

## Clinical Audit on Management of Central Nervous System Infections

ELSAYED K. ABD EL-KARIM, M.D.; DUAA M. RAAFAT, M.D. and SAFAA M. ABD EL-ALEEM, M.Sc.

The Department of Pediatrics, Faculty of Medicine, Assiut University, Egypt

### Abstract

**Background:** Central Nervous System (CNS) infections cause significant mortality and neurological morbidity throughout the world children.

**Patients and Methods:** All patients aged beyond neonates admitted to Assiut University Children Hospital (during six month duration) from 1/6/2017 to 30/11/2017 with any symptoms or signs of meningitis, encephalitis or meningoencephalitis including fever, convulsions, disturbed conscious level were included in this study to assess how much adopted protocols in management of CNS infections are applied.

**Results:** Shows that 100% of patients had lumbar puncture, CSF culture was done to 16.4% of all cases, the first choice of empirical treatment were Ampicillin plus cefotaxime in about 82% of all cases, vancomycin came after in 19.7% of them, then ceftriaxone in 18%, nearly all patients were treated with steroid except for one case, 88.5% were treated with antiviral, mainly all Children  $<3$  month with unconfirmed disease treated with cefotaxime + ampicillin for 14 day except for 25% of them, only 29.8% of Children  $>3$  month with unconfirmed disease treated with ceftriaxone for 10 days.

**Conclusion:** We need to stick with the international guidelines as a reference standard to avoid miss diagnosis and complications of CNS infections to improve the health services provided in Neurology Unit.

**Key Words:** Meningitis – Encephalitis – Management guidelines – Empiric antibiotics – Steroids – Acyclovair.

### Introduction

**MENINGITIS:** Is an inflammation of the membranes surrounding the central nervous system: Dura mater, arachnoid mater, and pia mater manifested by CSF pleocytosis [1].

It reflects an inflammation of the arachnoid mater and the CSF in both the Sub arachnoid space and the cerebral ventricles. Meningitis is caused by a myriad of pathogens that can incite different symptoms, often making diagnosis difficult. In younger age groups before speech development,

frequently few signs and symptoms can be detected. Meningitis, and in particular bacterial meningitis, carries very high morbidity rates (21%-56%), which stresses the importance of prompt and correct treatment [2].

The mortality of bacterial meningitis when untreated can approach 100%. There is also a great emphasis on promptly diagnosing and empirically treating meningitis because of the risk of permanent neurologic sequelae, which ranges from 10% to 30%, according to some sources for bacterial meningitis. Some authors argue that morbidity and mortality vary with geographical location and age and from one pathogen to another [3,9].

It is not surprising that failure to diagnose pediatric meningitis constitutes one of the most common causes of medical malpractice within pediatric emergency medicine [4]. There must always be a high degree of suspicion whenever certain symptoms arise as fever or hypothermia, convulsions, respiratory distress or apnea, bulging fontanelle, jaundice drowsiness, reduced feeding, failure to thrive, unconsciousness, lethargy, high-pitched cry, vomiting and Irritability.

**Encephalitis:** Which is defined as an inflammatory process of the brain parenchyma, shares some of the same etiology and symptoms. Encephalitis represents further disease invasion or progression. The presence or absence of normal brain function distinguishes meningitis from encephalitis [5]. The presence of flaccid paralysis and reduced reflexes is a manifestation of inflammation of the spinal cord, referred to as myelitis.

**Meningoencephalitis:** Is a disease in which there are features of both encephalitis and meningitis.

**Aseptic meningitis:** Is a clinical syndrome in which cultures for routine bacterial pathogens are

**Correspondence to:** Dr. Safaa M. Abd El-Aleem,  
E-Mail: [safaalkady13@gmail.com](mailto:safaalkady13@gmail.com)

negative and there were no antibiotics given before the Lumbar Puncture (LP). The causes can be infectious and noninfectious, but viruses remain the most common cause. For this reason, aseptic meningitis and viral meningitis are frequently interchangeable terms [6].

### Patients and Methods

All patients aged beyond neonates admitted to Assiut University Children Hospital (during six month duration) from 1/6/2017 to 30/11/2017 with any symptoms or signs of meningitis, encephalitis or meningoencephalitis including fever, convulsions, disturbed conscious level were included in this study to assess how much adopted protocols in management of CNS infections are applied.

*The following approaches were applied to all cases:* Assessment of history, clinical examination, and laboratory investigations that were done to the admitted cases:

- Complete blood count, serum glucose, lumbar puncture were done to all patients as a routine.
- Other investigations were done according to the symptoms of the patients.

#### Indices of the adopted protocols:

##### 1- Empiric antibiotics:

A- Third generation cephalosporins as cefotaxime (200-300mg/kg/day divided every 6 hours or ceftriaxone (100mg/kg/day divided every 6 hours).

B- Ampicillin (300mg/kg/day divided every 6 hours).

C- Vancomycin (60mg/kg/day divided every 6 hours).

2- Steroids (if the child age  $>3$  months) 0.15mg/kg to a maximum dose of 10mg, four times daily for 4 days).

3- Antiviral (acyclovir 60mg/kg/day divided every 8 hours).

4- Children  $<3$ mon with unconfirmed disease treated with cefotaxime + ampicillin or amoxicillin for at least 14 days.

5- Children  $>3$ mon with unconfirmed treated with IV Ceftriaxone for 10 days disease.

#### Inclusion criteria:

- 1 month-16 years.
- Cases of meningitis, encephalitis and meningoencephalitis.

#### Exclusion criteria:

- Partially treated meningitis.
- Syndromes.
- Patients known to have previous neurologic insult.
- CNS anomaly.

### Results

A total number of 61 cases, 32 females (52.5%), 29 males (29%) aged 2-192 months were admitted to Assiut University Children Hospital with meningitis, encephalitis and meningoencephalitis during this period.

*Our results are shown in the following tables:*

Table (1): Distribution of general investigation.

	No.	%
<i>Blood picture:</i> Yes	61	100.0
No	0	0.0
<i>WBCS:</i> Normal	23	37.7
Leucocytosis	38	62.3
<i>Blood culture:</i> Yes	0	0.0
No	61	100.0
<i>Blood glucose:</i> Yes	61	100.0
No	0	0.0
<i>Liver enzymes:</i> Yes	2	3.3
No	59	96.7

This table shows that leukocytosis was present in 62.3% of all cases, and 3.3% checked for liver enzymes elevation and the result showed elevated enzymes, finally there wasn't any blood culture.

Table (2): Distribution of specific investigation.

	No.	%
<i>Lumbar puncture:</i> Yes	61	100.0
No	0	0.0
<i>Protein in CSF:</i> Normal	40	65.6
Increased	21	34.4
Decreased	0	0.0
<i>Glucose in CSF:</i> Normal	47	77.0
Increased	0	0.0
Decreased	14	23.0
<i>Neutrophils in CSF:</i> Yes	13	21.3
No	48	78.7
<i>Lymphocytes in CSF:</i> Yes	27	44.3
No	34	55.7
<i>Normal CSF:</i>	18	29.5
<i>CSF culture:</i> Yes	10	16.4
No	51	83.6
<i>Result of CSF culture:</i> No growth	10	100
<i>CSF PCR:</i> Yes	0	0.0
No	61	100.0

This table shows that 100% of patients had lumbar puncture 29.5% of them had normal CSF, CSF culture was done to 16.4% of all cases and all results showed that there was no growth finally it was noticed that there wasn't any CSF PCR.

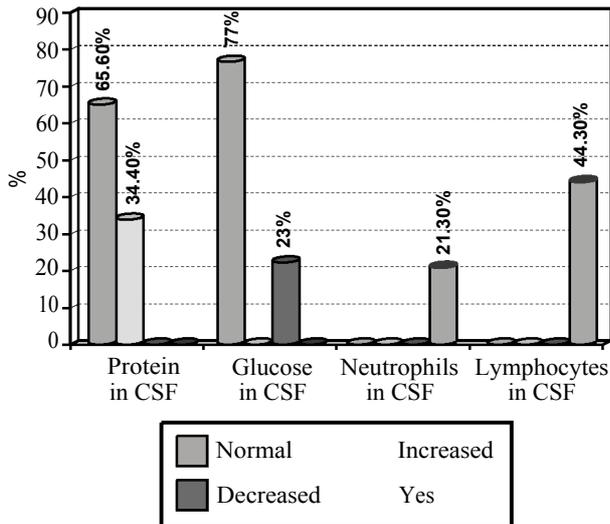


Fig. (1): CSF analysis results.

Table (3): Distribution of empiric treatment.

		No.	%
<i>Empiric antibiotic:</i>	Yes	61	100.0
	No	0	0.0
<i>Cefotaxime (200-300/kg/day):</i>	Yes	50	82.0
	No	11	18.0
<i>Ceftriaxone (100mg/kg/day):</i>	Yes	11	18.0
	No	50	82.0
<i>Ampicillin (300mg/kg/day):</i>	Yes	50	82.0
	No	11	18.0
<i>Vancomycin (60mg/kg/day):</i>	Yes	12	19.7
	No	49	80.3
<i>Antiviral (acyclovir 60mg/kg/day):</i>	Yes	54	88.5
	No	7	11.5
<i>Steroid (0.15mg/kg/day):</i>	Yes	60	98.4
	No	1	1.6
<i>Full volume maintenance fluids:</i>	Yes	47	77.0
	No	14	23.0
<i>IV mannitol:</i>	Yes	20	32.7
	No	41	67.2
<i>Control of convulsion:</i>	Diazepam	0	0.0
	Phenytoin	43	70.5
	No convulsion	18	29.5

This table shows that the first choice of empirical treatment were Ampicillin plus cefotaxime in about 82% of all cases, vancomycin came after in 19.7% of them, then ceftriaxone in 18%, nearly all patients were treated with steroid except for one case, 88.5% were treated with antiviral, about 77% of all patients received full volume maintenance fluids only 32.7% of all cases received one dose of mannitol and all patients who had convulsions were treated with phenytoin.

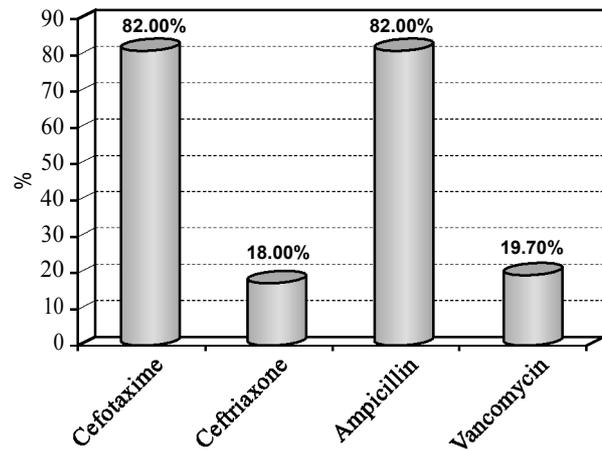


Fig. (2): Empirical antibiotic treatment.

Table (4): Distribution of diagnosis.

Diagnosis	No.	%
Meningitis	10	16.4
Encephalitis	45	73.8
Meningoencephalitis	6	9.8

This table shows that the main diagnosis was encephalitis in about 73.8% of all cases, meningitis came after in about 16.4%, Meningoencephalitis was the least one in about 9.8%.

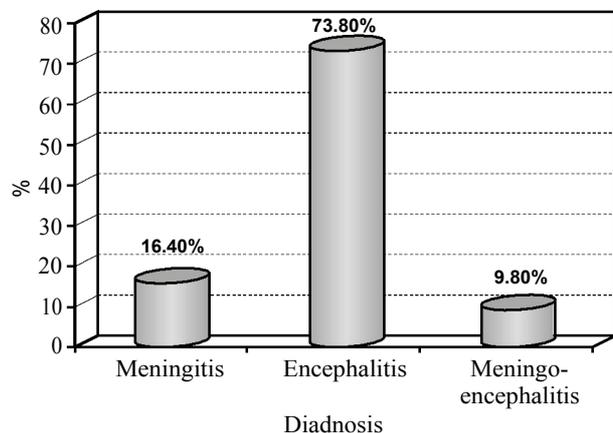


Fig. (3): Diagnosis.

Table (5): Distribution of treatment.

		No.	%
After culture result stop or continue antibiotic:	Continue	10	16.4
	Stop	0	0.0
Treatment of complication:	Yes	21	34.4
	No	0	0.0
	No complication	40	65.6
Children <3 month with unconfirmed disease treated with cefotaxime + ampicillin for 14 day:	Yes	3	7.5
	No	1	2.5
Children > 3 month with unconfirmed disease treated with ceftriaxone for 10 days:	Yes	17	29.8
	No	40	70.1
Acyclovir for 14 days:	Yes	52	85.2
	No	9	14.8

This table shows that antibiotic treatment was continued in all cases because the disease was unconfirmed; mainly all children <3 month with unconfirmed disease treated with cefotaxime + ampicillin for 14 day except for 25% of them, only 29.8% of children >3 month with unconfirmed disease treated with ceftriaxone for 10 days, about 85.2% of all patients were treated with Acyclovir for 14 days and it was also found that all cases followed by complications have been treated in the appropriate way.

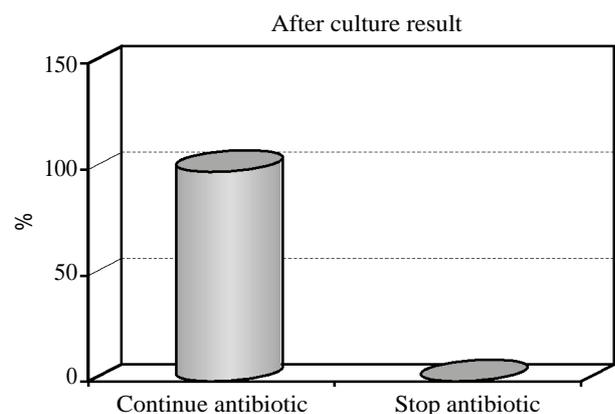


Fig. (4): After culture results stop or continue antibiotic.

Table (6): Distribution of outcome.

Outcome	No.	%
Good	46	75.4
No response	4	6.6
Icu	2	3.3
Neurological deficit	7	11.5
Death	2	3.3

This table shows that 75.4% had good outcome, 6.6% had no response, 11.5% had Neurological deficit (4 cases developed CP, 2 developed squint and one case developed ataxia), 3.3% were admitted in the ICU and 3.3% died.

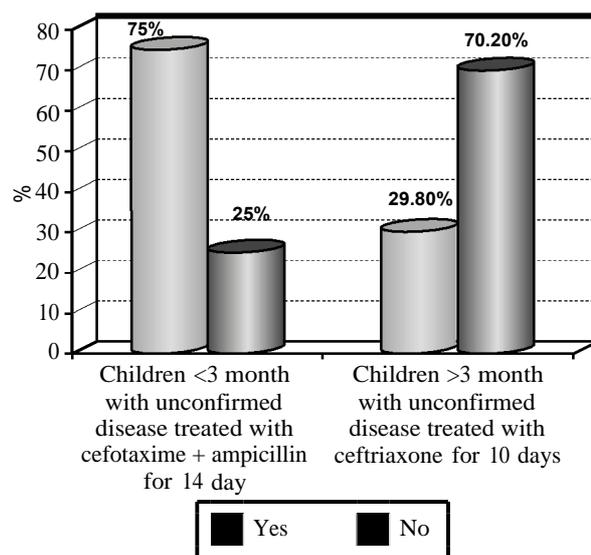


Fig. (5): Treatment of unconfirmed disease.

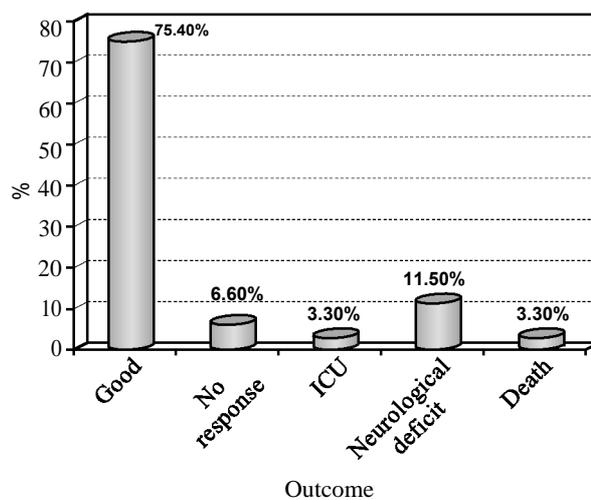


Fig. (6): Outcome.

**Discussion**

Infections of the Central Nervous System (CNS) can present with a wide variety of clinical symptoms and signs which are often non-specific, especially in infants and children. Both meningitis and viral encephalitis are neurological emergencies requiring urgent investigation and treatment [7]. Especially as distinguishing between the syndromes of meningitis and encephalitis and determining whether the underlying cause is bacterial or viral on clinical grounds which is not straight forward.

Proven or suspected CNS infections in children are frequent reason for hospital admission and a significant cause of morbidity and mortality [8,9].

In this study it was noticed that investigation following guidelines except for liver function test which was done in 2 cases only, blood culture which was not done at all, CSF culture which was done in 10 cases only, these investigation can easily be done to obtain sure diagnosis, and CSF-PCR was difficult to be done due to it's high cost.

Regarding to diagnosis it was a noticed that 73.8% were diagnosed as encephalitis, 16.4% were diagnosed as meningitis and 9.8% were diagnosed as meningoencephalitis.

Regarding treatment, it was found that there was defect in following guideline in the part of the treatment of unconfirmed disease related to patient's age, patients who were less than 3 months should be treated with ampicillin + cefotaxime and patients more than 3 months should be treated with ceftriaxone.

And finally the outcome of our patients was 75.4% had good outcome, 6.6% had no response, 11.5% had bad outcome (in the form of neurological deficit as cerebral palsy, squint, coma, ataxia), 3.3% were admitted in the ICU and 3.3% died.

#### *Conclusion:*

The practitioner should know the typical pathogens, understanding that timely and appropriate use of antimicrobials is essential. Empiric therapy should be administered promptly, once testing is complete, and should include a decision about whether adjunctive steroid therapy is appropriate.

Antimicrobial therapy should be targeted toward the suspected pathogens supportive care and monitoring are imperative, and the practitioner should anticipate and be prepared to treat complications. Although many practitioners are comfortable with the necessary plan of care and monitoring of the pediatric patient who has CNS infections, it is essential that such patients be cared for in a facility that has well-trained ancillary support personnel, including pediatric nursing, critical care, infectious disease, and radiologic staff. Once therapy is complete, all children treated for CNS infections should have follow-up hearing testing.

Evaluation for neurologic sequelae is necessary for all children treated for CNS infection.

#### *Recommendations:*

- A- Strict doing liver function test, blood culture and cerebrospinal fluid culture (before starting antibiotics) to obtain sure diagnosis by isolation of the causative organism so that we can describe the appropriate treatment.
- B- Improve the facilities for investigations like CSF PCR to verify viral etiology.
- C- Strictly follow the guidelines in the diagnosis of CNS infections and strictly follow the guidelines in the starting of treatment.
- D- Acyclovir should be given when a neonate is ill appearing, if there is history of maternal genital herpes and/or the presence of mucocutaneous vesicles, if the child presents with seizures or focal neurologic abnormalities, or if hepatic enzyme levels are elevated because of difficult in doing CSF-PCR which confirm viral etiology.
- E- Strictly follow the guidelines in continuation and duration of treatment to improve the outcome of the patient.

#### **References**

- 1- GRANDGIRARD D. and LEIB S.L.: Meningitis in neonates: Bench to bedside. *Clin. Perinatol.*, 37: 655-76, 2010.
- 2- MACE S.E.: Acute bacterial meningitis. *Emerg. Med. Clin. North Am.*, 26: 281-317, 2008.
- 3- CURTIS S., STOBART K., VANDERMEER B., et al.: Clinical features suggestive of meningitis in children: A systematic review of prospective data. *Pediatrics*, 126: 952-60, 2010.
- 4- CARROLL A.E. and BUDDENBAUM J.L.: Malpractice claims involving pediatricians: Epidemiology and etiology. *Pediatrics*, 120: 10-7, 2007.
- 5- TUNKEL A.R., GLASER C.A., BLOCH K.C., et al.: The management of encephalitis: Clinical practice guidelines by the Infectious Diseases Society of America. *Clin. Infect. Dis.*, 47: 303-27, 2008.
- 6- TAPIAINEN T., PREVOTS R., IZURIETA H.S., et al.: Aseptic meningitis: Case definition and guidelines for collection, analysis and presentation of immunization safety data. *Vaccine*, 25: 5793-802, 2007.
- 7- RASCHILAS F., WOLFF M., DELATOUR F., CHAFAUT C., De BROUCKER T., CHEVRET S., LEBON P., CANTON P. and ROZENBERG F.: Outcome of and prognostic factors for herpes simplex encephalitis in adult patients: Results of a multi-centre study. *Clin. Inf. Dis.*, 35 (3): 254-60, 2002.
- 8- GRANDGIRARD D. and LEIB S.L.: Meningitis in neonates: Bench to bedside. *Clin. Perinatol.*, 37: 655-76, 2010.
- 9- KIM K.S.: Acute bacterial meningitis in infants and children. *Lancet Infect. Dis.*, 10: 32-42, 2010.

## دراسة تدقيقية للطرق العلاجية لإلتهاب الجهاز العصبي المركزي بمستشفى الأطفال الجامعي بأسيوط

إلتهابات الجهاز العصبي المركزي يمكن أن تظهر في صورة مجموعة واسعة من الأعراض السريرية والعلامات التي غالباً ما تكون غير محددة، وخاصة في الرضع والأطفال. فكل من إلتهاب السحايا وإلتهاب الدماغ الفيروسي هي حالات طوارئ عصبية تتطلب تشخيصاً عاجلاً وعلاجاً خاصة وأن التمييز بين متلازمات إلتهاب السحايا وإلتهاب الدماغ وتحديد ما إذا كان السبب الأساسي هو بكتيريا أو فيروس ليس واضحاً. إلتهابات الجهاز العصبي المركزي يمكن الوقاية منها ومعالجتها. والمعرفة الوبائية هي أداة قوية لضمان التشخيص السليم والعلاج السليم.

بعد الدراسة التدقيقية لطريقة التشخيص والعلاج ل ٦١ حالة بمستشفى الأطفال الجامعي تبين أن نسبة الإصابة في الذكور والإناث تكاد متساوية وتبين أيضاً أن نسبة الإصابة بإلتهاب الدماغ تفوق بكثير نسب الإصابة بإلتهاب السحايا وإلتهاب السحايا الدماغى ووجد أيضاً قصور شديد في إجراء بعض الفحوصات الهامة مثل مزرعة السائل النخاعي حيث وجد أنها أجريت فقط ل ١٠ حالات مما أدى إلى تصنيف تشخيص الحالات تحت بند تشخيص غير مؤكد وبالتالي فمعظم الحالات خضعت لعلاج يشمل مضادات حيوية ومضادات فيروسية في أن واحد.

وكانت النتائج النهائية للمرضى جيدة حيث وجد أن حوالي ٧٥.٤٪ من الحالات قد شفيت شفاءً تاماً.

لتحسين نتائج علاج عدوى الجهاز العصبي المركزي نوصى:

- أ- بأخذ تاريخ مرضى دقيق من الآباء أو الأقارب مع وضع الوثائق المناسبة في ملف المريض.
- ب- الإهتمام بالفحص الجيد وكتابة الملاحظات التقديمية اليومية للمريض.
- ج- الإهتمام بعمل مزرعة دم بكتيرية ومزرعة بكتيرية للسائل النخاعي (قبل بدء المضادات الحيوية) وعمل وظائف الكبد.
- د- تحسين وسائل التشخيص وعمل بى سى آر للسائل النخاعي لمعرفة المسببات الفيروسية.
- هـ- إتباع المبادئ التوجيهية في تشخيص عدوى الجهاز العصبي المركزي وإتباع المبادئ التوجيهية في بدء العلاج.
- و- إتباع المبادئ التوجيهية في إستمرار ومدة العلاج لتحسين نتائج المريض.