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Background

Acute bacterial meningitis is an important cause of morbidity and mortality in children. The definition of meningitis is inflammation of pia and arachnoid membranes that cover the brain and spinal cord. Clinical signs and symptoms include sudden onset of fever, headache, stiff neck, nausea, vomiting and altered mental status. Signs and symptoms may occur within a few hours to several days. Acute bacterial meningitis should be promptly diagnosed and the appropriate therapy should be initiated early to prevent its complications such as convulsion, ventriculitis, hydrocephalus, subdural effusion and brain abscess. Meningitis can be diagnosed based on a medical history, physical examination, laboratory tests including complete blood count, acute phase reactant and blood culture. The most important diagnostic test is the evaluation of the cerebrospinal fluid (CSF) for cell count and protein and glucose levels. CSF gram staining, culture and multiplex PCR analysis can define the causative agent. Neuroimaging also can be used for diagnosis.

Causative agents may vary by age, underlying disease and geographical area. The most common pathogens are; *Streptococcus Pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae type b*. Despite of cerebrospinal fluid culture is accepted gold standard for diagnosis; it can result as negative especially in patient with previous antibiotic usage in history. Multiplex PCR (Biofire FilmArray®), ensures important advantages at diagnosis and timely treatment by resulting within first 1 hour of CSF examination and resulting positive despite of negative CSF culture due to previous antibiotic usage.

Methods

Multiplex PCR (Biofire FilmArray®), meningitis/encephalitis panel tests 14 pathogens that include *Escherichia coli* K1, *Haemophilus*

influenzae, *Listeria monocytogenes*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Cytomegalovirus*, *Enterovirus*, *Herpes simplex virus 1*, *Herpes simplex virus 2*, *Human herpes virus 6*, *Human parechovirus*, *Varicella zoster virus*, *Cryptococcus neoformans/gattii* and it is resulted in 1 hour.

In this study, we evaluated the value of multiplex PCR on diagnosis and treatment of acute bacterial meningitis, in patients between 0-18 years of age with the presumed diagnosis of meningitis who admitted to Marmara University Pendik Training and Research Hospital. Biofire Filmarray Multiplex PCR was performed in CSF samples of 59 patients and compared with CSF culture results.

Lumbar puncture was performed in patients with clinical signs or symptoms of meningitis such as fever, seizure, vomiting, rash, head ache, meningeal irritation findings, pulsatile fontanel, changes in consciousness. Glucose and protein levels, bacterial culture results, leucocyte count and multiplex PCR results were recorded.

Results

Multiplex PCR resulted as positive in 12 of 59 patients, while CSF bacterial culture resulted as positive in 4 of them. Viral pathogens were detected in 7 patients.

Neisseria meningitidis was detected in 3 patients with multiplex PCR in first hour of admission. The CSF culture was sterile in 1 of 3 patients. The antibiotic treatment, isolation precautions and postexposure prophylaxis for contacts performed rapidly.

Streptococcus pneumoniae was detected in 2 patients with multiplex PCR test while their bacterial cultures were sterile.

Viral pathogens were detected 7 patients and antibiotic treatment was stopped early in management (Table 1).

AGE	GENDER	SYMPTOMS	MIF	ANTIBIOTIC USE	CSF PROTEIN	CSF GLUCOSE	CSF LEUCOCYTE	CSF CULTURE	CSF MULTIPLEX PCR
10	FEMALE	VOMITING, HEADACHE	+	-	520	10	300	NEISSERIA MENINGITIDIS	NEISSERIA MENINGITIDIS
9	MALE	VOMITING, HEADACHE	+	-	39	55	320	NEGATIVE	ENTEROVIRUS
9	MALE	VOMITING, HEADACHE	+	-	110	45	1000	NEISSERIA MENINGITIDIS	NEISSERIA MENINGITIDIS
8	MALE	VOMITING, HEADACHE	+	+	37	65	300	NEGATIVE	ENTEROVIRUS
0	FEMALE	FEVER, CONVULSION	-	-	18	62	0	NEGATIVE	HHV 6
0	MALE	FEVER, CONVULSION	+	-	227	69	320	NEGATIVE	STREPTOCOCCUS PNEUMONIAE
8	MALE	VOMITING, HEADACHE	+	-	37	65	300	NEGATIVE	ENTEROVIRUS
0	FEMALE	FEVER, CONVULSION	-	-	18	62	0	NEGATIVE	HHV 6
8	MALE	FEVER, CONVULSION, VOMITING	-	-	74	68	0	NEGATIVE	NEISSERIA MENINGITIDIS
0	FEMALE	FEVER	-	-	37	48	0	NEGATIVE	HHV 6
0	MALE	FEVER, ALTERED MENTAL STATUS	-	-	45	268	840	NEGATIVE	STREPTOCOCCUS PNEUMONIAE
9	FEMALE	FEVER, HEADACHE	+	-	54	71	396	NEGATIVE	ENTEROVIRUS

Discussion

When the studies were evaluated, it has been shown that Multiplex PCR (Biofire FilmArray®), ensures important advantages in diagnosis and treatment due to its quick resulting time (1,2). In bacterial meningitis cases, one of the important reasons for sterile culture is the antibiotic usage prior to diagnosis. It has been shown that multiplex PCR may result positive while culture is sterile (3). Early initiation of appropriate treatment is provided by rapid positive results also negative results can prevent unnecessary antibiotic therapy (4).

References

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