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A 15-Year Retrospective Survey of the Cytopathologic Spectrum of Cerebrospinal Fluid Aspirate in a Teaching Hospital in Uyo, Southern Nigeria

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Abstract

Background: The cytopathologic evaluation of cerebrospinal fluid (CSF) aspirates is a vital diagnostic tool for neurological disorders. This research aimed to characterize the diverse range of cytopathological diagnoses encountered in the CSF specimens within 15 years in a teaching hospital while highlighting their clinical significance.
Materials and Methods: A thorough review of cytopathology records from January 1, 2006, to December 31, 2020, was conducted. CSF samples were collected through lumbar punctures and subsequently subjected to cytopathological examination. The data were collected from the Department of Histopathology, University of Uyo Teaching Hospital archives. The inclusion criteria encompassed all cases with available CSF cytopathology results during the study period. Cases with inadequate or missing data were excluded from the analysis. Data regarding patients' ages, sex, clinical, and cytopathologic diagnoses were extracted and analyzed.
Results: Thirty-four (34) CSF samples were analyzed during the study period. The mean age was 11.45 ± 12.20 years. The most common clinical indication for CSF analysis was suspected Burkitt's Lymphoma (34.78%), followed by other Non-Hodgkin Lymphoma (13.04%). The cytopathologic diagnoses exhibited a diverse spectrum, including Acellular Smear (26.5%), Inflammatory Smear (2.9%), Negative for Malignant Cells (52.9%), Positive for Malignant Cells (14.7%), and Suspicious for Malignant Cells (2.9%). This study also observed a significant association between age groups (particularly 0-10 years) and cytopathological diagnoses, with a p-value of 0.023.
Conclusion: A retrospective survey of CSF cytopathology in a Nigerian teaching hospital reveals diverse cytopathological diagnoses, providing insights for neuropathology clinicians and researchers.

Keywords: Cerebrospinal Fluid (CSF), Aspirate, Cytopathology, Retrospective Study, Spectrum, Uyo, Nigeria

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Introduction

Cerebrospinal fluid (CSF) analysis for cytopathological diagnosis plays a pivotal role in the diagnosis and management of a wide array of neurological disorders, including infections, neoplasms, and inflammatory conditions.[1–6] The cytopathologic examination of CSF specimens offers a minimally invasive means of obtaining

valuable diagnostic information, aiding in the identification of abnormal cells, infectious agents, and other pathological processes within the central nervous system (CNS).[1,3,4,7–15] CSF cytopathological evaluation is compulsory in suspected inflammatory, neoplastic, or hemorrhagic conditions and needs to be interpreted in the clinical context.[3–5,7–16] Indeed, the gold standard for CSF analysis is the microscopic examination by cytopathology screening technicians and neuropathologists, with a broad categorization of CSF cytopathological lesions into inflammatory, hemorrhagic, and neoplastic.[2] CSF cytopathological analysis is a valuable tool in understanding the pathogenesis of neuroinflammatory diseases, particularly multiple sclerosis.[16] The most common infectious, primary neoplastic, and secondary neoplastic lesions detected through CSF cytopathologic analysis include Cryptococcus neoformans infection, medulloblastoma, and non-Hodgkin lymphoma (NHL)/metastatic breast carcinoma respectively.[3,11–15,17] Also, the presence of siderophages or erythrophages on CSF cytopathological analysis can be used in confirming the diagnosis of subarachnoid hemorrhage as an alternative to CSF spectrophotometry to detect oxyhemoglobin or bilirubin.[4] The interpretation of CSF cytopathology requires meticulous examination and a comprehensive understanding of the diverse spectrum of cellular constituents that may be encountered.[1–6,10,13–18]

In Africa, the burden of neurological disorders remains significant.[19–24] However, there is a scarcity of cytopathological studies detailing the cytopathologic findings of CSF aspirates over an extended period in Africa, including Uyo. This study aims to bridge this gap by retrospectively analyzing the 15-year cytopathologic spectrum of CSF aspirates in a teaching hospital in Uyo, Southern Nigeria, as well as comparing the findings of this study with relevant existing literature.

Materials and Methods:

Study Design and Location: This is a retrospective analysis of cytopathology records from January 1, 2006, to December 31, 2020. This study was conducted at the University of Uyo Teaching Hospital (UUTH), Uyo, Akwa Ibom State, in the Department of Histopathology. UUTH, Uyo is a 500-bed tertiary healthcare facility in the South-South region of Nigeria.

Sample Collection and Processing: The CSF samples were collected through lumbar punctures performed by trained medical personnel (at diverse locations in the teaching hospital) using aseptic techniques. The samples were immediately transported to the Anatomical Pathology laboratory of the Department of Histopathology, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria, and subjected to cytopathologic processing according to standard operating procedure (SOP).[1,5,6] Also, following this SOP, conventional (i.e., Cytospin) smear preparations were made, stained using standard routine cytopathologic stains (hematoxylin and eosin, May-Grünwald Giemsa, and Papanicolaou), and examined by Anatomical Pathologists.

Data Collection and Analysis: Relevant data, including patients' ages, sex, clinical diagnoses, and cytopathologic diagnoses, were extracted from the department's laboratory information system and medical records. The inclusion criteria encompassed all cases with available CSF cytopathology results during the study period. Cases with inadequate or missing data were excluded from the analysis. Data regarding patient demographics, clinical, and cytopathologic diagnoses were extracted and analyzed. Data generated in this study were written in a Microsoft Office Excel 2016 document and transferred into IBM SPSS version 21.0 statistical software for statistical analysis. We used descriptive statistics, cross-tabulations, and Pearson's chi-square test to test for statistical differences between the variables. Statistical significance was set at a P value of ≤ 0.05. Following analysis, the results were presented as texts, frequency distribution tables, and figures.

Ethical considerations: This study was conducted following the World Medical Association's Helsinki declarations by ensuring patients' confidentiality.

Results

Thirty-four (34) cerebrospinal fluid (CSF) aspirate cases with previous cytopathologic diagnoses were included in this study. This accounted for 2.71% (34/1256) of non-gynecological cytopathology specimens received within the study period (2006 to 2020). Their mean, median, and modal age were

Table 1: A frequency distribution table of the age groups of study subjects

Age Groups	Frequency	Percentage
0-10	22	64.7
11-20	6	17.6
21-30	3	8.8
31-40	1	2.9
41-50	0	0.0
51-60	0	0.0
>61	2	5.9
Total	34	100.0

Table 2: A frequency distribution table of the provisional clinical and cytopathological diagnoses of the study subjects

Provisional Clinical Diagnosis		
Diagnosis	Frequency	Percentage
Acute Lymphoblastic Leukemias (ALL)	2	8.70
Acute Myelogenous Leukemia (AML)	2	8.70
Burkitt's Lymphoma	8	34.78
Carcinomatous Meningitis	1	4.35
Intra-abdominal Malignancy	1	4.35
Intracranial Tumor	1	4.35
Meningoencephalitis	1	4.35
Other Non-Hodgkin Lymphomas (NHL)	3	13.04
Retinoblastoma	1	4.35
Transverse Myelitis	1	4.35
Tuberculous Meningitis	2	8.70
Total	23	100.0
Cytopathological Diagnosis		
Acellular Smear (Non-Diagnostic)	9	26.5
Inflammatory Smear	1	2.9
Negative for Malignant Cells	18	52.9
Positive for Malignant Cells	5	14.7
Suspicious for Malignant Cells	1	2.9
Total	34	100.0

11.45 ± 12.20, 7, and 5 years respectively. Also, the minimum and maximum ages of the study subjects were 1 and 62 years respectively; with 25th, 50th, and 75th percentiles of 4.5, 7.0, and 13.5 years respectively. Furthermore, the most common age group of our study subjects was 0-10 years, accounting for 64.7% (22/34) of the cases (Table 1).

There were more males (61.8%; 21/34) than females (Figure 1), with a male-to-female ratio of 1.62:1.

The most common provisional clinical diagnosis was Burkitt's Lymphoma, accounting for 34.78% (8/23) of the cases (Table 2). Notably, the most

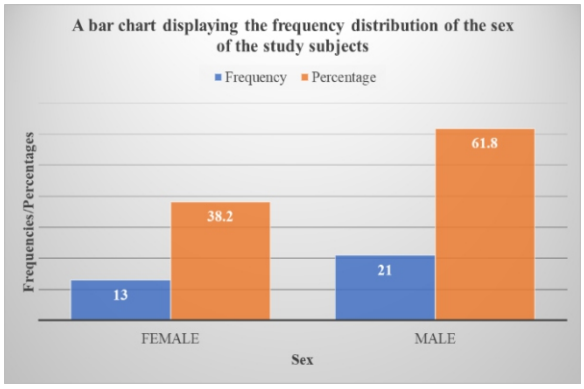

Figure 1: A bar chart showing the distribution of the sex of the study subjects

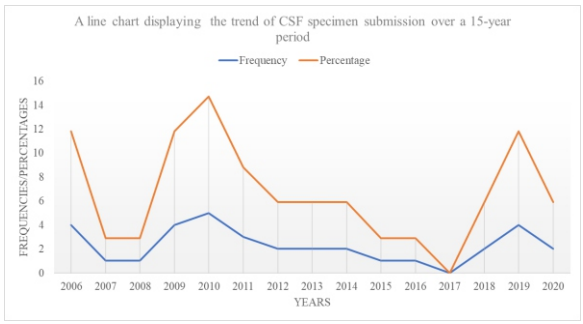

Figure 2: Aline chart showing the frequency distribution of the number of CSF specimens of the study subjects per year over 15 years (2006 to 2020)

common cytopathological diagnosis was Negative for Malignant Cells, accounting for 52.9% (18/34) of the cases (Table 2).

Most of the Negative for Malignant Cells diagnoses were found in males, comprising 66.67% (12/18) of the cases with Negative for Malignant Cells diagnoses, and 35.29% (12/34) of all the cases (Table 3). Also, both females and males share somewhat similar proportions for Positive for Malignant Cells diagnoses, comprising 5.88% (2/34) and 8.82% (3/34) of the cases respectively, with a non-significant p-value of 0.476 (Table 3). Notably, the 0-10 years age group accounted for 55.56% (10/18) of the cases with Negative for Malignant Cells diagnoses, and 29.41% (12/34) of all the cases, with a significant p-value of 0.023 (Table 3). Burkitt's Lymphoma accounted for 38.46% (5/13) of the cases with Negative for Malignant Cells diagnoses, and 21.74% (5/23) of all the cases, with a non-significant p-value of 0.260 (Table 3).

Table 3: A frequency distribution table of the cross-tabulations between cytopathological diagnoses, sex, age groups, and provisional clinical diagnoses of the study subjects.

Cytopathological Diagnosis and Sex							
Sex	Cytopathological Diagnosis						P-value
	Acellular Smear (Non Diagnostic)	Inflammatory Smear	Negative for Malignant Cells	Positive for Malignant Cells	Suspicious for Malignant Cells	Total	
Female	3	1	6	2	1	13	0.476
Male	6	0	12	3	0	21	
Total	9	1	18	5	1	34	
Cytopathological Diagnosis and Age Groups							
Age Groups	Cytopathological Diagnosis						P-value
	Acellular Smear (Non Diagnostic)	Inflammatory Smear	Negative for Malignant Cells	Positive for Malignant Cells	Suspicious for Malignant Cells	Total	
0-10	8	1	10	2	1	22	0.023
11-20	0	0	6	0	0	6	
21-30	0	0	0	3	0	3	
31-40	1	0	0	0	0	1	
41-50	0	0	0	0	0	0	
51-60	0	0	0	0	0	0	
>61	0	0	2	0	0	2	
Total	9	1	18	5	1	34	
Cytopathological Diagnosis and Provisional Clinical Diagnosis							
Provisional Clinical Diagnosis	Cytopathological Diagnosis						P-value
	Acellular Smear (Non Diagnostic)	Inflammatory Smear	Negative for Malignant Cells	Positive for Malignant Cells	Suspicious for Malignant Cells	Total	
Acute Lymphoblastic Leukemias (ALL)	1	0	1	0	0	2	0.260
Acute Myelogenous Leukemia (AML)	1	0	1	0	0	2	
Burkitt's Lymphoma	3	0	5	0	0	8	
Carcinomatous Meningitis	0	0	1	0	0	1	
Intra-abdominal Malignancy	0	0	1	0	0	1	
Intracranial Tumor	0	0	0	1	0	1	
Meningoencephalitis	1	0	0	0	0	1	
OtherNon-Hodgkin Lymphomas (NHL)	0	0	2	0	1	3	
Retinoblastoma	0	0	0	1	0	1	
Transverse Myelitis	0	0	1	0	0	1	
Tuberculous Meningitis	0	1	1	0	0	2	
Total	6	1	13	2	1	23	

Cross-tabulating cytopathological diagnoses with the sex of the study subjects revealed Kendall's tau-b ordinal by ordinal association of -0.067 (with a non-significant p-value of 0.686). Also, cross-tabulating cytopathological diagnoses with age groups of the study subjects revealed Kendall's tau-b ordinal by ordinal association of 0.277 (with a non-significant p-value of 0.067). Furthermore, cross-tabulating cytopathological diagnoses with the provisional clinical diagnosis of the study subjects revealed Kendall's tau-b ordinal by ordinal association of 0.075 (with a non-significant p-value of 0.614).

The peak of CSF specimen submission was in 2010 (14.7%; 5/34), while the trough was in 2017 (0.0%; 0/34) (Figure 2).

Discussion

In this study, the cytopathologic spectrum of CSF aspirates collected over 15 years in a teaching hospital in Uyo, Southern Nigeria, was retrospectively examined. The findings were also contrasted with pertinent prior research. The average age of the study subjects was 11.45 ± 12.20 years, and the age range from 0 to 10 years accounted for 64.7 percent (22/34) of the cases. Second, there were 1.62 times as many males as females. Thirdly, Burkitt's lymphoma was the most prevalent provisional clinical diagnosis, accounting for 34.78 percent (8/23) of the cases. Fourthly, Negative for Malignant Cells was the most frequent cytopathological diagnosis, accounting for 52.9 percent (18/34) of the cases. Notably, the age groups and cytopathological diagnosis were significantly

associated (with a p-value of 0.023).

The average age of our study subjects was not consistent with the average age of the study subjects of similar studies. Damiani D et al had an average age of ≤ 4 years, Rao R et al had an average age of 57 years, Schinstine M et al had an average age of 45 years, and Qian X et al had an average age of 6.1 years (pediatric group) and 38.7 years (adult group).[3,8,9,11] This is because Damiani D et al studied only pediatric patients, Rao R et al studied only adult patients, Schinstine M et al studied children and adults together (like in our study), while Qian X et al studied distinct pediatric and adult groups.[3,8,9,11] Most of these studies were on specialized patient groups unlike our study which was done on all patient groups; notably, Damiani D et al studied CSF in children with medulloblastoma, Rao R et al studied CSF in adults with metastatic breast carcinoma, Schinstine M et al studied CSF in patients with hematopoietic malignancies, and Qian X et al studied CSF in pediatric and adult groups with Ependymoma.[3,8,9,11] Ho CY et al studied distinct pediatric and adult groups with a general median age of seven years; this finding is consistent with the median age of our study subjects.[7]

We found that there were 1.62 times as many males as females. This finding is consistent with the findings of Ho CY et al and Schinstine M et al in their studies who found a male-to-female ratio of 58/29 and 19/13 respectively.[7,8] In contrast, Damiani D et al found a male-to-female ratio of 1:1.8.3 The reason for this difference may be that this CSF study was carried out in a specialized group of children with medulloblastoma rather than a general children and adults' group. Interestingly, Qian X et al in their study found contrasting male-to-female ratios in their pediatric and adult groups, being 19/14 and 4/11 respectively.[9] The reason for this contrasting group findings is unknown, hence calls for further study. Interestingly, there was no significant association between the sex of our study subjects and their cytopathological diagnoses; implying that the occurrence of the diagnostic category in any of the sexes is purely due to chance.

Notably, Burkitt's lymphoma was the most common provisional clinical diagnosis found in this study. This finding was generally inconsistent with similar studies because those studies were in specific lesions, cells, and methodologies with CSF correlation. However, Straccia P et al, Onur I et al, and Schinstine M et al in their studies done on metastatic neoplastic lesions with CSF involvement found that the commonest provisional clinical diagnosis were variable members of the Non-Hodgkin Lymphomas, and Burkitt's Lymphoma is a member of Non-Hodgkin Lymphoma.[8,12,17] Our study's sample size was quite low compared to that of similar studies reviewed, thus it is probable that if the sample size was larger, then the commonest provisional clinical diagnosis may also change. Interestingly, the provisional clinical diagnoses were not significantly associated with the cytopathological diagnoses, accordingly, none of these provisionally diagnosed Burkitt's Lymphoma cases had a "Positive for Malignant Cells" diagnosis after the cytopathological evaluations of their CSF samples.

Negative for Malignant Cells was the most frequent cytopathological diagnosis, in this study. This finding is consistent with studies by Prayson RA et al, Ho CY et al, Qian X et al, and Schinstine M et al.[7–10] This finding contrasted with the rest of the specialized metastatic neoplastic lesion CSF studies given that these studies were done only on samples that were already positive for malignant cells to further characterize the malignant cells. Also, for CSF studies on lesions that were initially diagnosed as "Negative for Malignant Cells", ancillary studies carried out majorly detected infectious agents such as Cryptococcus neoformans and Toxoplasma spp.[10,13,15] This implies that further testing for infectious agent identification will be a beneficial component of expert management of patients with neurological disorders who have a "Negative for Malignant Cells" diagnosis, particularly in our environment which has a high burden of infectious diseases.

Notably, there was a significant association between age groups and cytopathological diagnosis (with a p-value of 0.023). This suggests that the majority of the cytopathological diagnoses in our study were strongly related to the study subjects whose age bracket predominated (i.e., ages 0 to 10 years). The study subjects in this group provided the most CSF samples for cytopathological analysis, likely as a result of the high prevalence of neurological disorders in this age group in our teaching hospital or the fact that pediatricians requested CSF

cytopathological analyses more frequently than adult medicine specialists. Again, if we had a bigger sample size, this association might be altered. It is also interesting that none of the pertinent research we reviewed for this study reported such an association.

The limitations of this study stem from its retrospective nature, such that the pre-analytical, analytical, and post-analytical quality control variables in the laboratory processes leading to a cytopathological diagnosis were not under the control of the authors. Secondly, ancillary studies for further characterization of CSF samples such as microbiological evaluations, cell block analysis, cytochemistry, immunocytochemistry, and molecular biology studies could not be done because of a lack of facilities. Thirdly, the conventional cytologic technique (i.e., Cytospin) was used rather than the more modern liquid-based cytologic technique. Fourthly, differential cell count was not done in this study, and the radiological imaging data of the study subjects could not be assessed. For future studies, we would aim to conduct a prospective study in which all the quality control variables will be under the control of the authors as well as the incorporation of differential cell counting, ancillary cytopathologic techniques, and radiological investigation data.

Conclusion

This 15-year retrospective survey of the cytopathologic spectrum of cerebrospinal fluid aspirates (CSF) in a teaching hospital in Uyo, Southern Nigeria revealed the predominance of Negative for Malignant Cells diagnosis, with Burkitt's Lymphoma emerging as the most common provisional clinical diagnosis, as well as the significant association between age groups and cytopathological diagnoses. This highlights the importance of routine CSF cytopathology in the diagnosis and management of central nervous system disorders in our environment.

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