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Cerebro spinal fluid pleocytosis: A clinicopathologic analysis

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Abstract

Background: Cerebro Spinal Fluid (CSF) examination is very useful in patients of suspected CNS disease and the necessity of correlating it with the clinico-pathologic findings which will help in early diagnosis of CNS diseases and guide the further management of the disease. CSF examination with quantification of leukocytes and differential count of cellular subsets in the cerebrospinal fluid is a standard procedure in cases of suspected infectious conditions. Present study emphasises pleocytosis in the cerebrospinal fluid along with other laboratory parameters.

Materials and Methods: The study is consisting of 295 CSF samples from patients with clinically suspected CNS infections. The CSF findings were evaluated in all age group patients in relation to cell counts and pleocytosis.

Results: In Physical examination of CSF colour, appearance and received quantity were evaluated. Maximum specimen was received in 1 year to 18 year age group. CSF pleocytosis ($>5\text{cells}/\mu\text{l}$) was present maximum (48%) in 1 month to less than 1 year age. Pleocytosis $>5\text{leucocytes}/\mu\text{l}$ was found in 121 (41%) samples out of 295 samples.

Conclusion: CSF cell count examination is very common and useful investigation done for suspected various CNS diseases. Infectious and non-infectious diseases of CNS can cause pleocytosis of the cerebrospinal fluid. The type of cells depends mainly on the clinical scenario. However it seems to vary with total cell count also, such as lymphocytes predominating at lower total cell counts while neutrophils are at higher total counts.

Keywords: Cerebrospinal fluid, pleocytosis, central nervous system, CSF

Introduction

Migration of leukocytes to the cerebrospinal fluid (CSF) is a cardinal symptom of an infectious condition affecting the meninges or the cerebral parenchyma. Various CNS diseases and meningitis cannot reliably be differ clinically and requires lumbar puncture to analyse CSF [1, 2]. Accurate initial diagnosis is the corner stone for therapeutic decision making. Timelier diagnostic clues of meningitis on CSF analysis include an elevated white blood cell (WBC) count or protein concentration, and decreased glucose concentration relative to blood [3-5].

Patients suffering from viral meningitis present CSF leukocyte count varying from 10 to $1000/\mu\text{l}$, but typically below 500 [6]. In bacterial meningitis CSF leukocytes vary from below 100 to more than $10,000\text{leucocytes}/\mu\text{l}$, often between 1000 and $5000/\mu\text{l}$ [7]. However, pleocytosis in the CSF may also occur in other medical conditions, e.g. neurological, rheumatic or malignant disease [8, 9].

Analysis of cerebrospinal fluid (CSF) forms a key investigation. Despite the advances in diagnostic modalities, simple CSF examination remains a valuable test for the diagnosis of various pathologies of CNS. It is a rapid and sensitive method besides being cost-effective which is an important parameter for any diagnostic modality [10]. Present study aimed to analyse various clinicopathologic parameters assessed on CSF including age distribution, physical examination for received quantity, colour and appearance as well as cell count evaluation.

Materials and Methods

This is a prospective study consisting of 295 CSF specimen received in Trauma pathology laboratory of tertiary care hospital over period of one year. CSF specimens of all age groups were included for data analysis. Physical examination was done for received quantity of CSF (to check adequacy of specimen) along with colour and appearance. Microscopic examination was done for all received CSF samples which were assessed for total leucocyte count (TC) and differential leukocyte count (DC) by Romanowsky stain.

All CSF specimens received were included in the study. The traumatic lumbar puncture (LP) and those patients who had received antibiotic treatment before (as per clinical history) LP was excluded from the study.

Statistical Analysis

The data analysis was done by descriptive statistics for the percentage of pleocytosis CSF and distributed them by age and differential cell count.

Results

Total 295 CSF samples were evaluated. There were 170 male and 125 female patients. The CSF quantity received was < 1ml in 254 patients while ≥ 1 ml in 41 patients. [Table

1] illustrates details about colour, appearance and received quantity of CSF fluid in physical examination.

Table 1: Physical examination of CSF

Physical examination	Criteria	Number of Specimen
Colour	Clear	240
	Pale yellow	6
	Red	11
	Straw	35
	Yellow	3
Appearance	Clear	274
	Turbid	21
Quantity	<1 ml	254
	≥ 1 ml	41

In relation to age wise distribution, maximum specimens were received in 1 year to 18 year followed by newborn age group. CSF pleocytosis (>5 cells/ μ l) was present in 39% cases in newborn, 48% cases in 1 month to less than 1 year, 40% in 1 year to 18 year and 47% in more than 18 year age group. Out of 295 CSF specimens, 174 (59 %) patients showed cell count ≤ 5 and also maximum number of CSF specimen showed cell count of ≤ 5 in each age group. [Table 2]

Table 2: Age wise analysis of CSF cell count

Age	CSF Cell count/ μ l				CSF specimen with Pleocytosis (>5 cells/ μ l)	Total number of specimens
	≤ 5	6-100	101-1000	>1000		
Newborn	57(61%)	22	12	02	36(39%)	93
1 month to < 1 year	11(52%)	06	02	02	10(48%)	21
1 year to 18 year	87(60%)	40	12	06	58(40%)	145
>18 year	19(53%)	08	07	02	17(47%)	36
Total	174(59%)	76	33	12	121(41%)	295

[Table 3] shows distribution of differential cell count in relation to total cell count. It was observed that the differential count was lymphocytes predominated at lower cell counts (170 cases out of 174 for cell count ≤ 5 / μ l and

54 cases out of 76 for cell counts 6 -100/ μ l) while as neutrophils predominated only at very high cell counts (8 cases out of 12 for cell counts >1000 / μ l).

Table 3: Differential cell count analysis in CSF

Cells/ μ l	Number of cases	All Lymphocytes	All neutrophils	Mainly lymphocytes ($>60\%$)	Mainly neutrophils ($> 60\%$)	Lymphocytes and neutrophils equal
≤ 5	174	170	0	03	0	01
6-100	76	54	0	19	03	-
101-1000	33	06	0	24	02	01
>1000	12	0	01	04	07	-

Discussion

Cerebrospinal fluid (CSF) is a clear fluid circulating in the intracranial and spinal compartments. Under normal conditions, the composition of CSF remains constant. However, in various neurological diseases especially in acute conditions, the colour, appearance, composition, total count and its differential cell count can be altered. By measuring the levels of various CSF components using relevant laboratory techniques; diagnosis, severity and prognostication of pathological conditions can be done. Thus, CSF examination forms the cornerstone in the diagnosis of many neurological disorders [11]. Most common cause of abnormal CSF findings in most studies was

meningitis followed by demyelinating diseases and malignancy.

Physical examination of CSF begins immediately after collection of the specimen. It includes examination of parameters like colour and clarity which are important diagnostic characteristics of CSF. This must be done within 30 minutes of collection of the fluid, since red cell lysis after this time can affect the results. The normal CSF is crystal clear and colourless like distil water, and does not clot. The occurrence of pleocytosis is the usual reason for cloudy fluid. At least 200 white cells per cubic millimeter can be present without altering the clarity. Over 500 white cells per cubic millimeter usually produces cloudiness. A markedly

elevated protein can also alter the clarity of the CSF. Thus, clarity provides immediate indication of abnormality of the CSF.

The presence or absence of colour in CSF is crucial observation. Straw, pink, yellow, or amber pigments (xanthochromia) are abnormal and indicate the presence of bilirubin, haemoglobin, red blood cells, or increased protein. The most common cause of xanthochromia is subarachnoid haemorrhage^[12].

Cell count on CSF is done manually on the undiluted sample in a counting chamber. The number of white blood cells in CSF is very low, usually necessitating a manual WBC count. Total leukocyte count increases (pleocytosis) in various disorders and along with differential count provides important diagnostic information.

An increase in WBC cell count of CSF occurs in various pathological conditions of CNS like infection, allergy, leukaemia, multiple sclerosis, haemorrhage, traumatic tap, encephalitis, and Guillain-Barré syndrome. It is essential to do a microscopic examination of all CSF samples since white blood cell (WBC) count up to 200/cmm and red cell count up to 400/cmm are associated with the clear appearance of CSF^[13].

Differential Leukocyte Count of CSF provides information about relative proportion of various leukocytes. If CSF contains only a few cells, then it is centrifuged at high speed (3000 g) for 10 minutes and a smear is made from the sediment. If CSF contains many cells, then a smear is made directly from the uncentrifuged sample. After staining with a Romanowsky stain, smear is examined under the microscope for differential leukocyte count.

Simple centrifugation of CSF often causes cell breakage and distortion. Cytospin preparation with cytocentrifuge (high speed centrifugation to concentrate cells on a slide in a uniform monolayer) has been recommended as it improves the cell yield and preserves the cell morphology well. The WBC differential helps to distinguish many of these causes. For example, viral and tuberculous infection is usually associated with an increase in lymphocytes, while bacterial and fungal infections are associated with an increase in polymorphonuclear leukocytes (neutrophils)^[14].

Thus, Analysis of the CSF provides invaluable diagnostic information. Diagnosing alterations in CSF components by laboratory methods and its relevance to the emergency care physician is extremely helpful in the management of patients.

Conclusion

CSF analysis is a very useful investigation in patients presenting with acute neurological conditions. CSF examination for various laboratory parameters helps to establish diagnosis, prognosticate and to assess the effect of various therapies to treat the patient conditions. CSF analysis has evolved over years from basic analysis to assessment of various biomarkers to aid the clinician. Hence it is very informative for the clinician to understand importance of CSF examination.

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