

Fine needle aspiration cytology in malignant lymph nodes – A stepping stone

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Abstract

A hospital based cross-sectional study was carried out in all clinically suspected cases of malignant lymphadenopathy.

The present study was conducted on all clinically suspected cases of malignancy in lymph nodes over a period of 2 years from July 2015 to August 2017.

61 patients were included in this study to find the role of FNAC in cases of malignant lymph nodes and to correlate the findings with histopathology wherever possible. FNAC was carried out using a 23-gauge needle and 20 ml syringe after obtaining due consent of the patients. Cytological smears were examined. Statistical analysis was done and proportions of study variable were calculated and expressed in terms of percentages. The study showed 75.4% cases of metastatic malignancy and 24.5% primary with older age being more common.

Keywords: FNAC, lymph node, malignancy

Introduction

Malignancies in lymph nodes in our country are predominantly metastatic in nature with an incidence varying from 65.7% [1] to 80.4% [1] and lymphomas range from 2% [1] to 15.3% among lymph nodes aspirated from all the sites. Thus, the clinical recognition and urgent diagnosis of palpable lymphadenopathy is of paramount importance to differentiate between inflammatory, metastatic or primary neoplastic lesions. [2] However, it is difficult to determine the cause of these enlarged lymph nodes clinically or on gross examination. In our study the fine needle aspiration cytology (FNAC) is used as a primary tool in suspected cases of malignant lymphadenopathy and to correlate the findings of cytology with histopathology wherever possible. FNAC still holds a very important stepping stone in developing countries like India as it is cheaper and feasible compared to other methods.

NHL and Squamous cell carcinoma were the most common primary and secondary malignancies respectively. Cyto -histopathological correlation was 96.2% in metastatic cases.

Material and methods

Patients with lymphadenopathy who were clinically suspected to have malignant lesions of lymph nodes both primary and metastatic and those who were already diagnosed with leukemia along with lymphadenopathy were included in this study. After obtaining relevant demographic data and consent of the patient, FNAC was performed in all the clinically suspected patients of malignant lymphadenopathy using a 23- gauge needle and 20 ml syringe. Cytological smears were prepared and stained with Papanicolaou and hematoxylin and eosin stain. Smears were observed under microscope. Histopathological correlation was done wherever possible.

Table1: Age and sex distribution

Age in years	Mets in males	Mets in females	Primary in males	Primary in females
1- 10			2	1
11-20		1	3	1
21-30	1	1		
31-40	1	5		
41-50	4	6	3	
51-60	9	4	1	
61-70	8	1	2	1
71-80	2	4		
81-90	1			

Table 2: Types of malignancy and their frequencies

Sn.	Type of malignancy	No. of cases	percent
1	Non-Hodgkin’s lymphoma	11	16.6
2	Hodgkin's lymphoma	2	3.3
3	Squamous cell ca	18	30

All the patients with diagnosis of reactive, infective and inflammatory lymphadenopathy on FNAC were excluded. Only those cases which were suspected to be malignant on cytology were selected in this study and were followed through with clinical, radiological and histopathological evidence to confirm malignancy

Statistics

Statistical analysis was performed and proportions of study were expressed in terms of percentages.

Results

I. Age and sex distribution is shown in table 1 ranges from 1 year to 86 years. 51 cases (83.6%) 40 years of age and above while only 10 cases (16.6%) were seen in younger age group. Males (36/61, 60%) shows predominance over females (25/61,40%). These results coincide with various Indian studies like Dowerah.et al [3], Mehdi.et al [4] and Chaudhary. et al [5], Hemlata.et al [6]

4	Epithelial malignancy	12	20
5	Infiltrating ductal	8	13.3
	Carcinoma		
6	Melanoma	2	3.3
7	Adenocarcinoma	4	6.6
8	Granulocytic sarcoma	1	1.6
9	Germ cell tumor	1	1.6
10	Langerhans cell	1	1.6
	Histiocytosis		
11	Papillary thyroid ca	1	1.6

Out of 61 cases, 15 cases (24.5%) of primary malignancy and 46 cases (75.4%) of metastatic malignancy were reported.

Among metastatic cases, Squamous cell carcinoma showed highest frequency i.e. 18 cases (29.5%) as shown in various studies (Table 3). The cytological features showed typical keratinization, pleomorphism and anisonucleosis as shown in figure 4. Their primary

was found to be in oral cavity and upper aerodigestive tract as shown in table 4 corresponding to other studies.

13 cases were suspicious in which primary was known as shown in table 5. It is the No clinical suspicion in 5 cases (table 5) out of which two were suspected to have tuberculosis.

Commonest carcinoma to metastasize to cervical group of lymph node as shown in table 3.

Table 3: Distribution according to site and type of malignant lymph node

Sn.	Cytological diagnosis	Cervical	Supraclavicular	Submandibular	Axillary	Inguinal	Generalized
1	Squamous cell carcinoma	14	1	2		1	
2	Epithelial malignancy	8	1		1	2	
3	Infiltrating ductal carcinoma	1			7		
4	Adenocarcinoma	2	2				
5	Malignant melanoma				2		
6	Germ cell tumor		1				
7	Papillary thyroid carcinoma	1					
	primary malignancies						
1	Non-Hodgkin lymphoma	7		1			2

2	Hodgkin lymphoma	2					
3	Langerhans cell histiocytosis						1
4	granulocytic sarcoma	1					

Table 4: Aspirated lymph node sites showing tumor origin as confirmed by biopsy

Metastatic site	No. of cases	Tumor origin
Neck (cervical, supraclavicular)	15	tongue-3
submandibular)		oral cavity-4
		larynx-3
		thyroid-1
		ovary-1
		breast-1
		lung-2
Inguinal	4	skin -2
		prostate-1
		kidney-1
Axillary	7	breast -7

It is followed by epithelial malignancy 12 cases (19.6%), which did not have any characteristic features of squamous or adenocarcinoma as shown in figure 5. Similar findings were seen in study conducted by Wilkinson et al. Epithelial malignancy was not suspected in 10 cases and most of their origin could not be traced. Infiltrating ductal carcinoma appeared in 8 cases of patients (13.1%) showing its typical features as shown in figure 7. It was the most common malignancy in females and all were highly suspicious. (Table 5) it commonly metastasized to axillary nodes. It is followed by adenocarcinoma in 4 cases (6.5%) showing typical acinar arrangement or sheet like arrangement of cells as shown in figure 6. Primary site of 2 cases was traced back to lung who presented with enlarged lymph nodes in neck region. One case was Pancoast tumor in a

female. In other 2 cases, primary one case of Diffuse Large B-cell lymphoma was also reported. It presented as a retroperitoneal mass with site was not known. Two cases of metastatic melanoma were also seen. The first case who presented with metastatic melanoma was 55-year old male who was a known case of melanoma foot and previously operated for the same a few years back. The other case was that of a female patient who was 60-year-old, she had melanoma over her foot. Both the cases presented with inguinal lymphadenopathy as shown in table.3

One case each of metastatic germ cell tumor was seen in a previously operated patient for the same who presented with supraclavicular nodes showing features of vacuolated cytoplasm with background of lymphocytes as shown in figure 10.

One case of papillary thyroid carcinoma with intranuclear inclusions is also seen as shown in figure 9 was also diagnosed in a 68-year-old female with cervical lymphadenopathy. Studies conducted by Chaudhary.et al ^[5] , Ghartimagar.et al^[8] and Wilkinson.et al^[1], occasionally 1 or 2 cases were reported similar to ours.

In primary malignancies, 11 cases of Non-Hodgkin's lymphoma were diagnosed. All these smears showed high cellularity with monomorphic population of lymphocytes. In some smears, few lymphocytes show clumped chromatin, bi-nucleation and multinucleation with occasional mitotic figures as shown in figure 1.

As shown in table 2, NHL were mostly reported in male patients as compared to females. Most of the patients presented with cervical lymphadenopathy i.e., 7 cases and 2 cases presented with generalized lymphadenopathy as shown in table 3. One case of a 7-year-old male went for biopsy and IHC. His diagnosis was initially given as NHL. On histopathology and immunohistochemistry, it came out to be Burkitt's cell lymphoma. Lymphomas are difficult to classify on FNAC alone and as shown in studies like Wilkinson.et al¹ and Dowerah.et al ³ they require biopsy and IHC for final diagnosis.

Pelvic lymph nodes in a 40-year-old female patient. A USG-guided FNAC was done from the mass as well as lymph nodes. It was initially given as round cell sarcoma as few sheets and clusters of round cells with oval large hyperchromatic nuclei with scanty cytoplasm were seen. Only after histopathology and immunohistochemistry it was diagnosed as DLBCL. In

our study, the diagnosis of round cell sarcoma was given on FNAC keeping in mind that there was a retroperitoneal mass present. Two cases of Hodgkin's lymphoma were also there showing polymorphic population of lymphocytes, eosinophils, plasma cells and neutrophils with few large multinucleated RS- like cells as shown in figure 2. One case each of male and female presented with cervical lymphadenopathy and were clinically not suspicious. Both cases were lost to follow up. One case of granulocytic sarcoma was also seen in a diagnosed case chronic myeloid leukemia which showed a spectrum of myeloid differentiation with granulated promyelocyte, metamyelocytes and band forms. The patient was a 24-year-old male who presented with cervical lymphadenopathy with no other symptoms. On aspiration, his smears showed features of granulocytic sarcoma which was later confirmed on biopsy. Meanwhile his peripheral smears were also studied and he was diagnosed with chronic myeloid leukemia (CML). These cases are very rare in literature. One case of Langerhans cell histiocytosis was also seen in a 1-year-old female. She presented with generalized lymphadenopathy with involvement of occipital and inguinal group of lymph nodes. The smears revealed scattered atypical large histiocytes, eosinophils and lymphocytes (figure 3). Prominent nuclear grooves were seen giving it a coffee bean appearance. In a study conducted by Khajuria.et al [6], a solitary case was reported in a 3-year-old child as was in our case.

Table 5: Table showing clinically suspected and unsuspected cases of lymph node malignancies.

S.no	Cytological diagnosis	Clinically suspected	Clinically unsuspected
	Metastatic malignancy		
1	Squamous cell carcinoma	13	5
2	Epithelial malignancy	2	10
3	Ductal carcinoma	8	
4	Adenocarcinoma	2	2
5	Malignant melanoma	2	
6	Germ cell tumor	1	
7	Papillary thyroid carcinoma	1	
	Primary malignancy		
1	Non- Hodgkin's lymphoma	7	4
2	Hodgkin's lymphoma		2
3	Granulocytic sarcoma		1
4	Langerhans cell histiocytosis		1
	total	36(59.0%)	25 (41%)

In case of lymphoma, correlation was available only in 1 case which came out to be Burkitt's cell lymphoma

Discussion

FNAC is simple, cheap and economical tool used in the diagnosis of enlarged lymph nodes, especially in developing countries like India. It plays a major role in diagnosing both primary and secondary lymph nodes. Sometimes they are the only clue in diagnosing a malignancy even in unsuspected cases and in cases of occult primaries. As shown in table 5, there was no clinical suspicion in 25 cases (41%) which makes FNAC a very important tool for reaching the diagnosis especially in the cases of persisting lymphadenopathy without any notable cause. In some of the cases, the only presentation was enlarged lymph nodes. The histopathological type of most of these malignancies was epithelial malignancy, 10 cases (16.3%) as shown in table 5 The cyto-histopathological correlation was done in 28 cases. Out of which 24 cases were of metastasis and 4 cases were of primary malignancy. 24

cases showed the histopathological correlation. 2 cases of epithelial malignancy were later correlated on histopathology and were found to be renal and prostatic in origin. In case of primary malignancy, one case where histopathological correlation was done, the initial diagnosis was NHL which was diagnosed as Burkitt's lymphoma on histopathology. Only one case showed discrepancy. The case which presented clinically with a retroperitoneal mass was initially given a diagnosis of round cell variant of sarcoma on cytology, but later diagnosed as DLBCL on histopathology.

The sensitivity and positive predictive value of FNAC was found to be 100% and 96% respectively in cases of metastatic disease. Studies conducted by Dowerah.et al [3], Wilkinson.et al [1] and Mehdi.et al [4] also had sensitivity of 100% for metastasis. The studies conducted by Dowerah.et al [3] and Wilkinson.et al [1]

also showed FNAC was a highly sensitive technique for diagnosing lymphomas. In case of other primary malignancies like Langerhans cell histiocytosis and granulocytic sarcoma, FNAC was found to be accurate. A variety of factors influence the utility of fine needle aspiration cytology in the diagnosis of lymph node malignancy which includes technique, experience, training and adequacy of material. Different conclusions can be drawn from different cytological smears depending upon these factors. Most of the time ancillary techniques help us to reach a certain diagnosis. But at the end of the day, the cytology is to be correlated with histopathology and immunohistochemistry for a more reliable diagnosis.

Conclusion

In our study, FNAC proved to be a great help to form a preliminary diagnosis so that further work up can be carried out accordingly. It proved to be a highly efficient method for detecting metastasis. Some of the primary sites of malignancy could be detected with the help of clinical and radiological data. It provided us a clue for occult malignancies in some of the cases.

Legend Figures

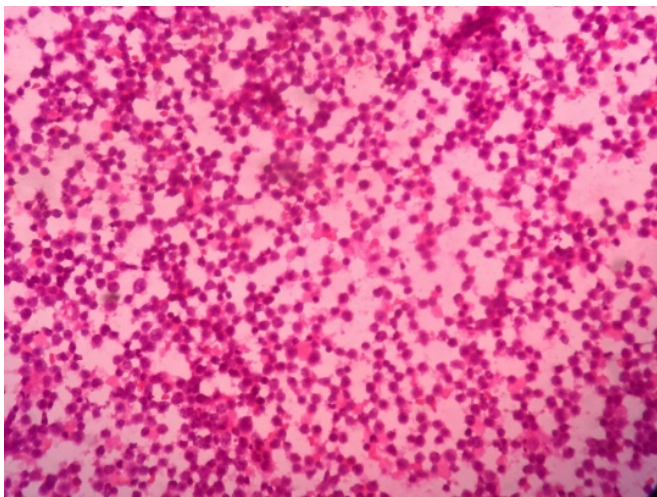


Figure 1: Photomicrograph showing cellular smears of Non-Hodgkin's Lymphoma. They reveal sheets of

monomorphic population of small lymphocytes at low power. (H&E X 10x)

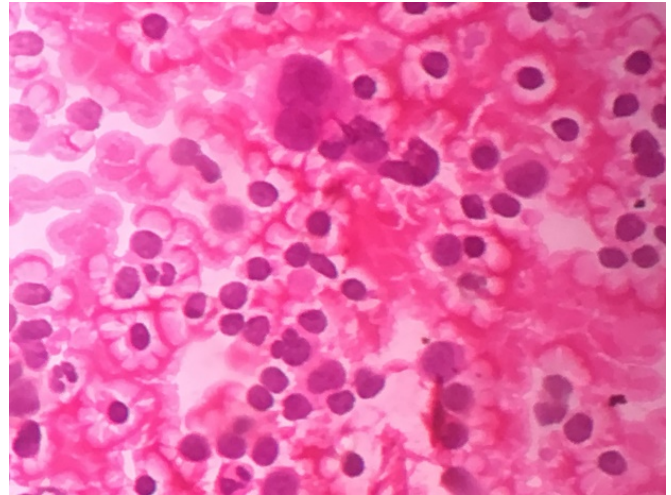


Figure 2: Photomicrograph Hodgkin's Lymphoma. They reveal monomorphic population of lymphocytes. Few cells show prominent nucleoli, clumped chromatin and high N/C ratio at high power. (H&E X 40x)

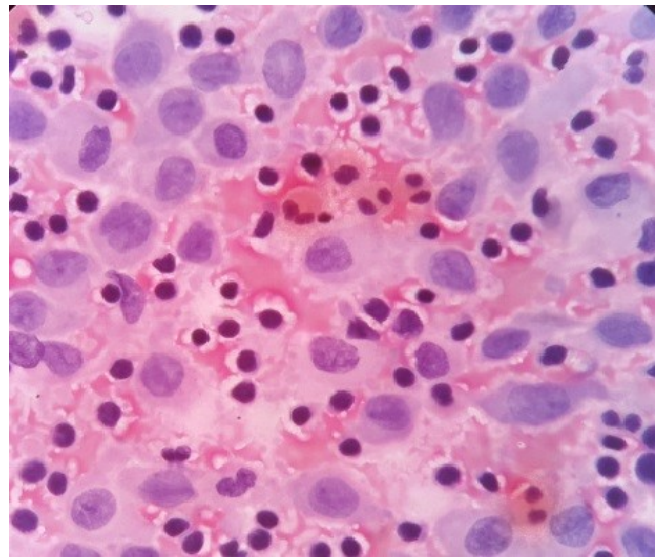


Figure 3: Photomicrograph shows Langerhan's cell histiocytosis showing large atypical histiocytes, eosinophils and lymphocytes. The histiocytes are large with moderate amount of cytoplasm and vesicular nuclei. The nuclei are grooved showing coffee bean appearance. (H&E X 40x)

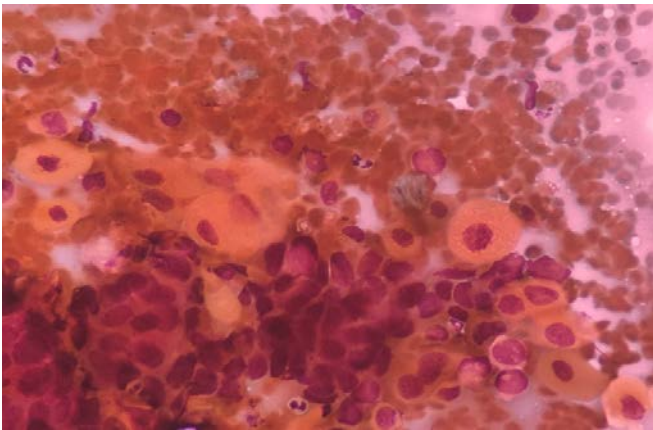


Figure 4: Photomicrograph showing Squamous cell carcinoma with cluster of round to polygonal cells with round hyperchromatic nuclei and moderate orangeophilic cytoplasm. Mild anisonucleosis and pleomorphism is also seen. (Pap X 40x)

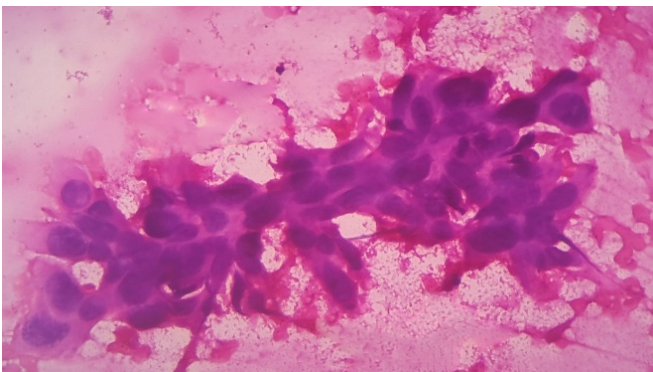


Figure 5: Photomicrograph epithelial malignancy showing sheet of round to oval cells with hyperchromatic nuclei and moderate amount of eosinophilic cytoplasm. Anisonucleosis and pleomorphism is also seen. (H&E X 40x)

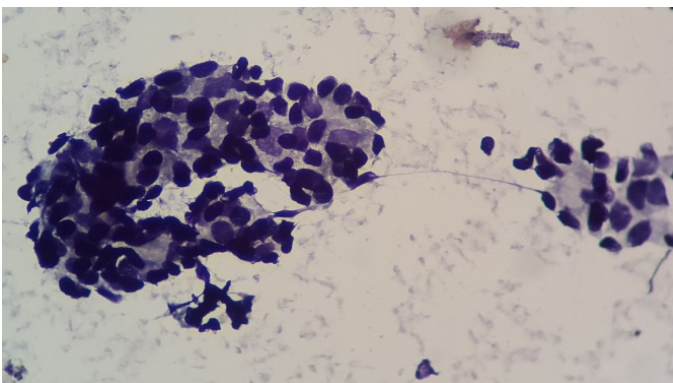


Figure 6: Photomicrograph reveals adenocarcinoma showing cluster and acinar arrangement of round to

oval cells with round nuclei and moderate amount of cytoplasm. Moderate pleomorphism and anisonucleosis is seen. (H&E X 40x)

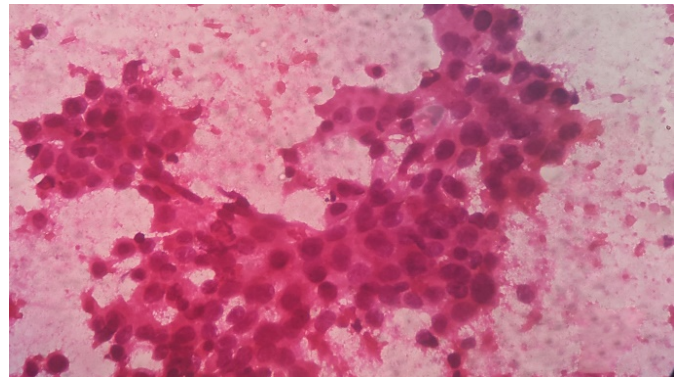


Figure 7: Photomicrograph showing Infiltrating ductal carcinoma reveal sheets, clusters and acinar pattern of ductal cells. The cells are round to oval with round nuclei and moderate amount of cytoplasm. Pleomorphism and anisonucleosis is seen. (H&E X 10x)

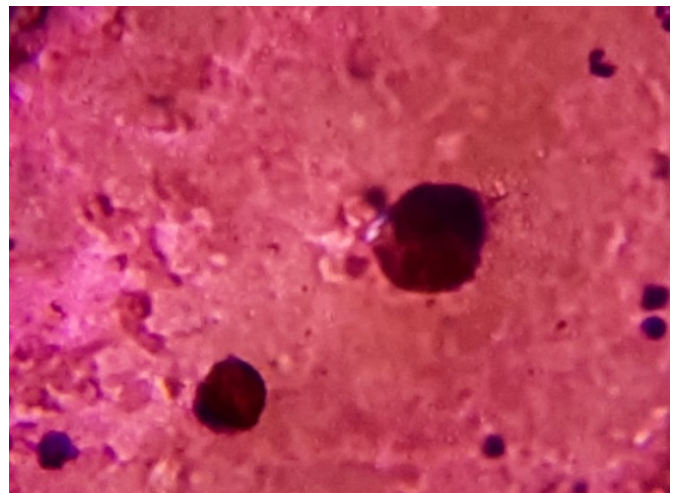


Figure 8: Photomicrograph showing melanoma reveals scanty cellularity. Few round to oval cells with hyperchromatic nuclei and moderate amount of cytoplasm are seen. Few bizarre cells are also present. There is presence of melanin pigment. Anisonucleosis and pleomorphism is also seen. (H&E X 40x)

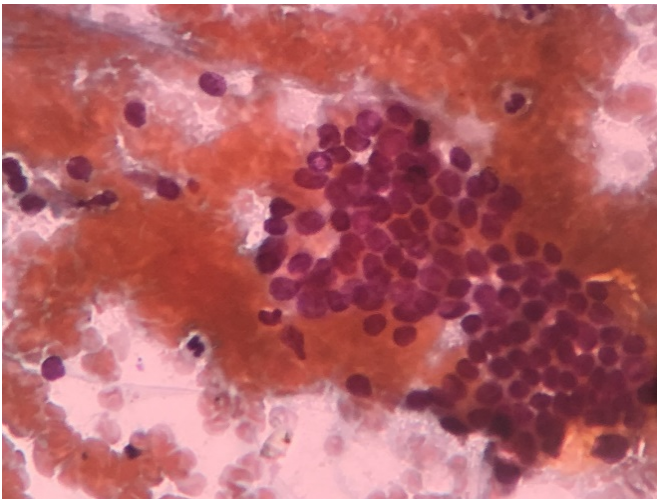


Figure 9: Photomicrograph reveals papillary thyroid carcinoma showing tumor cells arranged in sheets. They reveal round cells with round to oval nuclei and moderate cytoplasm. Nuclear grooves and intra nuclear inclusions are also seen at places. (Pap X 40x)

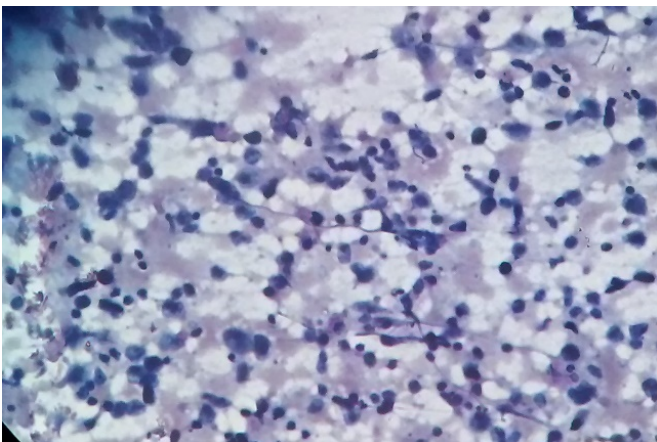


Figure 10: Photomicrograph showing Dysgerminoma which reveal mostly scattered and few clusters of round to oval cells with round to oval nuclei with prominent nucleoli and vacuolated cytoplasm. Background contains lymphocytes. (H&E X 40x)

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