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Original Research Article

Study of Cytomorphological Patterns of Lymph Nodes by Fine Needle Aspiration Cytology and Correlation with Histopathology

Dr. M. Jyothi Swaroopa, Dr. B. Vani*

Assistant Professor, Malla Reddy Institute of Medical Sciences, Hyderabad, Telangana State, India

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***Corresponding author:** Dr. B. VANI

Abstract

Lymphadenopathy is the most common presentation in the head and neck region and may occur due to inflammatory conditions, as well as primary and secondary neoplasms. An early and accurate diagnosis helps the clinicians in starting the specific therapy on time, thus reducing morbidity and mortality. The present study was undertaken to know the spectrum of lesions found in the Enlarged cervical lymph nodes in 628 patients. Cervical group of lymph nodes are the most common lymph nodes involved in head and neck region. Non-specific reactive lymphadenitis is the most common benign pathology associated with enlarged lymph nodes whereas metastasis is the most common malignant condition. Most common age group of enlarged lymph nodes in benign category was 3rd decade and in malignant category was 6th decade. The sensitivity and specificity of FNAC is fare enough with lot of various other advantages like rapid diagnosis, reliable, less traumatic, minimal complication, repeatability, economical and convenient. Fine needle aspiration cytology in our experience provides a reliable method of investigating lymph node enlargement, the efficacy of which approaches that of other similar diagnostic procedures and in the present study, over all accuracy and sensitivity was 94.8% and100% respectively.

Keywords: Lymph Node, Cytology, Fine Needle Aspiration, Histopathology, Hodgkin's Lymphoma, Lympadenitis, Tuberculosis, Carcinoma.

INTRODUCTION

Lymphadenopathy is one of the commonest clinical presentations of all age groups attending out-patient departments (OPD). The etiology can vary from an inflammatory process to a malignant condition. Most common tool used in the present day is Fine needle aspiration cytology. Fine needle aspiration cytology (FNAC) is the study of cells and other tissue components obtained by sampling of a palpable superficial lesion or radiologically localized deep seated lesion through a small gauge needle. FNAC is used routinely as a first line of investigation in the evaluation of patients with lymphadenopathy. Peripheral lymph nodes are easily accessible and amenable to FNAC. It has increased success rate of getting representative material with high accuracy of diagnosis. This diagnostic modality has gained considerable importance in the management of patients with lymphadenopathy over several years. It is highly reliable in its diagnostic accuracy and hence considered as a micro-biopsy with high degree of correlation with histopathology. FNAC can significantly reduce the number of open biopsies. In case of specific infectious etiology, not only the cause of lymphadenopathy is determined, but also the causative organism can be identified which help in planning the treatment.

AIM OF THE STUDY

This study was done to evaluate the role of FNAC in patients with cervical lymphadenopathy and also to study the different cyto-morphological patterns of FNAC associated with cervical lymph nodes; and correlate the FNAC findings with histopathology.

MATERIALS AND METHODS

It is a prospective study from June 2012 to May 2014 was done on patients who presented with lymphadenopathy and referred to the Upgraded Department of pathology, Osmania Medical College and General Hospital, Hyderabad for Fine needle aspiration cytology. All the patients were clinically examined and the procedure of aspiration biopsy was explained to the patient including reliability, limitations and complications. Aseptic precautions were taken and aspiration of the selected lymph node was done. After, the overlying skin was stretched, the lymph node was grasped between the index finger and the thumb of the left hand; a sterile 22 or 23 gauge needle fitted to a

10ml syringe was pierced obliquely into the lymph node. The plunger was then withdrawn and the negative pressure was created in the syringe, after entering the lymph node mass. The needle was moved back and forth several times with a constant suction. The negative pressure was released and the needle was removed from the mass. The needle containing the aspirated material was then detached and air was drawn into the syringe. After reattachment of the needle, content of the needle was ejected out on the clean, dry and grease free glass slides. Smears were prepared using another glass slide exerting light pressure. Smears were immediately fixed in 95% ethyl alcohol, and these smears were stained by hematoxylin and eosin stains (H & E), Papanicolaou stain (PAP) and Giemsa stain wherever necessary. Air dried smears were also prepared in some cases. Ziehl Neelsen stain (ZN stain) was done for all the cases where necrotic material was aspirated or clinically suspected tuberculosis and HIV. Smears were examined and cytological diagnosis offered. Data regarding relevant radiological, biochemical and hematological investigations done for diagnostic purposes were collected. Lymph nodes of the patients who underwent subsequent surgical biopsy were fixed in 10% formalin and subjected to gross examination. Biopsy specimens were routinely processed to obtain 3 – 6 µm paraffin sections, which were stained with haematoxylin and eosin stains. Special stains like Ziehl Neelsen stain, PAS were done when ever indicated. Histopathological study was done separately and then results of cytological and histopathological study were correlated to evaluate efficacy of the procedure.

All cases of lymphadenopathies where fine needle aspiration cytology was done and those cases undergoing subsequent biopsy are included in the study. All cases of lymphadenopathy where adequate aspirate was not obtained even after repeated aspirations were excluded from the study.

RESULTS

Fine needle aspirations (FNAC) of 628 patients were considered in the study, yearwise distribution of the cases are tabulated in Table-1. Out of 628 patients, 289 were male and 339 female with 46% and 54 % respectively. Age and gender wise distribution of the cases are shown in Table-2.

Table -1: Year wise distribution of aspiration of cervical lymph nodes

Year	No of FNAC	Percentage
June-Dec 2012	172	27
Jan-Dec 2013	297	47
Jan-May 2014	159	26

Table-2: Age and Gender wise distribution of lymph nodes aspirated

Age	Male	Female	Total	Percentage
0-10	25	27	52	8
11-20	36	67	103	17
21-30	82	116	198	32
31-40	38	52	90	14
41-50	37	34	71	11
51-60	22	26	48	8
61-70	27	19	46	7
>70	12	8	20	3
Total	289	339	628	100%

In this study, out of 628 cases, majority of the cases (483 cases) were benign (77%) and remaining 145 cases were malignant (23 %). Out of the 145 malignant lesions, 51 cases (35 %) were primary malignancies of the lymph nodes and 94 cases (65 %) were metastatic lesions. Out of 483 benign cases, most of the cases were in the age group 21-30 years and least in the age group 61-70 years.

When cytological diagnosis was done, majority of the cases were Nonspecific reactive lymphadenitis (220 cases) and least were Hodgkin's lymphoma (21 cases), remaining diagnostic entities were tabulated in Table-3.

Table-3: Cytological diagnosis of FNAC of cervical lymph nodes

Cytological diagnosis	No of cases	Percentage of cases	Male	Female	Age range(yrs)
BENIGN					
Non specific reactive lymphadenitis	220	35	103	117	2.5-63
Tuberculous lymphadenitis	144	23	75	68	7-76
Granulomatous lymphadenitis	119	19	52	67	12-60
MALIGNANT					
Hodgkins lymphoma	21	3	9	12	10-73
Non- hodgkins lymphoma	30	5	10	20	11-80
Metastasis	94	15	61	33	26-82
Total	628	100	289	339	2.5-82

Out of the 628 cases subjected to FNAC, only 94 cases turned up for biopsy as per indications, cytological and histopathological diagnosis correlation tabulated in Table-4. Table-5 showing the correlation of benign and malignant cases correlation of cytological and histopathological diagnosis.

Table-4: Demonstrating FNAC diagnosis with histopathological diagnosis

Cytological diagnosis	No of cases	Histological diagnosis	No of cases
Non specific reactive lymphadenitis	25	Non specific reactive lymphadenitis	20
		Tuberculous lymphadenitis	4
		Castleman`s disease	1
Tuberculous lymphadenitis	16	Tuberculous lymphadenitis	15
		Hodgkins lymphoma	1
Granulomatous lymphadenitis	17	Non specific reactive lymphadenitis	2
		Tuberculous lymphadenitis	12
		Non hodgkins lymphoma	1
		Hodgkins lymphoma	1
		Castleman`s disease	1
Hodgkins lymphoma	10	Hodgkins lymphoma	10
Non Hodgkins lymphoma	15	Hodgkins lymphoma	3
		Non Hodgkins lymphoma	12
Metastasis	11	Metastasis	11

Table-5: Correlation between cytological and histopathological diagnosis of cervical lymph nodes

Cytological diagnosis	No. of cases	% of cases	Histopathological diagnosis			
			Benign		Malignant	
			No of cases	% of cases	No. of cases	% of cases
Benign	58	62	55	95%	3	5%
Malignant	36	38	00	----	36	100%
Total	94	100%	55	59%	39	41%

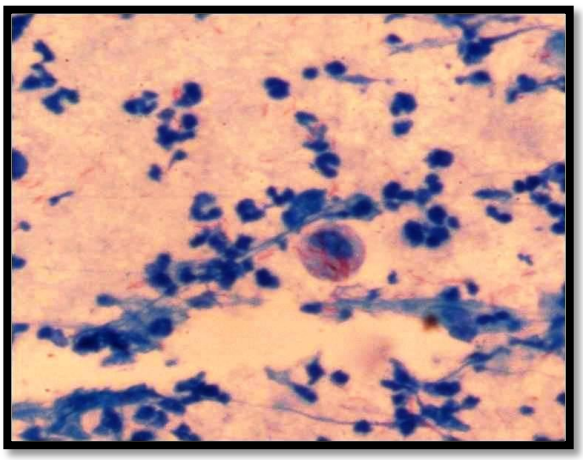

Fig-1: FNAC smear of tubercular lymph node showing tubercle bacilli (Acid fast bacilli-ZN Stain)

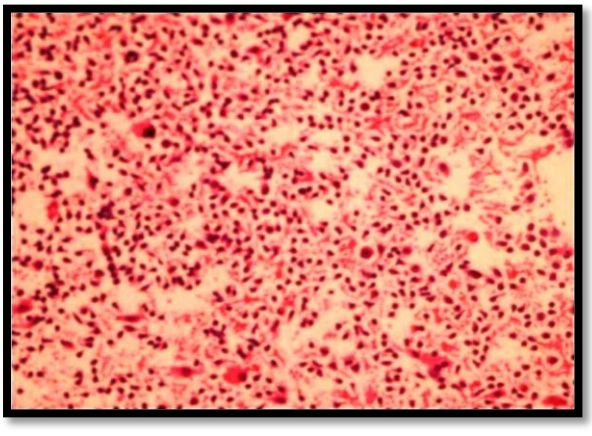

Fig-2: FNAC smear of lymph node of Hodgkin's lymphoma showing polymorphous tumor cells

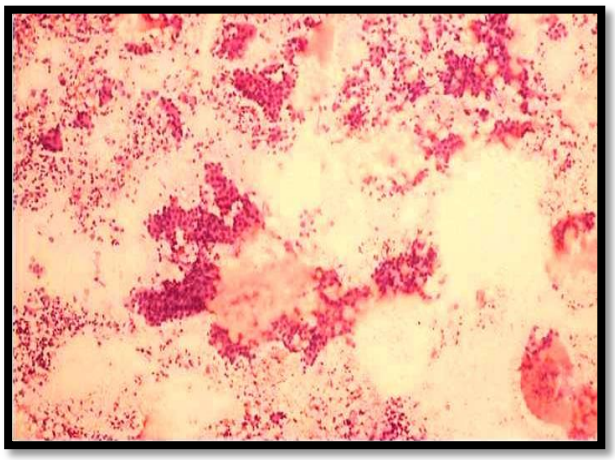

Fig-3: FNAC smear showing tumor cells arranged in acinar pattern (metastatic deposits of adenocarcinoma)

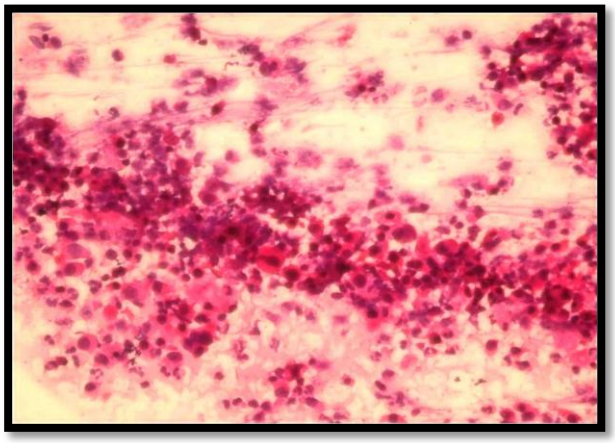

Fig-4: FNAC smear showing metastatic deposits of squamous cell carcinoma

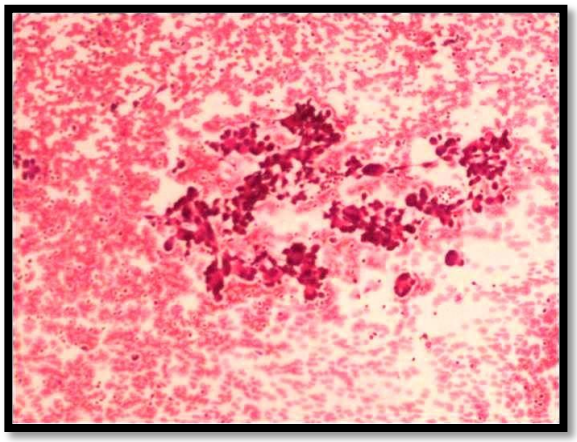

Fig-5: FNAC smear showing metastatic deposits of poorly differentiated carcinoma

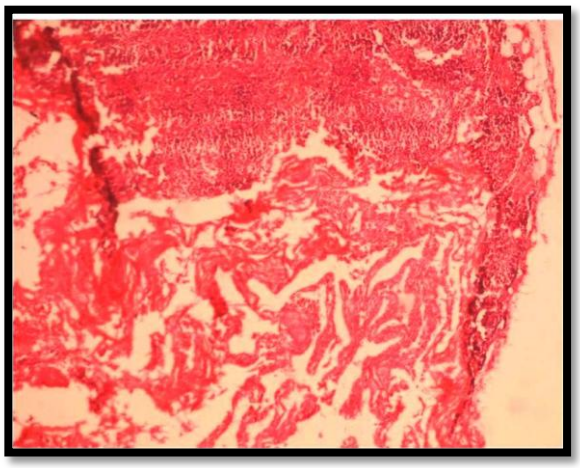

Fig-6: Histopathological section of lymph node showing metastatic deposits of papillary carcinoma of thyroid

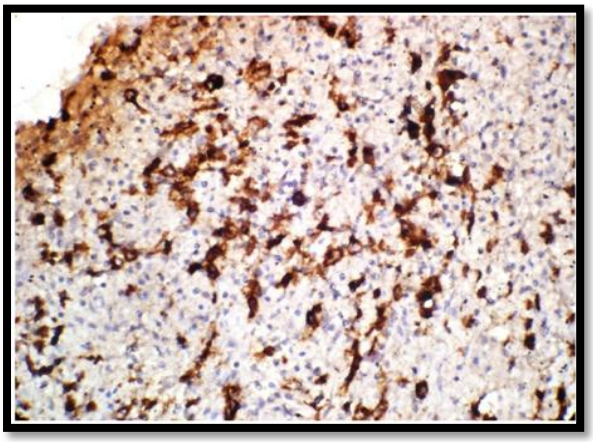

Fig-7: Immunohistochemistry showing positivity for CD15 marker in Hodgkin's lymphoma on histopathological section

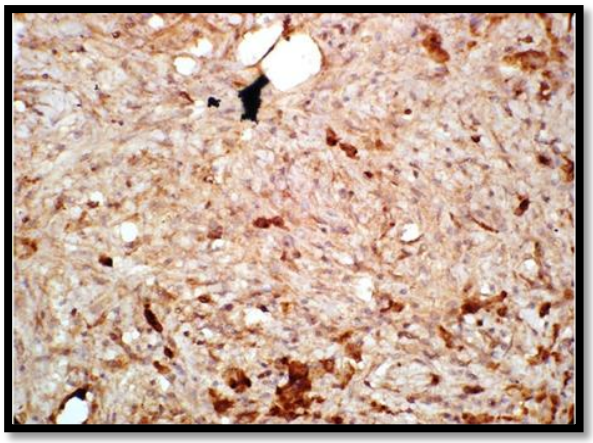

Fig-8: Immunohistochemistry showing positivity for CD30 marker in Hodgkin's lymphoma on histopathological section

DISCUSSION

The study duration was from June 2012 to May 2014, a 2 years prospective study of FNAC of cervical lymph nodes referred to the Department of Pathology. From June-Dec 2012, there were 172 cases. From Jan-Dec 2013 there were 297 cases and Jan-May 2014 the number of cases is 159. So totally in 2 years there were total 628 FNACs of cervical lymph nodes. Out of 628 cases, 94 cases had excision biopsies which were sent for histopathological study, and from June-Dec 2012 we had 23 cases from Jan-Dec 2013 we had 52 cases and from Jan-May 2014 we had 19 cases.

The age group of all the cases included in the study is in the range of 2.5 yrs to 82 yrs of age which is in correlation with other studies done by Rakhshan M *et al.*, [1]' Ishar T *et al.*, [2], Manjunath BS *et al.*, [3], Bharathi K *et al.*, [4] and Hirachand S *et al.*, [5]. In this study, the most common age group for cervical lymphadenopathy was 3rd decade, which is correlating with study of Narang *et al.*, [6], Pandit *et al.*, [7], Rakhshan M *et al.*, [1], Hirachand S *et al.*, [5].

In the study, benign lesions are more common than malignant one. Among benign lesions, Non-specific reactive lymphadenitis is the most common findings of enlarged cervical lymph node amounting to 35%, followed by tubercular lymphadenitis amounting to 23%, granulomatous lymphadenitis Includes 19%. Our findings are correlated well with the study of Ishar *et al.*, [2], Hirachand *et al.*, [5], Ahmad *et al.*, [8], and Lee *et al.*, [9].

Table-6: Comparison of various benign lesions of cervical lymphadenopathies with other studies

Cytological diagnosis	Non specific reactive lymphadenitis	Granulomatous lymphadenitis	Tuberculous lymphadenitis
Ishar T*et al*., [2]	52.4%	--	26.7%
Manjunath BS *et al*., [3]	33.3%	11.7%	35.7%
Bharathi K *et al*., [4]	28%	--	30%
Hirachand S *et al*., [5]	44.5%	9.2%	28%
Ahmed *et al*., [8]	53.6%	----	32.8%
Lee *et al*., [9]	51.5%	--	25.7%
Present study	35%	19%	23%

In our study, malignant lesions were 23% of all the cases undergone FNACs' of the cervical lymph nodes. Among 145 cases, 51 were primary malignancies. 21 cases were diagnosed as Hodgkin's lymphoma and 30 cases as Non-Hodgkin's lymphoma on cytology. Rests of the 94 cases were metastases to the lymph nodes.

All the 21 patients of Hodgkin's lymphoma presented with enlarged cervical nodes initially, later generalized. All cases show Reed-Sternberg cells on cytology. Majority of them are of classical type. One case showed lacunar type of RS cells. Background shows mixed inflammatory cells.

Among 21cases, 10 cases have histopathological correlation and all of them have turned out to be Hodgkin's lymphoma only. Immunohistochemistry shows positive for cytoplasmic and cell surface staining for CD30 and paranuclear deposit with cell surface and cytoplasmic staining for CD15.

Among 30 cases of Non-Hodgkin's lymphoma, one case showed large lymphoid cells with abundant cytoplasm, multinucleation and partly lobulated nuclei and prominent nucleoli. Background shows histiocytoid cells with phagocytic cells. On cytology, it was diagnosed as anaplastic large cell lymphoma. But on histopathology, it was finally diagnosed as Hodgkin's lymphoma. Another two cases were diagnosed as Non-Hodgkins lymphoma which turned out to be Hodgkin's on histopathology and Immunohistochemistry (IHC). According to Landgren O *et al*., Carter *et al*., study, about 13-15% of cases shows discordance between Hodgkins and Non Hodgkin's lymphoma on cytology [10, 11]. Out of 94 cases of metastatic deposits, majority of them were diagnosed as squamous cell carcinoma. The other deposits are that of adenocarcinoma, papillary carcinoma of thyroid, poorly differentiated carcinoma. 11 cases had histopathological correlation and all 11 cases correlated with cytological diagnosis. So, the most common metastates tumor to the lymph nodes of the Head and Neck region is squamous cell carcinoma. The most common group of lymph nodes is the cervical region. The most common age group is 6^{th} decade. All these findings are correlated well with study conducted by Bagwan *et al*., [12], Rakshan M *et al*., [1], Manjunath *et al*., [3] and Bharathi K *et al*., [4].

Table-7: Comparison of malignant lesions of cervical lymph node with various other studies

	Ishar T *et al*., [2]	Manjunath *et al*., [3]	Bharathi *et al*., [4]	Hirachand *et al*., [5]	Lee *et al*., [9]	Ahmed *et al*., [8]	Present study
Hodgkin's Lymphoma	7.3	2.3	1	6	3.5	4.5	7.9%
Non-Hodgkin's Lymphoma							
Metastasis	12.8	16.8	41	12.3	19.3	9.5	14.8%

Out of 628 cases, 94 cases have histopathological correlation. Cytological diagnosis of these 94 cases are as below: 25 cases were diagnosed as Non-specific reactive lymphadenitis, 17 cases as granulomatous lymphadenitis, 16 cases as tubercular lymphadenitis, 10 cases as Hodgkin's lymphoma, 15 cases as Non-Hodgkin's lymphoma and 11 cases as metastasis

On histopathology, out of 5 cases of Non-specific reactive lymphadenitis, 20 cases showed consistent diagnosis, 4 cases were tubercular lymphadenitis and another one turned out to be castleman's disease.

On histopathology, out of 17 cases of granulomatous lymphadenitis, 11 cases have consistent findings and diagnosed as tubercular lymphadenitis. These cases were not diagnosed as tubercular on cytology because of negativity of Acid Fast bacilli.

According to the study conducted by Hsu C *et al*., [13], shamshad AS [8], Narang RK [6], Adhikari P *et al*., [14], cases of tuberculosis which are in early stage or when load of bacteria is less or partially

treated patients, it is not possible to find the AFB on cytology. Hence, such cases will be diagnosed as granulomatous, most probably tubercular etiology and advised to correlate with the clinical signs and symptoms. Two cases were diagnosed as reactive lymphadenitis and 1 case each of Hodgkin's lymphoma, Non Hodgkins lymphoma, Castleman`s disease.

On histopathology, out of 16 cases, 15 cases of tubercular lymphadenitis have consistent findings and diagnosed as tubercular lymphadenopathy and one case as Hodgkin's lymphoma. The lymph node biopsy has been done in these patients because the patient is not responding to anti-tubercular treatment; some have non-healing sinuses which surgeons have excised as a part of treatment

On histopathology, 10 cases of Hodgkin's lymphoma have same diagnosis as cytology. These cases were subclassified as mixed cellularity type. Immunohistochemistry has been done and shows positive for cytoplasmic and cell surface staining for CD30 and paranuclear deposit with cell surface and cytoplasmic staining for CD15.

Three cases of Non-Hodgkin's lymphoma are diagnosed as Hodgkin's lymphoma on histopathology. Out of which one is of Nodular sclerosis type. Classical Reed-Sternberg cells are present in the background of mixed inflammatory cells. Nodular sclerosing type showed lacunar cells. Immunohistochemistry has been done to confirm. Due to absence of Reed-Sternberg cells on cytology they are misdiagnosed as Non-Hodgkin's lymphoma. Such misinterpretations have also been observed in the study done by Landgren O *et al*., and Carter *et al.*, [10, 11].

Finally out of 58 cases reported as benign on cytology, 46 cases have consistent findings with histopathology. In rest of the 12 cases,4 cases of tuberculous lymphadenitis and one case of Castleman`s disease is misdiagnosed as reactive lymphadenitis. One case of Hodgkin's lymphoma is misdiagnosed as tuberculous lymphadenitis.3 cases of reactive lymphadenitis,1 case each of Hodgkin's and Non Hodgkin's lymphoma and one case of castleman`s disease are misdiagnosed as granulomatous lymphadenitis

All the 36 cases reported as malignant on cytology has come out to be malignant on histopathology.

So, overall sensitivity, specificity and accuracy of FNACs' of enlarged cervical lymph nodes in the study is 100%, 92.3% and 94.8%. It is correlating well with the study done by Ahmad *et al.*, [8] and Bharathi K [4].

CONCLUSION

FNAC is a very useful and accurate approach in diagnosing various benign and malignant lymphadenopathies, as it has the diagnostic value of the first step, in the workup of patients with nodal enlargement. Although FNAC has proven to be a simple and cost effective diagnostic tool for lymphadenopathies, the limitation of this procedure in the diagnosis of low grade malignant lymphoma needs to be understood.

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