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Case study

Natural history of headache in patients with lymphocytic meningitis following lumbar puncture

Alexander Khlebtovsky *, Shlomit Yust-Katz, Arieh Kuritzky, Israel Steiner

Department of Neurology, Rabin Medical Center, Beilinson Hospital, Petach Tikva, Israel
Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

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ABSTRACT

Background: Analysis of cerebrospinal fluid (CSF) obtained by lumbar puncture (LP) is essential for diagnosis of meningitis. What is the impact of the procedure upon the natural history of headache and associated signs in patients with lymphocytic meningitis and what factors can have prognostic value for the future progression of symptomatology? This study was aimed at looking into these questions.
Methods: One hundred and one patients with clinical and laboratory diagnosis of aseptic meningitis answered a questionnaire intended at assessing the severity and nature of headache and meningeal irritation signs before and one, and twenty four hours after the LP. Later they were divided into three groups according to presence and type of headache after 24 h. Demographic and clinical data was obtained from patients files.
Results: There was almost 50% improvement in headache severity and associated signs after 24 hours from LP in the whole group of patients. Patients that did not have pain after 24 hours had higher BMI and lower headache severity one hour after LP compared to patients in the other groups ($p = 0.064$ and $p = 0.005$). Patients with papilledema had higher incidence of post dural puncture headache (PDPH).
Conclusions: Our study shows that patients with aseptic meningitis undergo improvement in all parameters of headache and also in signs of meningeal irritation following LP. Higher BMI and low headache intensity are positive prognostic factors for improvement of headache after 24 hours while papilledema is associated with a higher incidence of PDPH.

1. Introduction

Aseptic meningitis is defined as meningeal inflammation without identification of bacterial pathogen on gram staining [1]. Causes of aseptic meningitis include mainly infectious, inflammatory and neoplastic processes [2]. Enteroviruses and herpes simplex virus type 2 (HSV-2) are the most common viral pathogens, responsible for aseptic meningitis in adults [3]. The CSF reveals signs of inflammation: mononuclear pleocytosis, elevated protein and normal glucose levels and sometimes elevated intracranial pressure [4].

Lumbar puncture (LP) is an essential procedure for the diagnosis of meningitis [5]. Known for more than a century and despite many modifications, it is not an innocent, trivial procedure. Possible complications of LP include bleeding and local infection, and under conditions causing increased intracranial pressure brain herniation [6]. However, the most common complication is the distinctive type of head pain named post dural puncture headache (PDPH). It complicates almost 25% of LPs and is characterized by marked exacerbation on sitting or standing [7].

Does the LP have influence on the natural history of headache and on the other clinical signs of meningitis? Who are the patients that will continue to suffer from headache for an extended period of time? Are there conditions that are associated with quick improvement of headache? These issues are the focus of the present study.

2. Patients and methods

Patients were enrolled between January 2010 and December 2015 in a tertiary medical center. The study was approved by the local ethical committee. All patients recruited into the study were admitted to the neurological department with the diagnosis of aseptic meningitis. LP was performed using thraumatic needle of Quinke type, in the emergency room.

* Corresponding author at: Department of Neurology, Rabin Medical Center – Beilinson Hospital, Petach Tikva 49100, Israel. Fax: +972 3 9378220.
E-mail address: santech76@yahoo.com (A. Khlebtovsky).

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Following the results of the LP and the CSF analysis suggesting aseptic meningitis patients received an explanation about the study and were asked to sign the informed consent form. Including criteria was abnormal CSF content, and not clinical grounds. The cutoff for inclusion was more than 10 mononuclear cells in CSF and negative gram-staining of the liquor. Those patients that agreed to participate were asked to complete a questionnaire.

The questionnaire consisted of pre and post LP parts. The pre LP part was filled retrospectively, after the LP was performed, and following signature of the informed consent. It included information on history of headache episodes, headache intensity during the current event, and characteristics of the headache: quality, location, severity (rated on a scale from 1 to 10) and associated symptoms (nausea, vomiting, tinnitus, and phono- and photophobia). In addition, participants were asked to rate their stress before the LP on a scale from 0 (no stress) to 10 (extreme stress). In the post LP part of the questionnaire, patients were asked to report on the presence of headache at one and 24 hours after LP, quality and severity of the headache, its postural and associated symptoms and subjective relief of the headache severity one hour after the LP.

Data on patient characteristics (age, sex, BMI, fever, treatment with anesthetics before and after LP, papilledema) were collected from the medical records. Papilledema was diagnosed by ophthalmologist in emergency department using direct fundoscopy method. It also included needle size (22G or 24G), opening pressure, traumatic tap, number of punctures, physician experience when performing LP (recorded for the study as less than 1 year, 1–5 years and more than 5 years of experience). Data on CSF content (cells, glucose, protein), serum WBC and CRP levels were also collected.

Finally, according to the presence and type of headache after 24 hours patients were categorized into three groups: i) patients without headache after 24 h, ii) patients with headache after 24 h, iii): patients with PDPH that was defined according to the International Headache Society (IHS) guidelines (ICHS-II 7.2.1) [8].

Patients with non-infectious causes of meningitis such as inflammation (i.e. systemic lupus erythematosus) or malignancy (lymphoma) were excluded from the study. Likewise, because of the fact that low CSF pressure can be associated with pleocytosis, patients with suspected low pressure headache diagnosed according to IHS guidelines (ICHS-II 7.2.3) [8] were not included in the study.

In order to rule out the possibility of development of chronic headache after meningitis all patients were followed up for six months. Chronic headache was defined as new complaints of headache that lead to at least two visits to the physician. Patients that developed chronic headache or were lost for follow up were excluded from the study.

Based on these inclusion and exclusion criteria all patients that remained in the study conformed with the ICHS-II criteria of lymphocytic headache (code 9.1.2) [8].

3. Statistical analysis

The statistical analysis was based on SAS Software, Version 9.4. Continuous variables were presented by Mean ± Std, Categorical variables were presented by (*N*, %). *T* test was used to compare the value of continuous variables between study groups with two categories. ANOVA, with Tukey's correction for multiple comparisons, was used for study groups with more than two categories, and Chi-Square was used to compare the values of categorical variables between study groups. *P* values of less than 0.05 were considered significant.

4. Results

4.1. Patients characteristics (Table 1)

Hundred and one patients participated in the study. All suffered from headache before LP. Seventy-five had meningeal irritation signs on examination.

Demographic data of the entire group and division into the three groups of patients are presented in Table 1. Mean age of the patients in the study was 31.33 ± 10.3. Fifty one patients were females. Twenty three patients were chronic smokers. Twenty five had previous headache history. Thirty nine hospitalizations were during the summer and the month of September. Mean BMI for the entire group was 24.52 ± 4.7 m^2/kg. Patients with no headache after LP (group 1) had a trend for higher BMI compared to the other groups (26.73 ± 7.23 vs 23.98 ± 3.38 and 23.97 ± 4.17 for groups two and three respectively; $p = 0.064$). No other difference in season of hospitalization, age, gender and previous history of headache was identified.

4.2. Clinical features of meningitis (Table 2)

Almost fifty percent (46.39%) of patients had fever prior to LP. Sixty nine percent of patients had signs of meningeal irritation. There were 20 patients in whom there was no headache post LP (group 1). These patients did not differ from those with headache post LP (48 patients, group 2) and those with PDPH (33 patients Group 3) in respect of features characteristic of meningitis except for pain on moving the eyes one hour post LP. Level of stress before LP, nausea and vomiting, photo- and phono-phobia were all of no predictor value for continuation or disappearance of headache post LP. Of note was the observation that none of the patients with papilledema continued with headache post LP unless he developed PDPH. There were 7 patients with papilledema in our study. None suffered from headache that was unrelated to LP. Thus, 2 out of 20 (10%) patients without headache (group 1) and 5 out of 33 patients (15%) of patients with PDPH (group 3) had papilledema while none of those with headache due to other causes (group 2) had papilledema ($p = 0.033$).

Photo- and phonophobia, as well as pain while moving the eyes were reliable indicators for meningitis present in 71%, 61% and 74% of the patients respectively.

Sixty-one from ninety-eight patients (62.24%) that answered this item in the questionnaire felt subjective relief in headache intensity one hour after LP, When patients with PDPH had the lowest rates of relief (45.45% vs 77.78% and 68.09% for groups 1 and 2 respectively; $p = 0.044$).

4.3. Clinical features of headache (Table 3)

Mean headache severity was 8.68 ± 1.86. This parameter was similar to that present in patients who continued to suffer from headache after the LP. Likewise headache type and localization did not differ between the two groups.

The headache was mainly located at the forehead area (31 patients) and had pulsating quality (43 patients).

4.4. Auxiliary findings (Table 4)

No differences between the groups in the following parameters were found: physicians experience in performing LP, the size of the Quinke needle, the mean CSF opening pressure, mean number of CSF cells, mean glucose and protein levels, leukocytosis. Levels of CRP were slightly elevated in all patients (mean 1.75 ± 2.41 mg/dl normal range 0–0.5 mg/dl).