Short communication

Cerebrospinal fluid monocytes in bacterial meningitis, viral meningitis, and neuroborreliosis[☆]

Monocytes dans le LCS au cours des méningites bactériennes, virales et neuroborrélioses

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Abstract

Objective. – Cerebrospinal fluid (CSF) leukocytes analysis is commonly used to diagnose meningitis and to differentiate bacterial from viral meningitis. Interpreting CSF monocytes can be difficult for physicians, especially in France where lymphocytes and monocytes results are sometimes pooled.

Patients and methods. – We assessed SF monocytes in patients presenting with microbiologically confirmed meningitis (CSF leukocyte count > 10/mm^3 for adults or > 30/mm^3 for children < 2 months), i.e. bacterial meningitis (BM), viral meningitis (VM), and neuroborreliosis (NB).

Results. – Two-hundred patients (82 BM, 86 VM, and 32 NB) were included. The proportions of monocytes were higher in VM (median 8%; range 0–57%) than in BM (median 5%; range 0–60%, $P = 0.03$) or NB (median 5%; range 0–53%, $P = 0.46$), with a high value overlap between conditions.

Conclusion. – CSF monocytes should not be used to discriminate BM from VM and NB because of value overlaps.

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Keywords: CSF leukocytes; CSF monocytes; Meningitis

Résumé

Objectifs. – La présence de monocytes dans le LCS est source d'interrogation.

Patients et méthodes. – Étude des monocytes chez des patients hospitalisés pour méningite (leucorachie > 10/mm^3 ou > 30/mm^3 pour les enfants < 2 mois) bactérienne (MB), virale (MV) ou neuroborréliose (NB).

Résultats. – Deux cents patients (82 BM, 86 VM et 32 NB) ont été inclus. Les monocytes étaient plus élevés dans les MV (médiane 8 % ; extrêmes 0–57 %) que dans les MB (médiane 5 % ; extrêmes 0–60 %, $p = 0,03$) ou les NB (médiane 5 % ; extrêmes 0–53 %, $p = 0,46$), avec un chevauchement important des valeurs entre les trois groupes.

Conclusion. – La quantité de monocytes dans le LCS ne devrait pas être utilisée pour discriminer MB, MV et NB du fait d'un chevauchement important des valeurs.

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Mots clés : Leucocytorachie ; Méningite ; Monocytes

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1. Background

Meningitis is a life-threatening infection most commonly diagnosed by cerebrospinal fluid (CSF) analysis. Normal CSF leukocyte count is 0–5 cells/mm^3 with 70% lymphocytes and 30% monocytes [1,2]. However, normal CSF leukocyte count does not rule out meningitis, although most patients present with elevated CSF leukocyte counts (> 10/mm^3 for adults and > 30/mm^3 for children aged < 2 months) [2]. Discriminating between bacterial and viral infections is necessary to guide the initial treatment. Direct identification of pathogens via Gram staining, antigen detection, polymerase chain reaction (PCR) analysis, or culture methods remain the most reliable microbiological diagnostic techniques; however, the results may be false negative or not immediately available [3]. Thus, discriminating between bacterial and viral infection can be based on conventional parameters of CSF and blood, including CSF leukocyte counts and formula; CSF glucose, protein, and lactate; serum C-reactive protein (CRP) and procalcitonin (PCT) levels; or composite scores such as the Hoen score [4]. CSF leukocyte count and formula can quickly differentiate the types of infection. Bacterial meningitis (BM) is usually associated with a very high CSF leukocyte count of > 1000/mm^3, with a predominance of polymorphonuclear leukocytes (PMNs) of > 50% and low glucose and high protein levels. In viral meningitis (VM), CSF leukocyte count is usually < 100/mm^3 with a predominance of lymphocytes [1,2,5,6]. To date, no study specifically focused on monocytes (the 3rd population of CSF leukocytes) and most physicians are unaware of their significance. This retrospective study aimed to determine the diagnostic value of CSF monocytes in comparison with conventional CSF and blood parameters to differentiate BM from VM and neuroborreliosis (NB).

2. Materials and methods

The medical records of patients treated at the Hôpitaux Civils de Colmar, Northeastern France, from January 1st, 2004 to December 31st, 2016 were retrospectively reviewed. Meningitis diagnosis was obtained via the French Diagnosis Related Groups program database. Patient selection was based on the following criteria: CSF leukocyte count > 10/mm^3 for adults or > 30/mm^3 for children aged < 2 months, with a microbiological confirmation. Meningitis was defined as bacterial in case of a positive detection of *Streptococcus pneumoniae* antigen in CSF (BinaxNow *S. pneumoniae*, Alere, France) or a positive bacteriological culture or bacterial PCR. Meningitis was defined as viral in case of positive PCR results for enterovirus, herpes simplex virus (HSV)-1, HSV-2, cytomegalovirus, and Epstein-Barr virus (Argene, bioMérieux, Marcy-l'Étoile, France) or a positive serology for tick-borne encephalitis virus with immunoglobulin (IgM and IgG) (Institut Virion/Serion GmbH, Wurzburg, Germany). NB was either defined by CSF pleocytosis via blood serology and positive intrathecal synthesis (ITS) or via CSF pleocytosis associated with a positive CSF Lyme serology (Enzygnost, Siemens, Saint-Denis, France) if ITS was lacking. Patients with a CSF leukocyte counts without formula were excluded. Demographic, medical, and microbiological data was collected. CSF leukocyte count and formula were determined by microscopic examination (using a Kovacs slide and May-Grünwald Giemsa staining, respectively). CSF protein, glucose, and lactate levels and serum leukocyte count and PCT levels were determined according to standard procedures. The Hoen composite score was assessed as previously described; a score < 0.1 was not in favor of BM [7,8].

Comparisons among the BM, VM, and NB groups were conducted using the Kruskal-Wallis non-parametric test. When a statistical difference was observed, a comparison of 2 by 2 groups was performed using the Mann-Whitney-Wilcoxon test with correction of the probability (P) value according to Holm method to rule out an inflated alpha risk. A correlation test for the proportions of monocytes, PMNs, and lymphocytes in CSF was performed using Spearman's test. The alpha risk was 0.05% for all tests. All tests were performed using the program R version 3.1 R Development Core Team [9]. The study protocol was approved by the Ethics Committee of the Faculties of Medicine, Dentistry and Pharmacy, Strasbourg, France.

3. Results

Of the 222 patients eligible for inclusion, 22 (10%) were excluded (CSF leukocyte count > 10/mm^3 but no formula determination [altered cells]: 20; absence of medical charts: 2). A total of 200 patients (120 men and 80 women; 82 BM, 86 VM, and 32 NB) were thus included.

Significant differences in CSF leukocyte, protein, glucose, PMN, and lymphocyte counts (%) and blood CRP levels were observed among the three groups ($P < 0.00001$). This difference, although significant, was weaker for age ($P = 0.02$) and CSF monocytes ($P = 0.03$). The CSF monocyte count (%) was statistically higher in the VM group (median 8%; range, 0–57%) than in the BM group (median 5%; range, 0–60%, $P = 0.03$) or the NB group (median 5%; range, 0–53%, $P = 0.46$). Fifteen patients had a CSF monocyte count > 30% (3 BM, 3 NB, and 9 VM). The total leukocyte count and the proportion of PMNs (ratio PMNs/leukocytes) in CSF were greater in the BM group than in the VM group (1330/mm^3 with 91% PMNs vs. 108/mm^3 with 34% PMNs, $P < 0.00001$) or the NB group (147/mm^3 with 4% PMNs, $P < 0.00001$). The proportion of lymphocytes (ratio lymphocytes/leukocytes) in CSF was lower in the BM group (median 2%; range, 0–96%) than in the VM (median 48%; range, 1–100%, $P < 0.00001$) or NB group (median 86%; range, 2–100%, $P < 0.00001$). Total leukocytes in CSF were statistically not different between the NB and VM groups ($P = 0.3$), but the proportion of PMNs (ratio PMNs/leukocytes) in CSF was higher, and the proportion of lymphocytes (ratio lymphocytes/leukocytes) in CSF was lower in the VM group than in the NB group ($P < 0.00001$). Regarding PCT levels and Hoen scores, a comparison was conducted between the VM and BM groups only because these tests were not performed for patients presenting with NB. Data is summarized in Table 1 and Fig. 1.

Spearman's rank correlation coefficient was applied to explore correlations between the levels of PMNs, lymphocytes, and monocytes in the CSF of the 200 subjects, which revealed a strong negative correlation between CSF PMNs and