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Diagnosis of Meningitis With Special Reference to Adenosine Deaminase And C-Reactive Protein Level In Cerebro Spinal Fluid

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Abstract:
Introduction: *Cases of meningitis are medical emergencies which need rapid diagnosis. CRP and ADA can be used as rapid tests to diagnose and differentiate meningitis.*
Objective: *1) To estimate C-reactive protein (CRP) and adenosine deaminase (ADA) level along with other diagnostic parameters in cerebrospinal fluid of patients with meningitis. 2) To evaluate whether CRP and ADA level could be used to differentiate the various types of meningitis.*
Method: *CSF samples were collected from 108 patients who presented to M.O.P.D of our hospital during the period of 2014-2015. Diagnosis of meningitis was based on clinical presentation and CSF analysis.*
Results: *Out of 108 patients, highest no. of patients i.e. 46 patients (42.59%) were diagnosed as tubercular meningitis followed by 32 cases (29.62%) of viral meningitis and 28 cases (25.92%) of pyogenic meningitis. 65 cases (60.18%) were males and 43 cases (39.9%) were females. Most cases (44.44%) fall in the age group of 19-40 years. The mean ADA activity was 15.78 ±4.95 U/L in tubercular meningitis group. The sensitivity, specificity, positive predictive value and negative predictive value of ADA in TBM were 84.78%, 90.32%, 86.67% and 88.87% respectively.*
Conclusion*: CRP and ADA activity in CSF can help in differentiating pyogenic meningitis and tubercular meningitis .CRP is elevated in pyogenic where as ADA activity is higher in tubercular meningitis.*
Keywords: *Cerebrospinal fluid, Adenosine Deaminase, Meningitis, Tubercular meningitis, C-reactive protein, Viral meningitis, Pyogenic meningitis*

I. Introduction

Infectious diseases of CNS have always been a major cause of mortality and morbidity for millions of people around the world. CNS infection can result in devastating consequences and in many cases may result in both medical and neurological emergencies.Meningitis is an inflammation of the membranes that surround the brain and spinal cord. It is associated with a central nervous system inflammatory reaction. It is associated with a central nervous system inflammatory reaction that may result in decreased consciousness, varied intracranial pressure and stroke. The meninges, the subarachnoid space and the brain parenchyma are all frequently involved in the inflammatory reaction (Meningoencephalitis). Meningitis can be caused by many agents which includes bacteria, virus, fungi, protozoa, helminth and even by non infectious agents such as malignancy, chemical compounds, drug hypersensitivity etc.

Etiological diagnosis of meningitis remains a problem in clinical practice as CSF biochemical analysis & cellular response often overlap. Reliable, rapid and cost effective diagnostic tests which can be performed in any standard pathology laboratory and can be of help in differentiating the various types of meningitis is the need of the hour. In this regard, C-reactive protein level and Adenosine deaminase activity can be used as rapid tests in the differential diagnosis of meningitis. ADA estimation is useful in the diagnosis of tubercular meningitis. CRP estimation has been documentated to be useful in the diagnosis of pyogenic meningitis. The level of both ADA and CRP are found to be low in cases of viral meningitis.

This study is being done to find out the role of ADA and CRP level estimation in cerebrospinal fluid for differential diagnosis of meningitis

II. Aims & Objectives

- To estimate c-reactive protein (CRP) and adenosine deaminase (ADA) level along with other diagnostic parameters in cerebrospinal fluid of patients with meningitis
- To evaluate whether CRP and ADA level could be used to differentiate the various types of meningitis.

III. Materials & Methods

- CSF samples were obtained from 108 patients of all age group and either sex ,who presented to the inpatient and outpatient department of General medicine, Silchar medical college and hospital, Silchar during the period of September 2014 and August 2015.
- A detailed history of included patients was elicited and a complete general physical examination and systemic review of the patients was undertaken.
- The complete CSF count was done in a 6 part automated analyser (Sysmex X4000i) .
- CSF glucose and protein were estimated by automated chemistry analyser (Beckman Coulter AU 480)
- C –reactive protein in CSF was estimated by semiautomatic biochemistry analyzer (ERBA Chem 5x). C-reactive protein values greater than 22 mg/dl have been accepted as positive values for the present study.
- ADA was estimated by ADA-MTB reagent kit. For cerebrospinal fluid, the cut off value for ADA has fixed at 10 IU/L.

IV. Results & Observations

Out of 108 patients, highest no. of patients i.e. 46 patients (42.59%) were diagnosed as tubercular meningitis followed by 32 cases (29.62%) of viral meningitis and 28 cases (25.92%) of pyogenic meningitis.

65 cases (60.18%) were males and 43 cases (39.9%) were females. Most cases (44.44%) fall in the age group of 19-40 years.The mean ADA activity was 15.78 ±4.95 U/L in tubercular meningitis group. The sensitivity, specificity, positive predictive value and negative predictive value of ADA in TBM were 84.78%, 90.32%, 86.67% and 88.87% respectively. CSF-CRP is highest in pyogenic meningitis with a mean value of 30.86 ±14.58 mg/dl. The sensitivity, specificity, positive predictive value and negative predictive value of CRP in pyogenic meningitis were 82.14%, 97.5%, 92% and 93.98% respectively. All the results were statistically significant (p value <0.001).

Table 1: Distribution Of Various Types Of Meningitis

Types Of Meningitis	**Number Of Cases**	**Percentages**
Tbm	46	42.59%
Pyogenic	28	25.92%
Viral	32	29.62%
Fungal	2	1.85%
Total	108	100%

Table 2: Gender Distribution Of Meningitis

Gender	**Male**	**Female**
No Of Cases	65	43
Percentage	60.18%	39.81%

Table 3: Age Wise Distribution Of Meningitis

Type Of Meningitis	**0-18 Years**	**19-40 Years**	**41-60 Years**	**>60 Years**	**Type Of Meningitis**
Tbm	2 (8.69%)	31 (64.58%)	9 (36%)	4 (33.33%)	Tbm
Pyogenic	21(91.30%)	1 (2.08%)	4 (16%)	2 (16.66%)	Pyogenic
Viral	0	16 (33.33%)	10 (40%)	6 (50%)	Viral
Fungal	0	0	2 (8%)	0	Fungal
Total	23 (100%)	48 (100%)	25 (100%)	12 (100%)	Total

Table 4: Csf Cell Count In Different Meningitis

Types Of Meningitis	**Mean Cell Count /µl**	**Standard Deviation**
Tubercular	1401.5	± 224.73
Pyogenic	6963.75	± 818.83
Viral	49.84	± 46.39
Fungal	30	± 7.07

Table 5: Csf Neutrophil Percentage In Different Meningitis

Types Of Meningitis	**Mean Neutrophil %**	**Standard Deviation**
Tubercular	10%	± 6.50
Pyogenic	82.82%	± 8.97
Viral	14.5%	± 11.73
Fungal	29%	± 1.41

Table 6: Csf Lymphocyte Percentage In Different Meningitis

Types Of Meningitis	Mean Lymphocyte Percenatge	Standard Deviation
Tubercular	87.82%	± 14.67
Pyogenic	17.17%	± 8.97
Viral	85.5%	± 11.73
Fungal	71%	± 1.41

Table 7: Csf Protein Level In Different Meningitis

Types Of Meningitis	Mean Csf Protein Level (Mg/Dl)	Standard Deviation
Tubercular	101.08	± 34.37
Pyogenic	121.94	± 19.93
Viral	61.20	± 24.98
Fungal	142.1	± 2.68

Table 8: Csf Sugar Level In Different Meningitis

Types Of Meningitis	Mean Csf Glucose Level (Mg/Dl)	Standard Deviation
Tubercular	57.08	± 11.24
Pyogenic	30.28	± 11.33
Viral	68.37	± 13.99
Fungal	31	± 1.41

Table 9: Level Of Csf Ada In Different Meningitis

Type Of Meningitis	No Of Cases	Percentage	Mean Sd (Iu/L)
Tbm	46	42.59%	15.78(Iu/L) ± 4.95(Iu/L)
Pyogenic	28	25.92%	3.04(Iu/L) ± 2.73(Iu/L)
Viral	32	29.62%	3.99 (Iu/L) ± 3.47(Iu/L)
Fungal	2	1.85%	5.56(Iu/L) ± 1.70(Iu/L)
Total	108	100%	

Table 10: Level Of Csf- Crp In Different Meningitis

Type Of Meningitis	No Of Cases	Percentage	Mean Sd (Mg/Dl)
Tbm	46	42.59%	0.62± 0.15 Mg/Dl
Pyogenic	28	25.92%	30.86 ± 14.59 Mg/Dl
Viral	32	29.62%	2.26 ± 1.03 Mg/Dl
Fungal	2	1.85%	0.39 ± 0.09 Mg/Dl
Total	108	100%	

Table 11: Distribution Of Positive Ada (>10 Iu/L) And Positive Crp (>22 Mg/Dl) Cases

Parameters	Tbm	Pyogenic	Viral	Fungal	Total	Percentage
Ada	39	2	4	0	45	41.67%
Crp	0	23	2	0	25	23.15%

Table 12: Diagnostic Performance Of Ada In Relation To The Type Of Meningitis

Type Of Meningitis	Number Of Cases	Sensitivity	Specificity	Ppv	Npv
Tubercular	46	84.78%	90.32%	86.67%	88.87%
Pyogenic	28	7.14%	46.25%	4.44%	58.73%
Viral	32	12.5%	46.05%	8.89%	55.56%
Fungal	2	-	-	-	-

Table 13 : Diagnostic Performance Of Crp In Relation To The Type Of Meningitis

Type Of Meningitis	Number Of Cases	Sensitivity	Specificity	Ppv	Npv
Tubercular	46	-	-	-	-
Pyogenic	28	82.14%	97.5%	92%	93.98%
Viral	32	6.25%	69.73%	8%	63.85%
Fungal	2	-	-	-	-

V. Discussion

The Role Of C-Reactive Protein

- The results of the present study show that CRP level was significantly increased in bacterial meningitis as compared to tubercular & viral meningitis.
- Present study was consistent with the findings of various studies.
- In a study conducted by Vaishnavi C *et al*, CRP in CSF was significantly higher in patients with pyogenic meningitis compared to tubercular meningitis.[10]

- Riberio MH *et al* estimated the levels of CRP in CSF from 33 patients with bacterial meningitis, 21 patients with lymphocytic meningitis and 54 controls. 100% of these patients with bacterial meningitis were correctly classified on the basis of measurement of CRP levels in CSF.[(11)]
- A meta-analysis by Gerdes LU et al suggested that a negative CRP test in either CSF or serum can be used with a very high probability to rule out bacterial meningitis.[(12)]
- Hence, the present study tallies with other studies recommending the estimation of CRP in CSF in the differentiation of bacterial from non-bacterial meningitis

Various Studies On The Role Of Ada In Tubercular Meningits

Study	No. Of Patients Diagnosed With Tbm	Ada Cut Off Level (Iu/L)	Sensitivity	Specificity
Rajendra Prasad Et Al[(1)]	**29**	**3.3**	**100 %**	**97.87 %**
Kashyap Et Al [(2)]	**117**	**11.39**	**82 %**	**83 %**
Gautum N Et Al [(3)]	**20**	**6.97**	**85 %**	**88 %**
Pettersson Et Al [(4)]	**3**	**20**	**100 %**	**99 %**
Chotmongkol Et Al [(5)]	**16**	**15.5**	**75 %**	**93 %**
Choi Et Al [(6)]	**36**	**7**	**83 %**	**95 %**
Ribera Et Al [(7)]	**32**	**----**	**100 %**	**99 %**
Lopez Et Al [(8)]	**----**	**10**	**48 %**	**100 %**
Rohani My Et Al [(9)]	**14**	**9**	**----**	**87.69%**
Present Study	**46**	**10**	**84.78 %**	**90.32 %**

VI. Conclusions

- The study concludes that combine use of these two tests i.e. CSF CRP and ADA can be used for early differentiation of Bacterial, Tubercular, and Viral meningitis.
- This is necessary when gold standard test for meningitis like Smear and/or culture for AFB, smear and/or culture for bacteria, is not available or negative or time consuming.
- These tests for ADA and CRP in CSF are simple and can be carried out in a central laboratory with a rapid diagnosis, thus reducing unwarranted or harmful therapy for patients.

References

[1]. Prasad Rajendra, Kumar Anil, Khanna BK, Mukherji PK, Aagarwal SK, Kumar A, Srivastava VML. Adenosine deaminase in cerebrospinal fluid for diagnosis of tuberculous meningitis. Ind J Tub 1991; 38: 99-102

[2]. Kashyap RS, Kainthla RP, Mudaliar AV, Purohit GJ, Taori GM, Daginawala HF. Cerebrospinal fluid adenosine deaminase activity: a complimentary tool in the early diagnosis of tuberculous meningitis. Cerebrospinal fluid research 2006 March 30

[3]. Gautam N, Aryal M, Bhatta N, Bhattacharya SK, Basal N, Lamsal M. Comparative study of cerebrospinal fluid Adenosine deaminase activity in patients with meningitis. Nepal Med Coll J 2007; 9(2):104-6

[4]. Pettersson T, Klockars M, Weber TH. Diagnostic value of cerebrospinal fluid adenosine deaminase determination. Scand J Infect Dis 1991; 23: 97-100.

[5]. Chotmongkol V, Teerajetgul GY, Yodwut C. Cerebrospinal fluid adenosine deaminase activity for the diagnosis of tuberculous meningitis in adults. Southeast Asian J Trop Med Public Health. 2006; 37(5): 948-52

[6]. Choi SH, Kim YS, Bae IG, Chung JW, Lee MS, Kang JM, Ryu J, Woo JH. The possible role of cerebrospinal fluid adenosine deaminase activity in the diagnosis of tuberculous meningitis in adults. Clin Neurol Neurosurg 2002; 104:10-5

[7]. Ribera E, Martinez-Vazquez JM, Ocana I, Segura RM, Pascual C. Activity of adenosine deaminase in cerebrospinal fluid for the differential diagnosis and follow-up of tuberculous meningitis in adults. J Infect Dis 1987; 155: 603-7

[8]. Cortes LLF, Cruz-Ruiz M, Gomez MJ, Hernandez JD, Mejias JE, Pahon J, Castillo J. Adenosine deaminase activity in the cerebrospinal fluid of patients of aseptic meningitis: utility in the diagnosis of tuberculous meningitis or neurobrucellosis. Clin Infect Dis 1995; 20(3): 525-30

[9]. Rohani MY, Cheong YM, Rani JM. The use of adenosine deaminase activity as a biochemical marker for the diagnosis of tuberculous meningitis. Malays J Pathol. 1995; 17(2):67-71

[10]. Vaishnavi C, Dhand UK, Dhand R, Agnihotri N, Ganguly NK. C-reactive proteins, immunoglobulin profile and mycobacterial antigens in cerebrospinal fluid of patients with pyogenic and non tuberculous meningitis. 1992; 36(3):317-25

[11]. Ribeiro MA, Kimura RT, Irulegui. Cerebrospinal fluid levels of lysozyme, IgM and C-reactive protein in the identification of bacterial meningitis. J Trop Med Hyg 1992; 95(2): 87-94.

[12]. Gerdes LU, Jorgensen PE, Nexo E, Wang P. C-reactive protein and bacterial meningitis: A meta-analysis. Scand J Clin Lab Invest. 1998 Aug; 58(5):383-93.

VII. Photographs

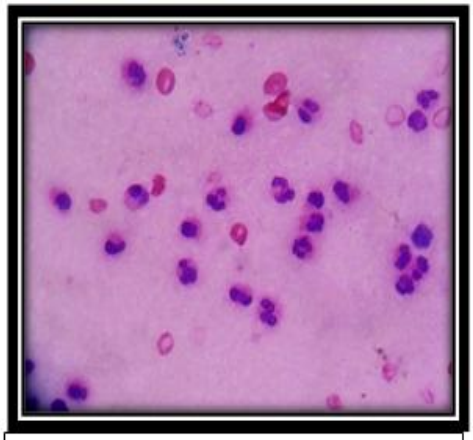

Figure 1: Giemsa stain(10 x 10X) neutrophils in CSF of a patient of pyogenic meningitis

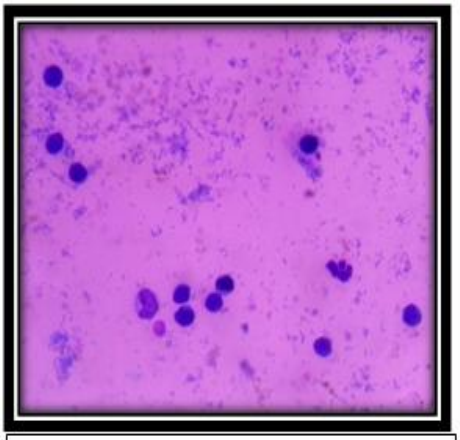

Figure 2 : Giemsa stain(10 x 10X). lymphoctes in CSF of a patient of tubercular meningitis.

Figure 5: plain CT brain showing ventricular dilation with minimal effacement of basal cisterns suggestive of non obstructive hydrocephalous in a patient of tubercular meningitis

Figure 6: PA view of chest X ray showing non homogenous opacity with internal cystic areas and surrounding fibrotic opacities noted in the upper zone of left lung with trachea mediastinal shift towards left side in a patient of pulmonary tuberculosis