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Case report

Metastatic nasopharyngeal carcinoma masquerading lymphoma- An unusual presentation

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ABSTRACT

Nasopharyngeal carcinoma is an Epstein-Barr virus associated malignancy of the nasopharynx. Although metastasis to the cervical region is known, initial presentation with cervical metastasis without an apparent mass in the nasopharynx is rare. Herein, we present a case of a 14-year-old male who presented with bilateral multiple cervical lymphadenopathies, clinically mimicking lymphoma, with no mass in the nasopharynx, even on CT scan. A biopsy of the lymph node revealed a syncytial arrangement of atypical cells with partially compressed lymphoid tissue. On immunohistochemistry, these cells were positive for Pan-cytokeratin and EBV-LMP1, with absent CD45 expression; and a possibility of metastatic deposit arising from nasopharyngeal carcinoma was suggested. MRI revealed a thickening of the posterior nasopharyngeal wall, thereby confirming the origin of the tumor.

This case highlights a possible clinical mimicker and the importance of biopsy and immunohistochemistry in reaching a conclusive diagnosis. Clinicians and pathologists must be vigilant, and the possibility of NPC must be ruled out even without any obvious mass in the nasopharynx, to avoid delay in further management.

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INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a malignant tumor arising from the epithelium of the nasopharynx.[1] It is an Epstein-Barr virus (EBV) associated malignancy of young adults with a high prevalence in South asian countries as compared to Western countries.[2] Clinically, patients may present with symptoms of nasal obstruction or cranial palsy.[3] Although early metastasis to lymph nodes is known, patients generally present first with nasal symptoms. Herein, we present an unusual case of metastatic nasopharyngeal carcinoma that presented with multiple bilateral cervical lymphadenopathies clinically mimicking lymphoma.

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CASE REPORT

A 14-year male presented with complaints of multiple bilateral cervical swellings for 6 months. At the time of presentation, there were no other complaints, particularly no nasal complaints, and a general physical examination revealed multiple enlarged lymph nodes present bilaterally in the neck, which were firm to hard in consistency. A biopsy of the cervical lymph node was done and sent for histopathology. Grossly, a single lymph node measuring 2cmx1cmx0.5cm was received. Microscopy revealed a partially encapsulated lymph node with effaced architecture. There was diffuse infiltration by sheets of syncytially arranged atypical cells. (fig.1A) These cells had large vesicular nuclei, prominent eosinophilic nucleoli, and moderate to ample cytoplasm. Frequent mitotic figures and focal nuclear pleomorphism were also noted. Peripherally compressed normal lymphoid tissue was also noted. Based on these morphological findings, the possibility of a secondary metastatic lesion of the lymph node was suggested, and immunohistochemistry (IHC) was advised. Meanwhile, the patient had one episode of epistaxis, which was managed conservatively. A CT scan of the head and neck was done, which did not reveal any mass in the nasopharynx. A panel of immunohistochemistry (IHC) markers was applied, which showed the atypical cells to be positive for Pan Cytokeratin, and negative for CD45, CD3, CD20, CD30, PAX-5, ALK, S-100, CD56, CD68, and Desmin. Diffuse weak positivity for EBV-LMP1 was also noted. (fig.1B & 1C) Based on these findings, a diagnosis of metastatic deposit, possibly nasopharyngeal carcinoma (non-keratinizing, undifferentiated type) was given. As there was no mass in the nasopharynx on the CT scan, an MRI was done, which revealed thickening of the posterior nasopharyngeal wall; thereby confirming the origin of the metastatic lesion. (fig. 1D)

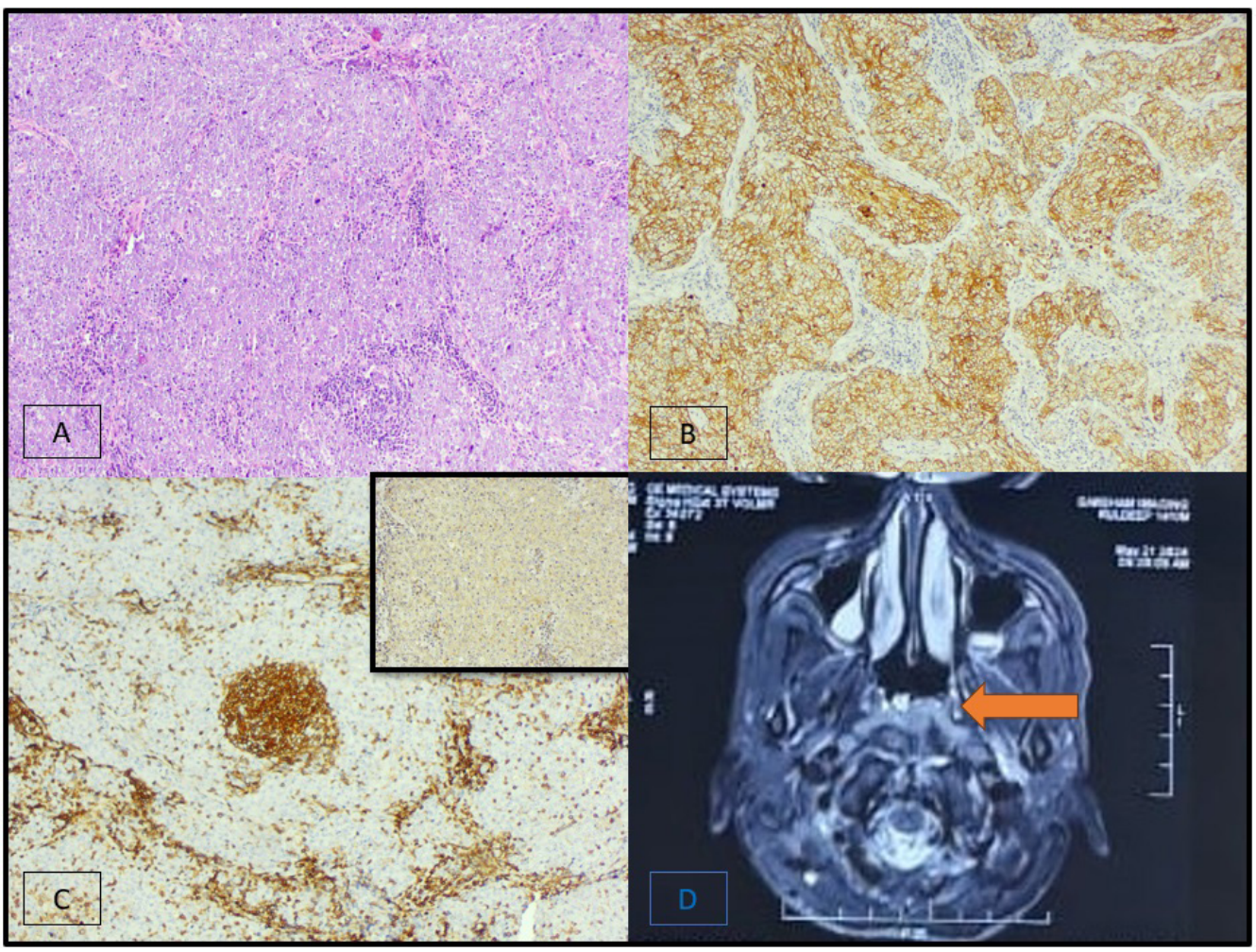

Figure 1: *A) Biopsy from the lymph node showing effacement of architecture with syncytial arrangement of tumor cells (HE stain; 100X). B) Tumor cells expressing Pan CK (IHC; 100X). C) Tumor cells negative for CD45 immunostain (the residual background lymphoid population expresses CD45). The tumor cells also showed faint positivity for LMP1 (IHC; 100x). D) MRI of the head and neck revealed thickening of the posterior nasopharyngeal wall (orange arrow).*

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DISCUSSION

Nasopharyngeal carcinoma predominantly occurs in young adults, although it can be seen in children. Its early detection may be a challenge due to the hidden location of the nasopharynx. On radiological examination, the nasopharynx may have a normal appearance or show fullness, surface granularity, or an overt mass.[4] However, the present case did not show an overt mass radiologically, due to which it was initially missed clinically. If an obvious mass is present, the diagnosis is usually based on its biopsy. However, NPC is known to have an early metastasis, and very rarely, patients may present directly with metastatic deposits in lymph nodes or distant metastases to bone (64–67%), liver (32–34%), and less commonly to lung (15–22%).[5] The present case had a similar presentation and was diagnosed based on the biopsy of the cervical lymph node.

The association between EBV infection and NPC is well known. Almost all NPCs in endemic regions are associated with infection by EBV. The expression of the EBV genome in NPC cells comes from the coding and non-coding genes. The coding genes include EBV latent membrane proteins (LMPs) and EBV nuclear antigens (EBNA). The non-protein genes include EBV-encoded small non-polyadenylated RNAs (EBERs) and microRNAs. Two small EBV-encoded RNAs, namely EBER1 and EBER2, are the most abundant viral transcripts in latent EBV-infected NPC cells, which can be detected by FISH. EBV infection, thus, has been proven to be an important factor in promoting NPC cellular motility and metastasis from different angles, involving multiple signaling pathways.[6]

According to the World Health Organization (WHO) classification, NPCs are classified morphologically into three types: keratinizing squamous cell carcinoma, non-keratinizing differentiated carcinoma, and non-keratinizing undifferentiated carcinoma.[7] However, this classification does not provide adequate information to predict the outcome of the patient, especially the occurrence of metastasis. Morphological characteristics of the undifferentiated type consist of uniform cells arranged in a syncytial pattern with cells having ovoid vesicular nuclei, prominent nucleoli, and indistinct cell borders.[4] This was similar to our case, wherein the lymph node showed a syncytial arrangement of these atypical cells. At times, distinguishing the undifferentiated type of NPC from lymphoma might be difficult, especially in cases of the syncytial variant of nodular sclerosis Hodgkin lymphoma. In such cases, a panel of IHC markers can help to differentiate Hodgkin lymphoma from NPC. Although CD45 is absent in both, NPC lacks CD30 and PAX5 expression as well.[4,8] There has been a single case report in the literature where NPC showed expression of CD30; however, the authors concluded that a panel of markers, including Pan CK, is useful in such cases, in which Hodgkin lymphoma will not show the expression of Pan CK.[4] IHC can easily help to differentiate undifferentiated carcinoma from Non-Hodgkin lymphoma. Pan CK and CD45 are the primary markers to differentiate undifferentiated carcinoma from NHL. However, a more robust panel of markers is essential to differentiate NPC from HL. In the present case, in addition to Pan CK and CD45, other markers for Hodgkin lymphoma (PAX5, CD30) were also applied to rule out the syncytial variant of nodular sclerosis Hodgkin lymphoma. Other markers like Desmin, CD68, and CD56 were also applied to rule out Rhabdomyosarcoma, and any histiocytic or NK cell tumors. However, positivity for Pan CK and EBV-LMP1 suggested the possibility of metastatic nasopharyngeal carcinoma.

CONCLUSIONS

Nasopharyngeal carcinoma presenting with multiple cervical lymphadenopathies without any obvious mass may be misdiagnosed as lymphoma clinically. Biopsy of the lymph node with a panel of IHC markers is essential in such cases to arrive at a conclusive diagnosis. It is also important to differentiate the syncytial variant of Hodgkin lymphoma from undifferentiated carcinoma. For this, immunohistochemistry is imperative. Clinico-radiologically, the possibility of NPC must be considered in a patient with multiple lymphadenopathies even without an obvious mass lesion in the nasopharynx.

Conflict of interests: The authors declare no conflict of interest.

REFERENCES

1. Nguyen Van et al. Unusual Site Metastases in Nasopharyngeal Carcinoma. Case Rep Oncol 2021;14:1821–6. DOI: 10.1159/000520977
2. Yu MC, Yuan JM. Epidemiology of nasopharyngeal carcinoma. Semin Cancer Biol. 2002;12(6):421–9.DOI: 10.1016/s1044579x02000858
3. Youssef AA, Raafat TA. Nasopharyngeal carcinoma: imaging features of unusual cancer in children. Egyptian J Radiol Nuclear Med 2015;46:943–7. DOI: 10.1016/J.EJRNM.2015.09.010
4. S. Hajra et al. A rare case report of nasopharyngeal carcinoma with multi-organ metastasis, clinico-radiologically mimicking lymphoma. Hematol Transfus Cell Ther. 2024;46 Suppl 6(Suppl 6):S389-92. DOI: 10.1016/j.htct.2023.03.024.
5. Ho FC, Tham IW, Earnest A, Lee KM, Lu JJ. Patterns of regional lymph node metastasis of nasopharyngeal carcinoma: a meta-analysis of clinical evidence. BMC Cancer. 2012; 12: 98. DOI: 10.1186/1471-2407-12-98
6. Guo LL, Wang HY, Zheng LS, et al. Metastasis of nasopharyngeal carcinoma: What we know and do not know. Visualized Cancer Medicine. 2021;2,4. https://doi.org/10.1051/vcm/2021003
7. Shanmugaratnam K. Histological typing of nasopharyngeal carcinoma. IARC Sci Publ (1971). 1978;(20):3-12. .PMID: 215516.
8. Jabbour MN, Nassif S, Chakhachiro Z. Undifferentiated Nasopharyngeal Carcinoma Mimicking Hodgkin Lymphoma With CD30 Expression. Int J Surg Pathol. 2016;24(8):715-7. DOI: 10.1177/1066896916664989