

## Research Article

# Point-of Care for Prompt Management of Infectious Meningitis and/or Encephalitis (IM/IE) in Gabon Military Hospital

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### Abstract

Infectious meningitis (IM) and/or infectious encephalitis (IE) can cause significant and irreversible damage to the central nervous system.

### Objective

The main objective of the study was to identify a pathogen which causes IM or Meningoencephalitis

(M/E) and evaluate the contribution of FilmArray (FA) M/E in patient management.

### Material and Method

Twenty-one (21) cerebrospinal fluid (CSF) samples tested simultaneously using the FilmArray M/E and bacteria culture. Each sample was tested per the manufacturer's instructions.

## Results

We received CSF from 21 patients, including one infant and children from three departments: pediatric, internal medicine and intensive care. Among all patients, 12 are living with HIV, 2 had trypanosomiasis and 7 were immunocompetent. Median age 41 years with an age range from 1 to 75 years. The sex ratio was 3,5. Only 3 patients presented with pneumococcal meningitis and including one living with HIV. The cultures incubation time took from 3 to 5 days and the Point-of-care testing took an hour and a half to perform.

## Conclusion

The detection of *Mycobacterium tuberculosis* in CSF samples is not yet included in all detection systems like GeneXpert or BioFire. We believe that in many epidemic areas for these diseases, developing tools to diagnose *Mycobacterium tuberculosis* or *Toxoplasma gondii* meningitis would be an important asset to help in the management of meningitis. Viruses remain a real problem for clinical diagnosis in countries with limited resources, therefore point-of-care development could improve treatment and reduce mortality.

## Introduction

Infectious meningitis and/or infectious encephalitis (IM/IE) can cause severe and irreversible damage to the central nervous system.

Meningitis or encephalitis is a medical emergency, especially if meningeal syndrome are present, patients should immediately go to a hospital for clinical evaluation. Realization of a lumbar puncture followed by a cerebrospinal fluid analysis could be

completed without delay and an empiric antibiotic therapy should be started immediately [1]. The association of meningeal syndrome and sign of encephalitis defines meningoencephalitis (M/E). Meningeal syndrome is classically characterized by a combination of stiff neck, headache, fever and altered mental status; other symptoms, including nausea, vomiting, and photophobia, are also commonly seen. IM/IE may be due to a bacterial, mycobacterial, fungal or viral agent [2].

Like all countries in sub-Saharan Africa, Gabon is faced with M/E despite an expanded vaccination program and compliance with preventive measures in health centers, IM/IE remains a public health problem in Gabon.

Low national vaccination coverage, increasing rate of people living with HIV (4.2%) contribute to increase in IM/IE [3,4].

The diagnosis of M/E must take into account many elements of the patient's history and symptomatology as well as regional epidemiology and background analyzes of cerebrospinal fluid (proteins, sugar, etc.) to enable the clinician to understand and stratify the etiological possibilities and rationally select additional diagnostic tests [2].

The main objective of the study was to identify an agent which causes M/E and evaluate the contribution of FilmArray M/E (BioFire Diagnostics, Salt Lake City, UT, USA) in patient management.

**Keywords:** FilmArray- Meningitis-Encephalitis-PCR; Multiplex

## Material and Method

Patients in this study were hospitalized in the intensive care unit (ICU), the internal medicine and pediatric department for meningitis or meningoencephalitis. All patients presented with fever (Temperature  $\geq 39^{\circ}\text{C}$ ), neck stiffness and/or loss of consciousness. A lumbar puncture was performed for all the patients. Twenty-one (21) samples of cerebrospinal fluid (CSF) were tested simultaneously by using FilmArray M/E and bacterial culture. Each sample was analyzed according to the manufacturer's instructions.

## Results

We received CSF from 21 patients, including an infant and children from three departments: pediatric, internal medicine and intensive care unit. Of all the patients, 9 are living with HIV, 2 had trypanosomiasis and 7 were immunocompetent. Median age 41 years with age range from 1 to 75 years. The sex ratio was 3,5 (Table 1).

## Patient symptoms and medical history

The clinical picture was dominated by meningoencephalitis in 6/21 patients, followed by altered state of consciousness in 5/21 patients; febrile convulsions in 3/21 patients and delirium in 2/21 patients. The other symptoms were marked by meningeal syndrome and / or meningeal syndrome associated with convulsions, only one patient presented with febrile meningeal syndrome, convulsions and hemiparesis.

## Clinical signs and pathogens

Enterovirus and *Streptococcus pneumoniae* were observed in patients with M/E. Only one of our 21

patients presented an M/E indicative of bacterial and parasitic co-infection such as Trypanosomiasis and Pneumococcal Meningitis.

*Herpes simplex virus 2* (HSV2) and Human Herpes virus 6 (HHV6) were found in 2 patients living with HIV who presented with confusional disorder and altered consciousness.

## Bacterial target

*Streptococcus pneumoniae* was the bacteria most represented for these diagnostic tools (FilmArray and culture), HHV6 was the main virus identified and the second most identified pathogen for all patients.

No virus could be identified with a standard culture, only FA/ME was able to diagnose them. One patient presented with co-infection with meningitis and sleeping sickness. Only one HIV patient developed a pneumococcal lung infection complicated by bacterial meningitis due to *Streptococcus pneumoniae*. We also diagnosed two patients with sleeping sickness.

The culture growth times range from 3 to 5 days and the Point-of-care testing took 1 hour and a half to carry out the diagnosis. Antibiotic treatment was administered before lumbar puncture in all patients admitted with suspected bacterial meningitis. A third-generation Cephalosporin (Ceftriaxone) at a meningeal dose was then administered and adapted secondarily as soon as the molecular diagnosis was confirmed by FilmArray in the CSF.

Patient number	Clinical symptoms	Medical history	BIOFIRE Results	Culture
1	Meningeal syndrome + Seizure	Ischemic stroke	Not Detected	Nothing
2	Meningo-encephalitis syndrome	Trypanosomiasis	<i>Streptococcus pneumoniae</i>	<i>Streptococcus pneumoniae</i>
3	Meningo-encephalitis syndrome	Nothing	Not Detected	Nothing
4	Meningeal syndrome -Fever Hemiparesis - convulsive seizure	Nothing	Not Detected	Nothing
5	Meningeal syndrome	Trypanosomiasis	Not Detected	Nothing
6	Convulsive seizure disorder-febrile state	Nothing	Not Detected	Nothing
7	Febrile Seizure	HIV-Toxoplasmosis	Not Detected	Nothing
8	Meningo-encephalitis syndrome	HIV	<i>Streptococcus pneumoniae</i>	<i>Streptococcus pneumoniae</i>
9	Tuberculosis -inconsistent statements	HIV	<i>Human Herpes virus 6</i>	Nothing
10	Meningo-encephalitis syndrome	HIV Stage C	Not Detected	Nothing
11	Non-febrile seizure	HIV stage C	Not Detected	Nothing
12	Febrile altered consciousness	Nothing	<i>Streptococcus pneumoniae</i>	<i>Streptococcus pneumoniae</i>
13	Meningo-encephalitis syndrome	HIV	Not Detected	Nothing
14	Cough + Altered consciousness	HIV	Not Detected	Nothing
15	Confusional disorder- cervical polyadenopathies	HIV	<i>Herpes simplex virus 2</i>	Nothing
16	Altered consciousness	HIV	Not Detected	Nothing
17	Febrile seizure	Nothing	Not Detected	Nothing
18	Febrile Altered consciousness	HIV	Not Detected	Nothing
19	Altered consciousness	HIV	Not Detected	Nothing
20	Altered consciousness	HIV	<i>Human Herpes virus 6</i>	Nothing
21	Meningo-encephalitis syndrome	Nothing	Enterovirus	Nothing

**Table 1:** Patient symptoms and medical history

BACTERIAL target	FilmArray BIOFIRE	CULTURE
Escherichia coli K1		
Haemophilus influenzae		
Listeria monocytogenes		
Neisseria meningitidis		
Streptococcus agalactiae		
Streptococcus pneumoniae	X	X
VIRUSES target		
Cytomegalovirus (CMV)		

Enterovirus (EV)	X	
Herpes simplex virus 1 (HSV-1)		
Herpes simplex virus 2 (HSV-2)	X	
Human Herpes virus 6 (HHV-6)	X	
Human parecho virus (HPeV)		
Varicella zoster virus (VZV)		
<b>YEAST</b>		
Cryptococcus neoformans/gattii		

**Table 2:** Pathogen detected

### Discussion

In Gabon, patients are generally treated with probabilistic antibiotic therapy before bacteriological and antibiogram results. However, in the context of our study, the antibiotic therapy was secondarily adapted to the pathogen and antibiogram upon receipt of the microbiological results. This situation is common in sub-Saharan African country where microbiological diagnosis is not developed for many diseases. For this reason, rapid point-of-care diagnosis (POC) like FilmArray helps clinicians manage meningitis in hospital [5]. POC diagnosis would ensure appropriate treatment is given on time before hospital discharge ensuring patient will have appropriate prescription. In some cases, patient can't be easily traced after their hospitalization and proper treatment before hospital discharge is paramount in proper case management. Some centers lack proper diagnosis equipment and empiric treatment is used without ever pushing the etiologic diagnosis. POC tools would permit a higher etiologic diagnosis allowing public health institutions to better track meningitis etiology in Gabon. Knowing that Gabon is an endemic country for Toxoplasmosis and Tuberculosis like many countries in sub-Saharan

Africa, unfortunately the FilmArray does not detect *Mycobacterium tuberculosis* and *Toxoplasma gondii*. Therefore, the use of other diagnostic tools such as polymerase chain reaction (PCR) for the diagnosis of *Mycobacterium* [6] and neurotoxoplasmosis [7], would help in the microbiological diagnosis of these two pathogens. Therefore, prompt diagnosis to detect mycobacterial meningitis and cerebral toxoplasmosis remain more important for the management of meningitis [8]. The association of seizures and febrile meningeal syndrome is frequently observed in people living with HIV who present with cerebral toxoplasmosis as an opportunistic infection [9]. Most of our patients presented with clinical signs of M/E and altered consciousness, as seen in the literature [10]. Among our 21 patients, clinical signs of meningoencephalitis were mostly observed in patients living with HIV and in patients with trypanosomiasis. We did not find in the literature a direct link between co-infection associating Trypanosomiasis and meningitis caused by *Streptococcus pneumoniae*. However, we were able to observe that the diagnosis of Trypanosomiasis preceded that of Pneumococcal meningitis in terms of kinetics of events and medical history of the patient. *Streptococcus pneumoniae* was the most frequent

pathogen in our result. According to the medical literature, pneumococcal meningitis is the most common bacterial meningitis and causes about 40% of bacterial meningitis cases [11,12].

In our region, we have empirically treated meningitis with third generation cephalosporin antibiotics. This probabilistic antibiotic therapy is usually administrated before the lumbar puncture, therefore, partly responsible for the decapitated meningitis and probably involved in the negativity of cultures; explaining why we did not find any pathogens when we performed the majority of the CSF samples [13]. In our practice, physicians routinely used cephalosporin (ceftriaxone) in case of suspected meningococcal meningitis [14]. The main challenge will be to prevent antibiotic resistance. Gabon is also an endemic area for sleeping sickness, we have reported two cases of sleeping sickness and this disease must be systematically diagnosed in all laboratories and confirmed by RT-PCR [15]. We have found two types of Herpes virus, HSV2 and HHV6 in people living with HIV. These viruses infect people living with HIV and are prevalent in this population as an opportunistic infection [16,17]. Despite the prevalence of Herpes around the world, more than four decades of research have yet to produce an effective vaccine against its various forms. A patient with encephalitis or herpetic meningitis can be protected by a vaccine and prevent this infection, because this diagnosis is life threatening. One patient was an infant and another adolescent, these two patients not being able to justify a follow-up of pentavalent vaccine that also prevents infections to *Haemophilus Influenzae* type B. The Expanded Program on Immunization (EPI) was developed for infants and pregnant women. After

this period, you can only get the vaccine if you are traveling abroad where the infectious disease was endemic. Indeed, before the pandemic situation and during the period of COVID19, we observe the decline in overall vaccination coverage. We also observe that vaccination observance rate is not effective in adolescents [18,19]. In our study, the median age was 41 years for people living with HIV and immunocompetent people. Unfortunately, in Gabon, this type of adult population, does not benefit from an Expanded Program on Immunization. Indeed, Gabon's EPI does not have a vaccination program including people over 40 and people living with HIV [20]. In December 2020, the Gabonese government introduced a pregnancy immunization program for all countries according to the WHO recommendation but not yet for adults [21,22]. This public health problem is a real challenge for our country, due to the lack of molecular diagnosis meningitis. More than half of the patients were immunocompetent, which shows that meningitis, whether bacterial, viral or fungal, affects the entire population regardless of age and HIV status. The global roadmap to end meningitis by 2030 aims to accelerate progress through visionary and strategic goals focused on meningitis prevention through vaccination [23]. Gabon is not in the countries of the African meningitis belt and does not present any epidemic risk, but we believe that making efforts to achieve the objectives of the global roadmap in our country must be beneficial for the population [24]. We found the presence of pneumococci in patients on three occasions. It is known that the effectiveness of vaccination depends on the different strains of pathogens involved in the disease, which is why it is more important to identify and sequence all strains of

pneumococci. The pneumococcal meningitis vaccination policy is not yet clear in Gabon, because there is a lack of knowledge of vaccine introduction and unidentified circulating serotypes to assess and support the vaccination program [25].

### Conclusion

The detection of *Mycobacterium tuberculosis* in CSF samples is not yet in all detection systems like GeneXpert or BioFire FilmArray. We believe that in many epidemic areas of these diseases, developing tools to perform *Mycobacterium tuberculosis* or *Toxoplasma gondii* will better help in the management of meningitis or M/E.

Viruses remain a real problem for clinical diagnosis in developing countries, so the emphasis on point-of-care could improve treatment and reduce mortality. The management of the re-emergence of sleeping sickness in urban and semi-urban areas should be improved and lead to better routine diagnosis by RT-PCR. The Expanded Program on Immunization must consider setting up a vaccination program over more than 21 years to protect this type of the population.

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### Declaration of conflicting interests

The Authors declares that there is no conflict of interest

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