



Estimation of C-Reactive Protein (C-RP) in Serum and Cerebrospinal Fluid (CSF) to Differentiate between Pyogenic and Tubercular Meningitis

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Abstract

Meningitis is one of the commonest and most feared neurological disease in children and adults with high morbidity and mortality. So, this study was conducted to measure the serum and CSF C-reactive protein to differentiate between pyogenic and tubercular meningitis.

Method: *This study was conducted in Department of Medicine, S. N. Medical College, Agra. Adult between 12 - 50 years of age admitted with history of fever and seizure were included. CSF was sent for CRP estimation and other laboratory investigations. Patients were divided into three groups based on clinical and CSF finding. Group 1 (Bacterial Meningitis), Group 2 (Tubercular Meningitis) and Group 3 (Control Group). Statistically analysis was done by Chi-square test and Student "t" test.*

Result: *60 patients were enrolled in our study. The mean ages of our cases in pyogenic tubercular and control group was 22.38 years, 26.38 years and 28.95 years respectively. 8 cases had pyogenic meningitis, 32 cases had tubercular meningitis and 20 cases had no meningitis. Serum value of CRP in case of pyogenic meningitis which is statistically significantly raised than that in tubercular group (mean value 36.52mg/L) (p value < 0.0001). The value of mean CRF level was found to be significantly higher in the pyogenic meningitis (91.13 mg/L), compare to tubercular meningitis (2.70 mg/L) and control group (1.54 mg/L with p value <0.0001), which is statistically significant.*

Conclusion: *Serum CRP and CSF - CRP estimation in meningitis is good parameter to differentiate pyogenic from other meningitis.*

Introduction

Acute pyogenic meningitis is the most common cause of suppurative infection in the central nervous system (CNS). The prognosis of pyogenic meningitis is critically dependent on a rapid and causal implementation of immediate treatment.

However, clinical and biochemical parameters available are not reliable enough except when bacteria are found in the cerebrospinal fluid (CSF) under a microscope. Therefore, the initial treatment of acute pyogenic meningitis is most of the time presumptive.¹⁻² Meningitis in view of

their acute morbidity and long term risk of brain damage, learning disabilities, mental retardation, hearing loss or death, differentiation between pyogenic meningitis and tubercular meningitis is extremely important because of their therapeutic and prognostic significance.

Till date there are various tests available which are helpful in establishing the etiological diagnosis but each and every test has some drawback. The rapid diagnostic tests including counter immunoelectrophoresis and enzyme linked immunosorbent assay (ELISA), are helpful in establishing etiologic diagnosis, but these tests are costly, difficult to perform and not easily available. If the patient has received inadequate antibiotics and ATT the CSF becomes sterile. Biochemistry may be altered and pleocytosis persists though nature of the cells changes. It poses a difficult problem in the differential diagnosis from bacterial and tubercular meningitis. In such circumstances the estimation of serum and CSF CRP concentration provides a new dimension to the specific diagnosis of meningitis. Some of the studies conducted abroad and in india, have shown that serum and CSF CRP can be used as a diagnostic tool to differentiate between pyogenic and tubercular meningitis⁴.

So we have conducted this study to establish the credibility of CRP as a diagnostic tool in differentiation between pyogenic and tubercular meningitis.

C-Reactive protein (CRP) is an acute phase reactant. Almost any inflammation in the body causes CRP to be detected in serum or other body fluids associated with the affected tissue^{3,10}. In Western countries, attention has differentiate bacterial and viral infections. Few studies have reported CSF C-reactive protein to have high sensitivity and specificity in differentiating pyogenic meningitis from aseptic meningitis.

Objective

The present study was conducted to evaluate the role of serum and CSF CRP in differentiation of pyogenic meningitis and tubercular meningitis.

Methods

This study was carried out in the Department of Medicine, S. N. Medical College, Agra from June 2007 to November 2008. Clinically suspected 40 cases of meningitis between the age group of 12 - 50 years were selected from the medicine indoor and outdoor clinic. The enrolled patients were subjected to a protocol which includes detailed clinical history. Haemogram, X-ray chest PA view, CSF-Cytology & Biochemistry, CSF-Gram's stain and culture, CT Scan / MRI Brain and CSF-CRP values estimation were done. Patients less than 18 years. Patients with severe hepatic dysfunction females on contraceptives and intrauterine devices, patients on steroids, severe dyslipidemias, pregnancy and lactation. and inflammatory conditions eg. Arthritis, SLE, and obesity reduced are not included in the study as these factors independently affect CRP levels.

Patients were divided into three groups based on clinical and CSF finding. Group 1 – pyogenic meningitis, Second Group – included Tubercular meningitis and Third Group included age and sex matched control group. Control group consisted of patients with acute respiratory tract infection, with meningismus and febrile convulsions. CRP level was estimated by liquid phase immune precipitation assay with nephelometric and point detection. Observation were tested statistically by the Chi-square test and student “t” test and for sensitivity, specific and positive predictive value of CSF in different types of meningitis.

Result

The mean ages in pyogenic, tubercular control group was 22.38 years, 26.38 years and 28.95 years respectively. The male-to-female ratio in each groups is described in Table 1 which compares the three groups on gender parameter.

Table 1: Gender distribution in the three groups

Sex	Pyogenic Meningitis	Tubercular Meningitis	Control
Male	6	16	11
Female	2	16	9
Total	8	32	20

Table 2: CSF C – Reactive protein in Study group & Control group

Group	No.	Mean(mg/L)	SD
Tubercular	32	2.70	1.55
Pyogenic	8	91.13	11.21
Control	20	1.54	0.59

The value of mean CSF-CRP level was found to be significantly higher in the pyogenic meningitis (91.13 mg/L), compare to tubercular meningitis (2.70 mg/L) and control group (1.54 mg/L with p value <0.0001), which is statistically significant.

Table 3: Serum C-Reactive protein in Study Group and Control Group

Group	No.	Mean(mg/L)	SD
Tubercular	32	36.52	24.93
Pyogenic	8	204.11	14.93
Control	20	2.55	0.774

The mean value of serum CRP in the case of pyogenic group is 204.11 mg/L which is statistically significantly raised than that in tubercular group (mean value 36.52 mg/L) (p value <0.0001)

Table 4: Comparison of Serum CRP in Tubercular and Pyogenic Group

Group	No.	Mean (mg/L)	SD	t-value	p-value
Tubercular	32	36.52	24.93	18.108	<0.0001
Pyogenic	8	204.11	14.93		

Table 5: Comparison of CSF CRP in Tubercular and Pyogenic Group

Group	No.	Mean (mg/L)	SD	t-value	p-value
Tubercular	32	2.70	1.55	44.607	<0.0001
Pyogenic	8	91.13	11.21		

Table 6: Diagnostic utility of C-reactive Protein Test in CSF

Meningitis	No.	CR P +ve	CR P -ve	Sensitivity	Specificity	Positive Predictive Value
Pyogenic	8	8	0	100	100	100
Tubercular	32	2	30	6.25%	100	100
Control	20	-	20	-	-	-
Total	60	10	50	-	-	-

Table 6 shows estimates of CRP in CSF for pyogenic meningitis with 100% sensitivity, specificity and positive predictive value.

Absence of CRP rather than its presence is more important for the diagnosis to tubercular meningitis.

Table 7: Diagnostic utility of C-reactive Protein Test in Serum CRP

Meningitis	No.	CR P +ve	CR P -ve	Sensitivity	Specificity	Positive Predictive Value
Pyogenic	8	8	0	100	100	100
Tubercular	32	32	-	100	100	100
Control	20	-	20	-	-	-
Total	60	40	20	-	-	-

Table 7 shows estimates of CRP in serum for pyogenic and tubercular meningitis with 100% sensitivity, specificity and positive predictive value.

Discussions

CRP is mainly synthesized in the liver. But studies shows that CRP can also be synthesized in the neurons and lipopolysaccharide-S can induce CRP synthesis in extrahepatic sites. CRP levels are affected by factors such as hepatic dysfunction, dyslipidaemia, females on oral contraceptive pills, and patients on steroids, and hence were not included in the study.

In this study we found that the mean value of CSF CRP are pyogenic meningitis (91.14 mg/L) and tubercular meningitis (2.70mg/L) which is significantly higher than that in control group (1.54mg/L) with p value <0.0001 which is statistically significant. Gaur et al⁷ conducted study and results shows sensitivity of 80% and 100% specificity and 100% positive predictive value.

Similar study conducted by Corral et al² initiated that CSF-CRP value appeared to be more sensitive in differentiating bacterial and not-bacterial meningitis than the usual parameters measured in CSF like cell count, protein, sugar and Gram stain. Our result also correlate with their findings. Similar study conducted by Przulalkowski et al, indicated that CRP levels in CSF were elevated significantly in pyogenic meningitis compared to tubercular meningitis.

The mean value of serum CRP are- pyogenic (204.11 mg/L) and tubercular meningitis (36.52 mg/L) which is significantly higher than that in control group (2.55 mg/L) with p value < 0.0001 which is statistically significant. Sutinen J et al⁸ states that value of serum CRP in differentiating CNS infections of varying etiology was investigated. Mean CRP was higher in the bacterial group than in the viral groups (207+111 mg/l Vs 39+34 mg/l; p value<0.001)

Similar study conducted by Siriyaichingkul S et al (2005)⁴ : Serum C-reactive protein can be used as a diagnostic tool to differentiate between bacterial and aseptic meningitis as a serum CRP in bacterial meningitis is significantly higher than that in aseptic meningitis (p value < 0.0001).

Peltola³, H.O. (1982) and Debeer⁹, F.C., Kirsten et al (1984) used serum CRP levels to monitor the infections of central nervous system and also to differentiate between tubercular, pyogenic and viral meningitis, since the CRP levels have been found to be significantly lower in the cases of tubercular and viral meningitis.

Shimentani et al also showed a substantial increase in CSF and serum CRP level in case of meningitis.

Vaishnavi et al⁵ and Tankhiwale et al⁶ observed a similar trend with the level of CSF CRP.

Sutinen J, Sombrero L et al (1998/1999): Mean CRP was significantly higher in the bacterial group than in the viral group (207 ± 111 mg/L Vs 39 ± 34 mg/L ; p value < 0.0001).

Hansson I O and Axelsson et al (1993): Serum CRP to differentiate between acute bacterial and viral meningitis was evaluated in 235 patients. Serum CRP value was higher in bacterial meningitis than viral meningitis.

Conclusion

We conclude that estimates of CRP in serum and CSF is a valuable, rapid, bedside diagnostic test for differentiating between pyogenic and tubercular meningitis with reasonably good sensitivity, specificity and positive predictive value. Absence of CRP in CSF rather than its

presence is more important for the diagnosis of Tubercular meningitis. Maximum prediction of pyogenic meningitis can be made if the test is positive.

However, recommending it for routine clinical application needs further evaluation with bigger sample size, utilizing accurate and precise quantitative assay for measuring CRP levels in serum and CSF.

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