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CERVICAL LYMPH NODE METASTASIS OF NASOPHARYNGEAL CARCINOMA POSING AS A DIAGNOSTIC DILEMMA

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ABSTRACT

Background: Nasopharyngeal carcinoma (NPC) is a malignant tumor arising from the epithelial lining of the nasopharynx, most commonly presenting as undifferentiated carcinoma. A hallmark of NPC is early and frequent metastasis to cervical lymph nodes, often presenting before primary site symptoms, making diagnosis challenging. **Case Presentation:** We report the case of a 45-year-old female who presented with a persistent, painless left postauricular swelling for over one year. Clinical examination revealed a firm, non-tender mass suggestive of lymphadenopathy. Radiological imaging identified multiple cervical lymph nodes with necrotic centers and a suspicious lesion in the left nasopharynx. Fine needle aspiration cytology from the swelling revealed features of metastatic undifferentiated carcinoma. A tru-cut biopsy from a cervical lymph node confirmed the diagnosis, supported by immunohistochemistry findings: pancytokeratin, EMA, p63, and EBV-LMP-1 were positive, while LCA and HMB-45 were negative. These results were consistent with **metastatic nonkeratinizing squamous cell carcinoma, undifferentiated subtype (NPC)**. The patient was treated with chemotherapy and showed a favorable clinical response. **Discussion:** This case highlights the diagnostic difficulty posed by NPC presenting solely as cervical lymphadenopathy, without nasopharyngeal symptoms. NPC is strongly associated with Epstein-Barr virus (EBV) infection, which aids in its identification through immunohistochemical markers. Proper radiological evaluation and an accurate panel of IHC markers are crucial for distinguishing NPC from other causes of cervical lymphadenopathy, such as lymphoma. **Conclusion:** A high index of suspicion, combined with thorough imaging, cytopathology, and IHC analysis, is essential for the early diagnosis and appropriate management of NPC.

KEYWORDS

1. Nasopharyngeal carcinoma
2. Cervical lymphadenopathy
3. Epstein-Barr virus
4. Immunohistochemistry
5. Undifferentiated carcinoma
6. Metastasis

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a form of poorly differentiated squamous cell carcinoma of the nasopharyngeal mucosal origin. It is also known as lymphoepithelioma.[1] NPC is a leading cause of death in South- East Asian population. There is a strong association of NPC and Epstein-Barr virus (EBV). EBV infection is probably the initiation factor in combination with environmental factor. EBV has also been demonstrated in the metastatic NPC in cervical lymph node with the help of PCR.[2] NPC commonly presents as a metastatic lymph nodal mass. The tumour has a bimodal age incidence, with one peak around 25 year age and another around 60 years.[3]

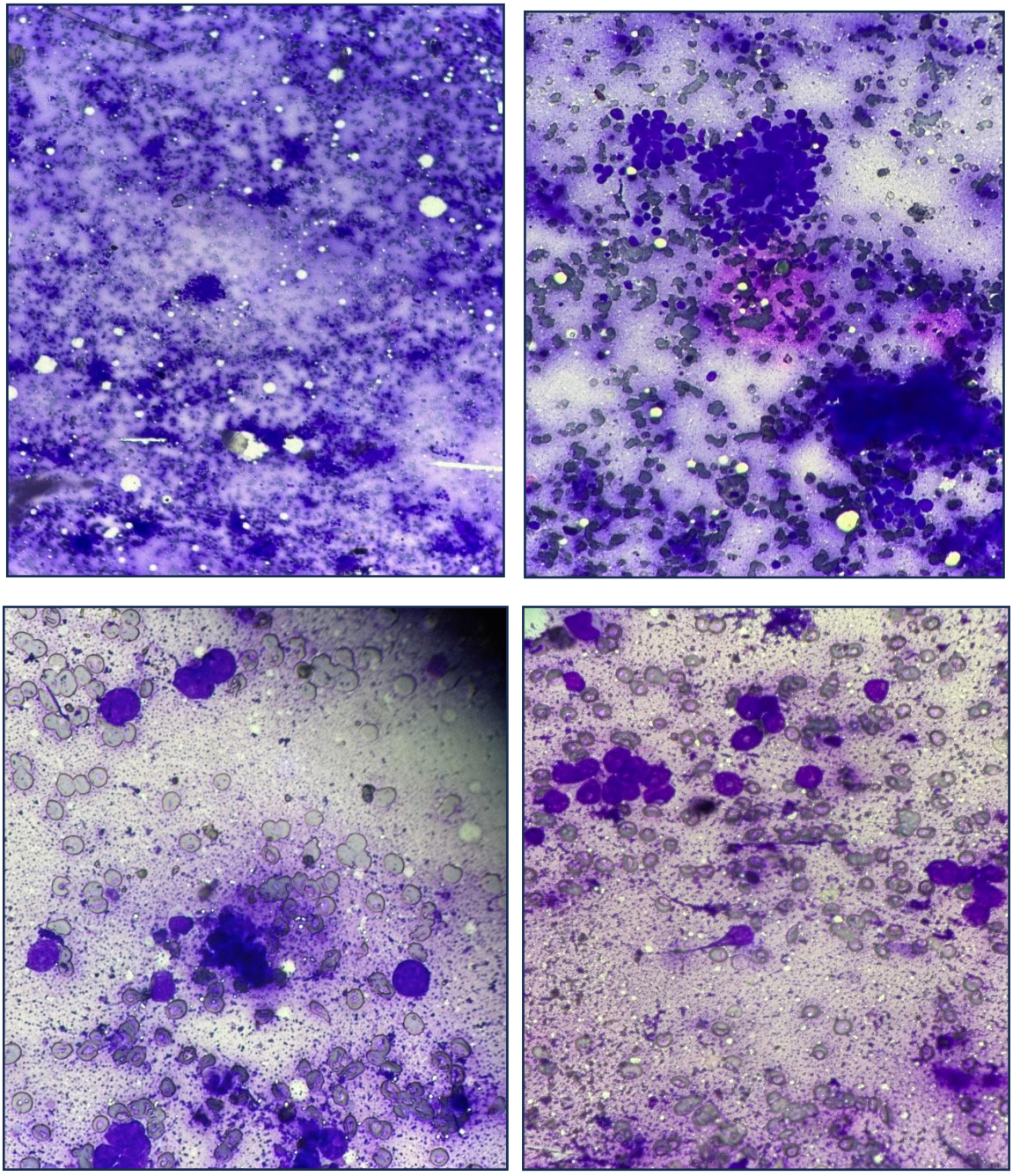
MATERIALS AND METHODS

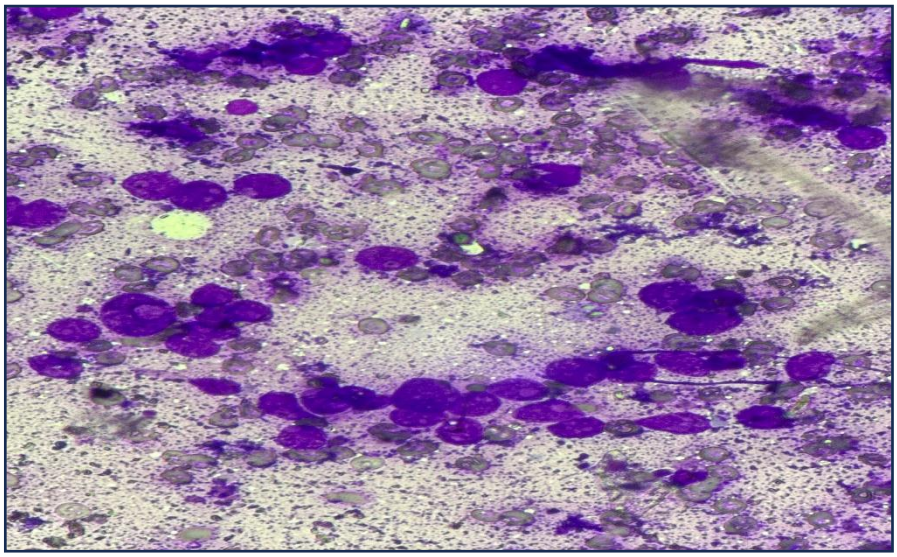
A 45 years old female patient presented to surgery department with complaint of left posterior auricular swelling. Patient gave history that swelling was persistent since 1 year for which she was prescribed antibiotics. Even after taking on-off course of antibiotics there was no response and swelling remained same. On examination swelling was firm to hard, measuring approximately 3.0x2.0 cm. Swelling was similar to consistency of lymph node. No other lymph nodes were enlarged. No history of fever and cough. Then for further evaluation patient was advised for radiological investigations. CECT neck, PNS and chest was done which revealed multiple enlarged lymph nodes with internal hypodense necrotic area seen in bilateral cervical region at level 2 and 3; with largest measuring 32x28x33

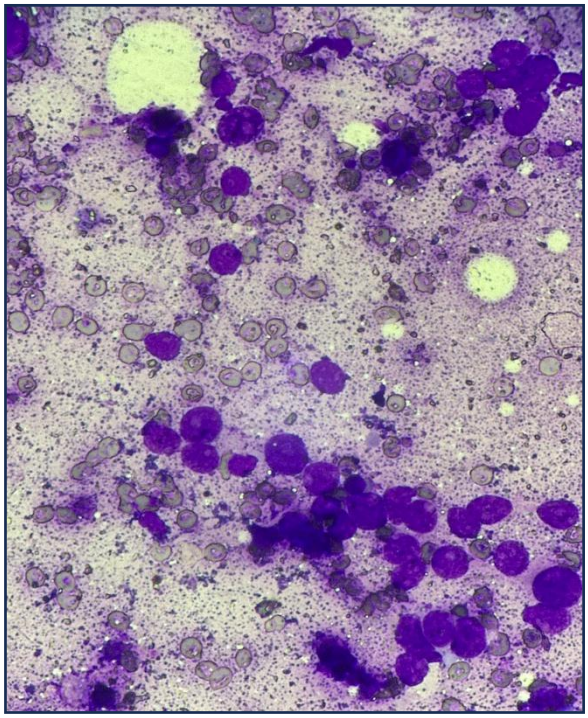
mm on left side at level 5. Overall the features were suggestive of soft tissue density lesion centred in left nasopharyngeal region- likely neoplastic etiology- Ca Nasopharynx.

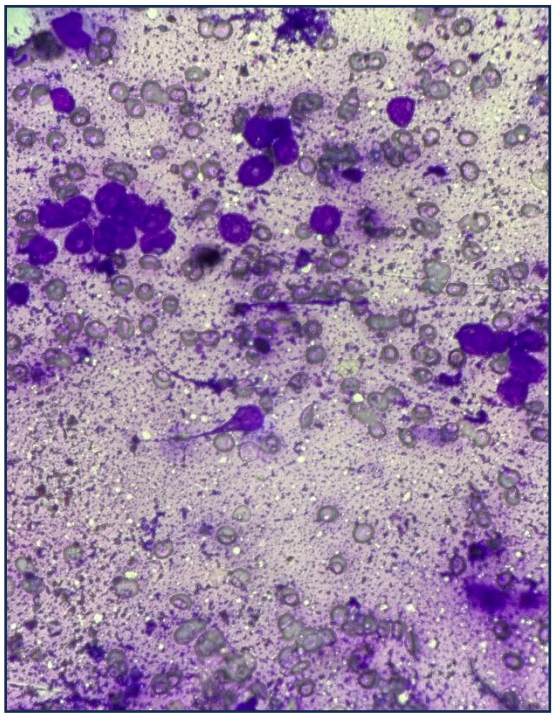
For pathological examination patient was advised FNAC. FNAC was done for left post auricular swelling/? upper cervical region lymph node. FNAC was done using 22 gauge needle and slides were stained with MGG.

Giemsa stained cytosmears reveal cells arranged in loose clusters and singly scattered cells. The individual cells have moderate cytoplasm with indistinct margin. Nuclei show mild nuclear pleomorphism. Nuclear chromatin is fine with single-to multiple prominent nucleoli. Occasional cells have prominent macronucleoli, total dissociation of the tumour cells, nuclei are large, with fine chromatin, prominent nucleoli and abundant basophilic cytoplasm. Background shows abundant reactive lymphoid cells admixed with dissociated malignant cells and hemorrhage is also seen.









Features were overall suggestive of Metastatic Carcinoma- Undifferentiated. Clinical, radiological evaluation and biopsy was advised for confirmation and further evaluation.

PET scan was performed which showed lesion in the left lateral wall of the nasopharynx with extension. Left retropharyngeal, left sided cervical lymph nodes-likely metastatic disease. No definitive scan evidence of abnormal metabolism elsewhere in the body was present in that study. For histopathological examination trucut biopsy was done for left cervical lymph node.

Grossly, multiple soft tissue cores were received measuring 0.4 to 1.0 cm. After processing paraffin blocks were made and slides were stained with haematoxylin and eosin stain. H&E stain sections revealed lymph nodal tissue infiltrated by nests and sheets of loosely cohesive cells with indistinct cell margins. Tumour cells have moderate eosinophilic to amphophilic cytoplasm, round nuclei, prominent eosinophilic nucleoli and vesicular chromatin. Apoptosis and brisk mitotic activity were present. Immunohistochemistry was done for confirmation. Pancytokeratin was positive in tumour cells, p63 -positive, epithelial membrane antigen (EMA)-positive, EBV-LMP-1 was positive, LCA(CD-45) and HMB 45 were negative for tumour cells.

The morphological findings together with the immunophenotype were consistent with diagnosis of – Metastatic Nonkeratinising Squamous Cell Carcinoma, Undifferentiated subtype. (Undifferentiated nasopharyngeal carcinoma).

Following diagnosis of undifferentiated nasopharyngeal carcinoma patient was treated with chemotherapy and responded well to treatment, currently patient is doing fine.

DISCUSSION

Nasopharyngeal cancer (NPC) has a high propensity of cervical node metastasis. The most commonly involved cervical lymph node regions include lateral retropharyngeal nodes and level II nodes. These first echelon nodal groups are followed by levels III, VA, and IV. Nasopharyngeal carcinoma rarely comes to medical attention before it has spread to regional lymph nodes. Enlargement and extension of the tumour in the nasopharynx may result in symptoms of nasal obstruction, changes in hearing and cranial nerve palsies, though the most common physical findings are neck mass consisting of painless, firm lymph node enlargement. According to the World Health Organization (WHO), nasopharyngeal carcinoma is classified into three subtypes namely, keratinizing squamous cell carcinoma, nonkeratinizing squamous cell carcinoma and undifferentiated or poorly differentiated carcinoma including lymphoepithelioma and anaplastic variant.[4] Nasopharyngeal carcinoma is positive for pan-cytokeratin, EMA and EBV-LMP and usually positive for markers of squamous differentiation like p40 and p63.[5] The association between EBV infection and undifferentiated nasopharyngeal carcinoma is well documented. Morphological characteristics of the undifferentiated type consist of uniform cells with ovoid vesicular nuclei, prominent nucleoli, and indistinct cell borders arranged in a syncytial pattern. IHC markers are of immense help to distinguish undifferentiated carcinoma from lymphoma. So, an initial panel of markers should include Pan-Cytokeratin and LCA. If pan-cytokeratin comes positive, then next panel should be markers of squamous differentiation like p40 and P63. EBV-LMP can be used in tumours which are negative for p40, and p63.[5] These findings are important for the management of NPC, particularly in defining proper treatment fields for definitive radiation therapy. Most patients are admitted to the hospital with advanced disease. Evidence of histopathology and immunohistochemistry is required to prove NPC origin. Multidisciplinary consultation is required for these uncommonly specific metastases.

CONCLUSION

This case emphasizes patterns of NPC metastasis and how through proper workup we can arrive at early and accurate diagnosis. It also highlights the importance of using correct IHC panel of markers to arrive at the final diagnosis. Paying attention to the specific lymph node metastasis sites of NPC plays an important role in accurately diagnosing the stage, thereby giving an appropriate treatment strategy. It is also important in determining radiotherapy volumes because radiotherapy is the standard therapy for this disease.[6] Radiological aid, cyto-histopathological correlation and with IHC we can get confirmed diagnosis. With robust of knowledge pathologists can create great difference in providing quick and early patient relief.

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