource limited settings, cerebral malaria, tuberculous meningitis and bacterial meningitis are close differential diagnoses in patients with fever and impaired mental status. In these settings clinicians cannot always perform a lumbar puncture or lack access to cerebrospinal fluid (CSF) microscopy. They, therefore, use clinical signs to distinguish meningitis from encephalopathy such as cerebral malaria. It is important for the clinicians to know if the signs of meningeal irritation are accurate enough to obviate the need for CSF examination. We carried out this study to find out the diagnostic accuracy of four physical signs – nuchal rigidity, jolt

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accentuation of headache (hereafter called head jolt sign), Kernig's sign and Brudzinski's sign – to detect meningitis among hospitalized patients, 12 years of age or older, suspected to have meningitis with cerebrospinal fluid cell count as the reference standard.

2. Subjects and methods

2.1. Patients, setting and data collection

This study was performed at a 620 bed teaching hospital with 400,000 patient visits and about 10,000 patient admissions to the internal medicine wards, each year. Typically about 200 patients with fever, headache and altered mental status (clinically classified as acute encephalitis syndrome or AES) seek care at this hospital every year [8]. These patients typically are usually tested for malaria (microscopy and rapid diagnostic tests) and evaluated for a metabolic encephalopathy (glucose, electrolytes and renal panel tests). Patients testing negative for malaria and not found to have a metabolic encephalopathy undergo a lumbar puncture and CSF microscopy to determine cause of AES. Treating physicians use on admission Glasgow coma score (GCS) to grade severity of disease, and make a final diagnosis based on clinical profile, results of CSF based tests, clinical biochemistry, and neuro-imaging.

For a period of 1-year, beginning May 2008, we prospectively enrolled all consecutive patients with AES (fever, headache, and altered mental status, with or without seizures or focal neurological deficit) in whom treating physicians had ordered CSF examination. Blind to the diagnosis, physical findings and laboratory data, the ICU residents, who were aware of the study, used standardized examination techniques [1] to elicit the following physical signs on each patient before they underwent a lumbar puncture.

Physical sign	Method of elicitation	Positive test
Nuchal rigidity	With the patient in the supine position, the resident gently flexed the neck, asking the patients to touch their chin to sternum	Resistance to flexion
Jolt accentuation of the patient's headache	The resident asked the patients to turn their heads horizontally at a frequency of 2–3 rotations per second	Worsening of the base line headache
Kernig's sign	With the patient in the supine position, the resident lifted the knee in flexed position until maximal hip flexion was obtained. The leg was extended at the knee and resistance was checked	Resistance to extension at the knee to >135° or pain in the lower back or posterior thigh
Brudzinski's sign	With the patient in the supine position, the resident flexed the neck, and looked for flexion of both the lower limbs	Flexion of the knees and hips

ICU resident recorded the results of these tests on a specially designed sheet. This sheet was folded, and sealed to ensure that index tests were interpreted blinded to and independent of the reference standard. Before performing lumbar puncture the sealed recording-sheet was deposited in a box placed in the intensive care unit of the hospital.

Since lumbar punctures are often done in the middle of night and cells in the CSF need to be counted within 30 min of a lumbar puncture, a medicine resident (SW) underwent training to do CSF cell counting using a haemocytometer (Neubauer's chamber). The methodology was pilot tested and cell counts performed by the medical resident and an experienced microscopist were compared and shown to be reproducible in a set of 25 patients. It was ensured that time-interval between recording of physical signs, lumbar puncture, and CSF cell counting does not exceed 60 and 30 min, respectively. The resident (SW) was blind to the history and results of the physical examination until after the CSF counts were entered in data collection forms.

Meningitis was defined as >5 white blood cells/μL of CSF. Patients were excluded from the study if lumbar puncture was traumatic (defined as either grossly bloody CSF, or if red blood cell count in CSF was >400 cells/μL). A differential count was also obtained from the wet smear. Additional tests (CSF sugars, proteins, and bacterial cultures) were performed in all samples as a standard of care. Further CSF tests (e.g. mycobacterial cultures, specific viral diagnostics) were ordered based on discretion of the treating physician, cost, and availability.

The study protocol was approved by the institutional ethics committee, and consent was obtained from patients or their relations to elicit physical signs and to do lumbar punctures.

2.2. Statistical analysis

We assessed the accuracy of physical signs in diagnosing meningitis by calculating sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios. In a post hoc analysis we estimated diagnostic accuracy of physical signs by sub-classifying individuals with meningitis by [1] severity of meningeal inflammation: mild (CSF cells 6–100/μL), moderate (101–1000 cells/μL) and severe (>1000 cells/μL); [2] predominant cells in CSF: lymphocytes, neutrophils, and mixed, using 75% cells as a cutpoint; [3] tertiles of Glasgow coma score and [4] discharge diagnosis of type of meningitis (aseptic, tuberculous or bacterial). We used diagti command in STATA (version 10, Stata Corp. College Road, TX, USA) to calculate point estimates of accuracy and their 95% confidence intervals.

3. Results

We have used STARD (Standards for Reporting Diagnostic Accuracy Study) guidelines to report this study. Figure shows the study profile. Between May 2008 and July 2009, we enrolled 204 patients. We could not use data from 14 patients because the lumbar puncture was traumatic. Thus, our final sample consisted of 190 patients (119 men, 71 women); ages 13–81 years [mean 38 (SD 18) years]. CSF analysis identified meningitis in 99 of 190 (52%) patients. The diagnosis based on clinical profile, cerebrospinal fluid findings, and neuro-imaging for these 99 patients was aseptic meningitis ($n = 62$ (63%)), tuberculous meningitis ($n = 30$ (31%)) and bacterial meningitis ($n = 7$ (7%)). There were only seven patients with confirmed bacterial meningitis, and 13 with a predominantly neutrophilic leucocytosis. The final discharge diagnosis of those classified in non-meningitis group ($n = 91$) consisted of acute encephalitis of undermined etiology, acute hepatic encephalopathy, metabolic encephalopathy, alcoholic encephalopathy, cerebral malaria, brain abscess, delirium, pesticide poisoning, seizure disorder, sepsis, stroke and subdural haemorrhage.

Table 1 describes patient characteristics according to the presence ($n = 99$) or absence ($n = 91$) of meningitis. Also, shown in this