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Case Report

Ear, Nose and Throat Section

Diagnostic Pitfalls and the Critical Role of Excisional Biopsy in Non-Hodgkin's Lymphoma: A Case Report

MEGHA DOIPHODE[1], PRIYA ELANGBAM[2], APURVA JARANDIKAR[3], GUNDAPPA D MAHAJAN[4], VINOD SHINDE[5]

ABSTRACT

Lymphomas often pose significant diagnostic challenges, particularly when they present with atypical clinical features that can mimic other conditions. This complexity can lead to delays in accurate diagnosis and appropriate treatment. A 30-year-old female patient presented with a recurrent swelling in the cervical region. Despite multiple Fine Needle Aspiration Cytologies (FNACs) performed on the swelling, the diagnosis remained unclear and initial results were misleading. These cytological evaluations failed to definitively identify lymphoma, contributing to a delay in establishing the correct diagnosis. The present highlights common diagnostic pitfalls encountered in lymphoma detection, especially when relying solely on minimally invasive procedures like FNAC. While FNAC is a useful initial tool for evaluating lymphadenopathy, it has limitations in distinguishing lymphoma from reactive or other malignant processes due to sampling error and cytological overlap. Consequently, an excisional biopsy, which provides a larger tissue sample for detailed histopathological and immunohistochemical analysis, is essential for accurate diagnosis. This approach allows for a comprehensive examination of tissue and cellular characteristics, which are critical for classifying lymphoma subtypes and guiding treatment decisions. Despite advances in less invasive diagnostic techniques, histopathological examination of excised tissue remains the gold standard for definitive diagnosis in suspected lymphoma cases. Clinicians should maintain a high index of suspicion and proceed to excisional biopsy promptly when lymphoma is suspected but FNAC results are inconclusive, to avoid delays in diagnosis and improve patient outcomes.

Keywords: Fine needle aspiration cytology, Lymphadenopathy, Malignancy

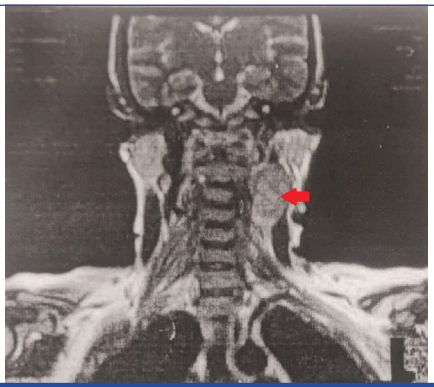
CASE REPORT

A 30-year-old female presented to the Ear, Nose and Throat (ENT) outpatient department with a swelling on the left side of her neck, which had been present for three years. Over the past two months, she noticed a sudden increase in the size of the swelling [Table/Fig-1], accompanied by pain, an evening rise in fever, and weight loss. She reported having undergone fine needle aspiration of the swelling three times over the previous three years, each time resulting in a temporary reduction in size, but the cytology from these procedures was inconclusive.

[Table/Fig-1]: Preoperative image- arrow showing the swelling.

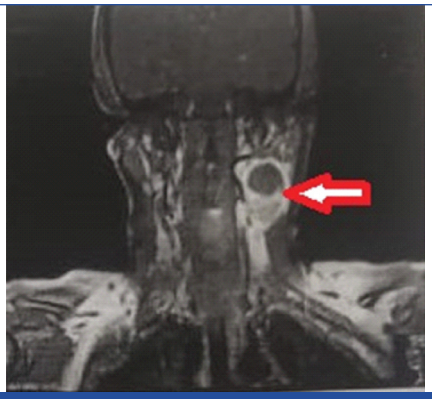
On clinical examination, a swelling measuring 4×3 cm was palpated on the left side of the neck, extending from 1 cm below the angle of the mandible superiorly to 8 cm above the clavicle inferiorly, 3 cm from the midline medially, and 1 cm from the mastoid tip laterally. The mass was firm to hard in consistency, non tender, mobile, and showed no local rise in temperature. There were no other palpable neck swellings or lymph nodes. Pan-endoscopy revealed no abnormalities. The provisional diagnosis was lymphoma, and the differential diagnoses included tubercular lymphadenitis, lymphoma, and granulomatous lymphadenitis.

Ultrasonography demonstrated a well-defined hypoechoic lesion at left level II with peripheral vascularity on colour Doppler imaging, without evidence of calcification. Magnetic resonance imaging revealed a fairly well-defined lesion in the left parapharyngeal space adjacent to the deep lobe of the parotid gland, measuring 4.5×3.2 cm. The lesion appeared hyperintense on both T1 and T2 sequences [Table/Fig-2]. Post-contrast imaging showed perivascular enhancement with internal non enhancing areas, suggestive of an abscess or nodal abscess [Table/Fig-3].



[Table/Fig-2]: MRI- arrow showing a fairly well-defined lesion in the left parapharyngeal space adjacent to the deep lobe of the parotid gland, measuring 4.5×3.2 cm, which appeared hyperintense on both T1 and T2 sequences.

Despite imaging features suggestive of an abscess, the absence of clinical signs of infection prompted an ultrasound-guided FNAC, which did not yield a definitive diagnosis. The FNAC revealed medium to large lymphocytes with a high nuclear-to-cytoplasmic ratio and prominent nucleoli, along with moderate cytoplasm. The background showed tingible body macrophages, necrosis, and haemorrhage.

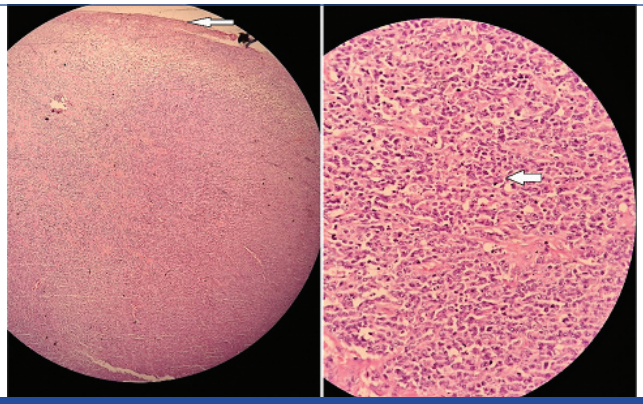


[Table/Fig-3]: Post-contrast showing perivascular enhancement with internal non-enhancing areas, suggestive of an abscess or nodal abscess.

In view of the previous inconclusive non-ultrasound-guided FNACs and the current ultrasound-guided FNAC suggestive of possible non-Hodgkin lymphoma, an excisional biopsy was performed under general anaesthesia after appropriate preanaesthetic evaluation and informed consent from the patient and her relatives.

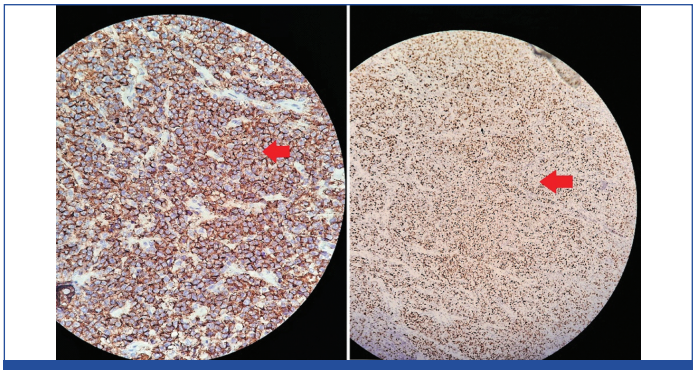
The excisional biopsy [Table/Fig-4], along with histopathological examination Haematoxylin and Eosin (H&E) demonstrated complete effacement of the lymphoid architecture by a diffuse infiltrate of medium to large atypical lymphoid cells [Table/Fig-5a,b]. These cells exhibited pleomorphic nuclei with vesicular chromatin and, in some areas, prominent nucleoli. There were also foci of variable mitotic activity and apoptosis, as well as large areas of necrosis.

[Table/Fig-4]: Gross pathological image of the specimen.



[Table/Fig-5]: a) Arrow showing capsule; b) Arrow showing complete effacement of the lymphoid architecture by a diffuse infiltrate of large to medium-sized cells (H&E, 10X) The atypical lymphoid cells have pleomorphic nuclei with vesicular chromatin and at places prominent nucleoli. (images from left to right)

Immunohistochemistry [Table/Fig-6] showed strong positivity for Leukocyte Common Antigen (LCA), Cluster of Differentiation 20 (CD20) and B-cell Lymphoma 6 (BCL6), with scattered positivity for Cyclin D1. B-cell Lymphoma 2 (BCL2) was negative in tumour cells but positive in background T cells. The Ki-67 proliferation index was 50-60%. Tumour cells were negative for CD3, TdT, and CD5. This immunoprofile supported a diagnosis of Diffuse Large B-Cell Lymphoma (DLBCL).



[Table/Fig-6]: Tumour cell positive for CD20 and Ki-67, respectively.
a) CD20 in high power magnification; b) Ki-67. (images from left to right)

The final diagnosis, based on excisional biopsy with histopathological examination and immunohistochemistry, was high-grade B-cell non-Hodgkin's lymphoma. The patient is currently undergoing chemotherapy and remains on regular follow-up.

DISCUSSION

Lymphomas are a diverse group of haematologic malignancies that often pose diagnostic challenges, particularly when presenting in the head and neck region. They can clinically mimic infectious or reactive conditions, making early and accurate diagnosis crucial for appropriate management and prognosis [1]. In the present case, the patient presented with a long-standing cervical swelling that showed a sudden increase in size, accompanied by constitutional symptoms. Despite undergoing multiple FNACs, including a recent ultrasound-guided one, the diagnosis remained inconclusive. This diagnostic delay reflects the limitations of FNAC in evaluating lymphoproliferative disorders, where cellular morphology alone may not be sufficient for definitive classification [2,3].

Magnetic resonance imaging suggested an abscess or nodal collection; however, the lack of corresponding clinical signs of infection prompted further evaluation. Ultimately, an excisional biopsy was performed, revealing a diagnosis of high-grade B-cell non-Hodgkin's lymphoma, specifically DLBCL. This supports the crucial role of tissue biopsy, which offers architectural and immunophenotypic details necessary for accurate subtyping and treatment planning [4,5]. Though image-guided core needle biopsies can improve diagnostic accuracy, they still carry a risk of false negatives or inadequate sampling in lymphomas. Excisional biopsy remains the gold standard, particularly when FNAC is non diagnostic, providing complete lymph node architecture essential for histological and immunohistochemical analysis [5,6].

Head and neck lymphomas comprise about 12% of all malignancies in the region, ranking behind squamous cell carcinoma and thyroid carcinoma. Because they often present as asymptomatic masses or mimic benign conditions, misdiagnosis or delayed diagnosis is common. Features such as persistent unilateral lymphadenopathy, especially without clear signs of infection, should raise suspicion for lymphoma [7].

The FNAC has demonstrated high specificity for detecting metastatic disease but has limited diagnostic utility in suspected lymphomas due to a lack of architectural context and challenges in subclassification [6]. Kim YH and Cho JH highlighted that, in patients with cervical lymphadenopathy, excisional biopsy was essential for achieving a definitive diagnosis when FNAC and imaging findings were ambiguous [8]. Early excisional biopsy is essential in cases where lymphoma is suspected and FNAC is inconclusive. This approach enables timely and accurate diagnosis, guiding appropriate therapy and ultimately improving clinical outcomes [7,8].

CONCLUSION(S)

Lesions in the head and neck region, due to their accessibility, should always prompt early biopsy when clinical suspicion arises. This is

especially true for extranodal NHL, which involves the head and neck in 20-30% of cases. A comprehensive diagnostic approach, including biopsy, should be adopted when evaluating lesions in areas such as the oral cavity, salivary glands, oropharynx, nasopharynx, paranasal sinuses, and larynx. Clinical features such as unilateral lymphadenopathy without a clear tumour mass or systemic signs should raise suspicion for lymphoma—even in the absence of B-symptoms or blood abnormalities. Excisional biopsy remains a cornerstone in establishing a definitive diagnosis, especially when FNAC results are inconclusive or misleading.

REFERENCES

[1] Storck K, Brandstetter M. Clinical presentation and characteristics of lymphoma in the head and neck region. Head Face Med. 2019;15(1):1. Doi: 10.1186/s13005-019-0191-6.

[2] Vasudevan PA, Ramachandran R. Effectiveness of fine needle aspiration cytology versus excisional biopsy in cervical lymphadenopathy. Formos J Surg. 2021;54(3):79-84. Doi: 10.4103/fjs.fjs_71_20.

[3] Loubeyre P, McKee TA. Diagnostic precision of image-guided multisampling core needle biopsy of suspected lymphomas in a primary care hospital. Br J Cancer. 2009;100(11):1771-76. Doi: 10.1038/sj.bjc.6605090.

[4] Marton I, Hrgović Z. Primary Hodgkin's lymphoma of the breast initially treated by surgical excision and axillary dissection. Acta Clin Croat. 2020;59(2):365-67. Doi: 10.20471/acc.2020.59.02.21.

[5] Bayhan Z, Ozdemir K. Analysis of diagnostic excisional lymph node biopsy results: 12-year experience of a single center. Acta Clin Croat. 2023;62(1):58-64. Doi: 10.20471/acc.2023.62.01.07.

[6] Schleder S, Jung EM. Efficacy and safety of ultrasound-guided core needle biopsies in cervical lymphadenopathy in patients with suspected head and neck cancer during the COVID-19 pandemic. Clin Hemorheol Microcirc. 2023;83(3):397-408. Doi: 10.3233/CH-221552.

[7] Lee JW, Lee SM. Characteristics and outcomes of primary extranodal lymphoma of the head and neck: A single-center analysis. BMC Cancer. 2020;20:254. Doi: 10.1186/s12885-020-06776-3.

[8] Kim YH, Cho JH. Diagnostic challenges and clinical features of non-Hodgkin's lymphoma presenting with cervical lymphadenopathy: A retrospective study. Eur Arch Otorhinolaryngol. 2021;278(6):2093-99. Doi: 10.1007/s00405-020-06242-0.

PARTICULARS OF CONTRIBUTORS:

1. Resident, Department of ENT, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.
2. Resident, Department of ENT, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.
3. Assistant Professor, Department of ENT, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.
4. Professor, Department of ENT, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.
5. Professor, Department of ENT, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Priya Elangbam,
Carnation Girls' Hostel, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Sant Tukaram Nagar, Pimpri, Pune, Maharashtra, India.
E-mail: elangbam.priya1995@gmail.com

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