Journal of the Neurological Sciences 393 (2018) 72–79

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Where there is no brain imaging: Safety and diagnostic value of lumbar puncture in patients with neurological disorders in a rural hospital of Central Africa

Deby Mukendi[a,b,*], Jean-Roger Lilo Kalo[a], Tharcisse Kayembe[b], Pascal Lutumba[a,b], Barbara Barbé[c], Philippe Gillet[c], Jan Jacobs[c,d], Cedric P. Yansouni[e], François Chappuis[f], Kristien Verdonck[g], Marleen Boelaert[g], Andrea S. Winkler[h,i], Emmanuel Bottieau[c]

[a] Institut National de Recherche Biomédicale, Kinshasa, DR, Congo
[b] Département de Neurologie, service de Neurologie Tropicale, Université de Kinshasa, DR, Congo
[c] Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium
[d] Department of Microbiology and Immunology, KU Leuven, Leuven, Belgium
[e] JD MacLean Centre for Tropical Diseases, McGill University Health Centre, Montreal, Canada
[f] Division of Tropical and Humanitarian Medicine, Geneva University Hospitals and University of Geneva, Switzerland
[g] Department of Public Health, Institute of Tropical Medicine, Antwerp, Belgium
[h] Center for Global Health, Department of Neurology, Technical University of Munich, Munich, Germany
[i] Centre for Global Health, University of Oslo, Oslo, Norway

A B S T R A C T

Analysis of cerebrospinal fluid (CSF) obtained by lumbar puncture (LP) is an essential step for the diagnostic approach of neurological disorders, in particular neuro-infections. In low-resource settings, it is even often the only available diagnostic method. Despite its key contribution, little is known on the risks and benefits of LP in the large tropical areas where hospital-based neuroimaging is not available. The objectives of this study were to assess the safety and diagnostic yield of LP in a rural hospital of central Africa and to identify predictors of CSF pleocytosis (white blood cell count > 5/μL) as surrogate marker of neuro-infections.

From 2012 to 2015, 351 patients admitted for neurological disorders in the rural hospital of Mosango, Kwilu province, Democratic Republic of Congo, were evaluated using a systematic clinical and laboratory workup and a standard operating procedure for LP. An LP was successfully performed in 307 patients (87.5%). Serious post-LP adverse events (headache, backache or transient confusion) were observed in 23 (7.5%) of them but were self-limiting, and no death or long-term sequelae were attributable to LP. CSF pleocytosis was present in 54 participants (17.6%), almost always associated with neuro-infections. Presenting features strongly and independently associated with CSF pleocytosis were fever, altered consciousness, HIV infection and positive screening serology for human African trypanosomiasis. In conclusion, the established procedure for LP was safe in this hospital setting with no neuroimaging and CSF analysis brought a substantial diagnostic contribution. A set of presenting features may help accurately selecting the patients for whom LP would be most beneficial.

1. Introduction

Laboratory analysis of cerebrospinal fluid (CSF) obtained by lumbar puncture (LP) is a key diagnostic step to distinguish between inflammatory, infectious, metabolic, neoplastic, demyelinating, and degenerative causes of neurological disorders [1]. In low-resource settings, CSF analysis is often the only available investigation in the search for a specific and treatable neurological diagnosis, primarily infections. Basic analyses such as measurement of glucose or protein concentration, white blood cell (WBC) count and differential, and identification of pathogens by microscopy provide invaluable information for clinical management [1, 2]. In particular, CSF pleocytosis, defined as a WBC count above 5/μL of CSF, is a key surrogate finding usually pointing to infections of the central nervous system (CNS). Moreover, the WBC differentiation helps to further consider subgroups of etiological pathogens which have to be urgently and specifically treated.

Safe performance of LP and accurate analysis of CSF require adequate staff training and appropriate equipment, which are far from optimal in low-resource settings. In such situations, the decision to perform an LP relies on a difficult-to-apprehend balance between the expected diagnostic benefits and the risks of the procedure. Indeed, multiple complications can occur after LP. Headache, backache, and nerve root irritation are the most frequently reported adverse events, in up to 60%, 40% and 13% of procedures, respectively [3–5]. Other complications are rare but may be life-threatening. Cerebral herniation, the most feared adverse event, occurred in about 1% of diagnostic LPs

* Corresponding author at: Institut National de Recherche Biomédicale, Kinshasa, DR, Congo.
E-mail addresses: debymukendi@yahoo.fr, debymukendi@gmail.com (D. Mukendi).

https://doi.org/10.1016/j.jns.2018.08.004
Received 19 April 2018; Received in revised form 10 July 2018; Accepted 2 August 2018
Available online 09 August 2018
0022-510X/

in historical studies prior to neuroimaging [3]. Other more rare but serious complications include post-LP infection (cellulitis, discitis, spinal abscess, and meningitis), transient cranial nerve palsies and bleeding (spinal subdural/epidural hematomas or subarachnoid hemorrhages) [3].

In high-income settings, patients with neurological disorders usually undergo neuroimaging to identify the etiology of their problem and to detect cerebral abnormalities that may precipitate herniation if an LP is performed. Neuroimaging has become part of the standard initial evaluation, even if there is some evidence that clinical evaluation should remain key in the decision to urgently perform, or defer, an LP [4, 6, 7]. In contrast, the risks and benefits of an LP have been hardly studied in the countless low-resource hospitals where neuroimaging is not available, at the exception of some facilities specialized in HIV care [8, 9]. Since evidence-based guidance is lacking, many first-line clinicians feel uncomfortable with the decision to perform an LP and too often, this leads to its inappropriate omission in situations where it is clearly indicated [10].

For a clinical study that was part of the NIDIAG project ("Better Diagnosis for Neglected Infectious Diseases", www.nidiag.org) and that investigated the causes of neurological disorders in the rural hospital of Mosango in the Democratic Republic of the Congo (DRC), we had to elaborate a standard operating procedure (SOP) on when and how to perform an LP [11, 12]. This local guideline had to rely on clinical and fundoscopic examination only. To develop the SOP, we first looked at recommendations for high-income countries [5], which were then adapted to the setting of a rural hospital by a study team of neurologists with experience in tropical medicine (see the corresponding SOP in French and English as Supplemental Table). The NIDIAG study provided a unique opportunity to assess the risks and usefulness of LP in this particular setting.

The primary objectives of the present study were to report on the safety of LPs performed according to the elaborated guideline, and to determine the diagnostic yield of basic CSF analysis in NIDIAG study participants. A secondary objective was to identify the clinical and first-line laboratory predictors of CSF pleocytosis, the main observed abnormal finding, in order to improve the selection of patients with neurological disorders who would most benefit from a diagnostic LP in similar settings.

2. Methods

2.1. Study design

This study about LP was nested in a larger observational and prospective cohort study which was part of the NIDIAG project. The larger NIDIAG study had as objectives to (1) investigate the etiology and outcome of neurological disorders in a rural hospital of DRC and (2) assess the diagnostic value of clinical and laboratory predictors, including a set of rapid diagnostic tests (RDTs), for identifying severe and treatable CNS infections. Detailed information on the inclusion criteria, neurological workup, priority neurological infections, case definitions, and index and reference diagnostic methods is available in Mukendi D et al. [13].

2.2. Study setting

The NIDIAG study was conducted in the "Hôpital Général de Référence" (HGR) of Mosango, a health facility with very limited resources, located in Mosango health district (a rural area of 3350 km^2 with about 110,000 inhabitants), Kwilu province at about 400 km from the capital, Kinshasa. General practitioners with minimal training in neurology provided the medical care. Besides the laboratory facilities set up to conduct the study described in detail in [13], advanced methods for neurological diagnosis, and in particular neuroimaging, were not available.

2.3. Participants

All patients older than five years presenting at the HGR of Mosango with non-traumatic and progressive neurological disorders were enrolled in the NIDIAG clinical and diagnostic study [13]. Briefly, for inclusion, at least one of the following symptoms or signs had to be present: (1) altered state of consciousness; (2) changes in sleep pattern; (3) cognitive decline; (4) changes in personality/behavior; (5) epileptic seizure (within < 2 weeks); (6) recent, severe and progressive headache; (7) meningism; (8) new onset cranial nerve lesion; (9) new onset sensorimotor focal deficit; and (10) new onset gait/walking disorders.

2.4. Study procedures

All study participants were subjected to a thorough clinical/neurological examination and a set of laboratory reference and study assays. LP was an integral part of the diagnostic workup (except in case of contra-indication, see below). All diagnoses were established according to strict composite case definitions, with a particular focus on the following set of priority (severe and treatable) neuro-infections prevalent in the region: bacterial meningitis, unspecified meningo-encephalitis, second-stage human African trypanosomiasis (HAT), cerebral malaria, central nervous system (CNS) tuberculosis, HIV-related neurological disorders and neurosyphilis [13].

2.5. Performance of lumbar puncture, analysis of cerebrospinal fluid and patient follow-up

A set of clinical criteria that were absolute and relative contra-indications for LP were established in an SOP that also described the procedure itself (Supplemental Table). Absolute contraindications included unresponsive coma (Glasgow coma scale [GSC] < 8), rapid deterioration of consciousness, recent (< 30 min) and/or repeated epileptic seizure, symptoms/signs of hemodynamic or respiratory failure, papilledema at fundoscopy, bleeding diathesis, skin infection at the puncture site or severe vertebral deformities/opisthotonus. Relative contraindications included altered consciousness (GCS between 8 and 13) and focal neurological deficits; LP could be performed if these clinical manifestations were not progressing rapidly.

After the patient (or his/her representative) consented to participate in the study and contraindications were excluded, about 10 mL of CSF was collected. Investigations that were immediately performed in the study hospital included WBC count with differentiation and search for trypanosomes in all participants, as well as India ink and a reference Cryptococcal Antigen Latex Agglutination test (CrAg LAT) in HIV-positive patients. CSF was systematically inoculated into bacterial and mycobacterial growth indicator tube (MGIT) cultures and cryopreserved; bacterial species identification and additional molecular testing were done in reference laboratories in Kinshasa, DRC, and Antwerp, Belgium, as detailed in [13]. CSF pleocytosis was defined as the presence of more than five WBC/μL of CSF. For CSF WBC counts between 5 and 20/μL, a second cell count was performed and we categorized the patient as having pleocytosis when both results were above the cut-off of 5/μL. WBC differentiation with measurement of the proportion of neutrophils or lymphocytes was performed only when the WBC count was above 20/μL. Determination of glucose and protein concentration in CSF was not performed due to the technical difficulties related to additional sampling and analyses for a likely limited diagnostic output. When CSF pleocytosis was present, additional investigations included Gram and Ziehl staining in the study hospital, and Pastorex Meningitis antigen assay (Bio-Rad, Hercules, CA) and polymerase chain reaction for herpes simplex and zoster viruses in reference laboratories in Antwerp, Belgium [13].

All enrolled patients were admitted to the hospital and were offered targeted or empirical therapy according to pre-established clinical SOPs; they were re-evaluated on a daily basis (or more often if required)