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Original Article - Case Report

Dedifferentiated Liposarcoma of the Nasopharynx - A Case Report of a Rare Enigmatic Entity

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ABSTRACT

Liposarcoma is the second most common soft tissue sarcoma and is usually encountered in the retroperitoneum and lower extremities. Nasopharyngeal liposarcoma is exceptionally rare, with only four cases being reported to this date. Additionally, diagnosis of the dedifferentiated subtype of liposarcoma becomes particularly challenging on biopsy samples obtained from non-retroperitoneal sites, as it exhibits a wide morphological spectrum, less commonly shows an absence of a component of well-differentiated liposarcoma, and at times displays low-grade dedifferentiation. We report a case of nasopharyngeal low-grade dedifferentiated liposarcoma in a 36-year-old male, the diagnosis of which was limited by all the above-mentioned factors. However, a diligent search for lipoblast-like cells and the use of appropriate immunohistochemical markers lead to a conclusive diagnosis. We have also commented on the differential diagnoses that could compound the diagnostic dilemma and have attempted to probe into the site-specific prognostic implication of this rare malignancy. Accurate identification of DDL is foremost owing to the differences in management from its close mimickers and may confer a good prognosis, especially when it occurs in nasopharynx.

Abbreviations

Well-differentiated liposarcoma (WDL), Dedifferentiated liposarcoma (DDL), Magnetic resonance imaging (MRI), Positron emission tomography and computed tomography (PET-CT), Fluorodeoxyglucose (FDG), Smooth muscle actin (SMA), Immunohistochemistry (IHC), Fluorescence in-situ hybridization (FISH).

Keywords

Diagnosis, dedifferentiation, immunohistochemistry, liposarcoma, nasopharynx.

INTRODUCTION

Liposarcoma is one of the most common malignant soft tissue tumors in adults. The retroperitoneum and lower extremities are the usual sites of tumor development. The incidence of this malignant neoplasm in the head and neck region is extremely low, accounting for only 1.8–6.2% of all cases[1,2,3]. Nasopharyngeal liposarcoma is exceptionally rare, with only four cases being reported in the existing literature[1,3-5]. Further, the dedifferentiated subtype of liposarcoma is likely to be underdiagnosed at non-retroperitoneal sites, particularly when it is not associated with a component of well-differentiated liposarcoma (WDL), or in patients without an antecedent history of WDL[6]. The present paper aims

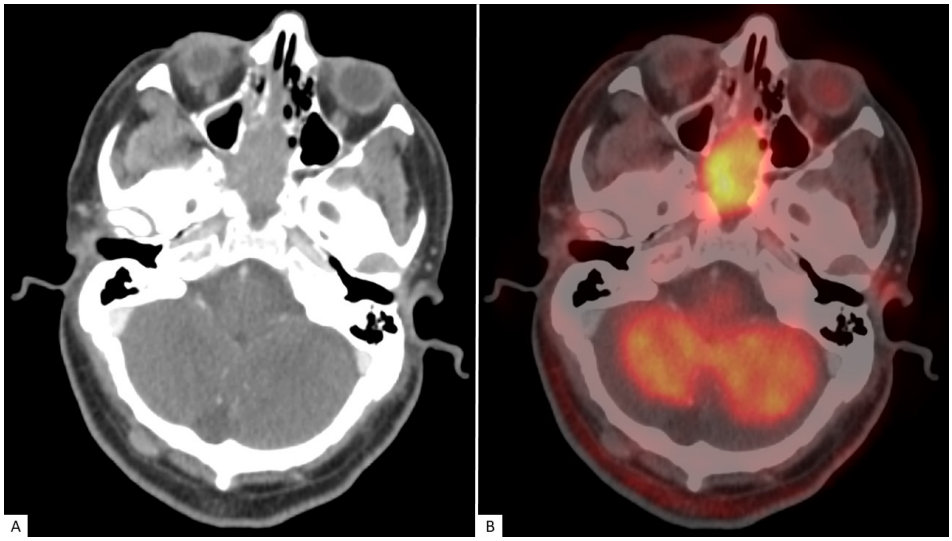

Figure 1. PET-CT images of the presented case
A. CT image of the presented case (axial plane); **B.** PET image of the presented case (axial plane)

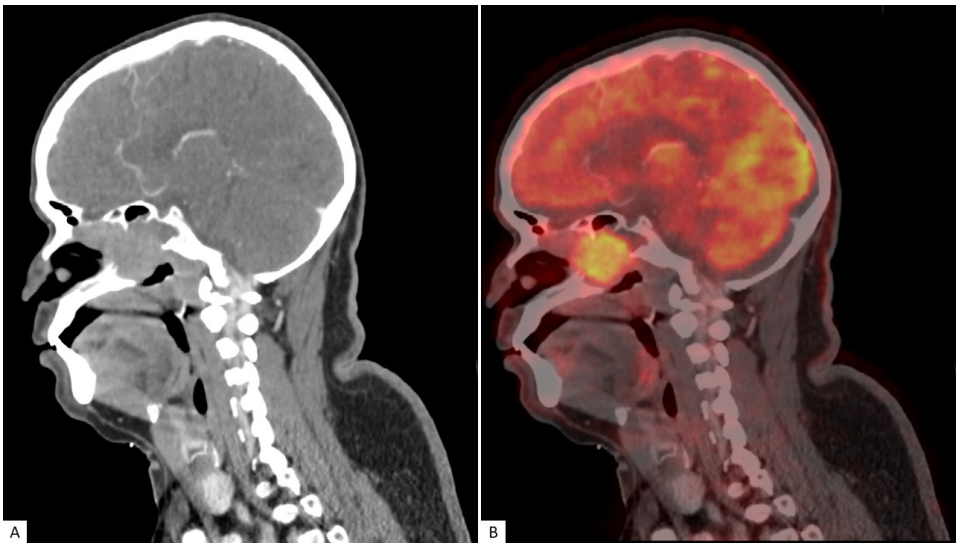

Figure 2. PET-CT images of the presented case
A. CT image of the presented case (sagittal plane); **B.** PET image of the presented case (sagittal plane)

to report an additional case of dedifferentiated liposarcoma (DDL) of the nasopharynx in a 36-year-old patient, with emphasis on diagnostic challenges for the precise diagnosis and the prognostic implication at this rare site.

CASE REPORT

A 36-year-old male presented to the Head and Neck OPD with right nasal bleeding for 4 months and right nasal blockage for 10-15 days. On examination, blood-stained right nasal mucosa was noted with no obvious mass/ growth. Magnetic resonance imaging (MRI) of the paranasal sinuses revealed a heterogeneous lobulated soft tissue mass in the right nasopharynx, measuring approximately 4.4x3.0x4.2cm with no regional lymphadenopathy. Subsequently, positron emission tomography and computed tomography (PET-CT) were performed, which showed *fluorodeoxyglucose (FDG)* avid soft tissue mass involving the nasopharynx, eroding the sphenoid sinus and extending into the ethmoid sinus

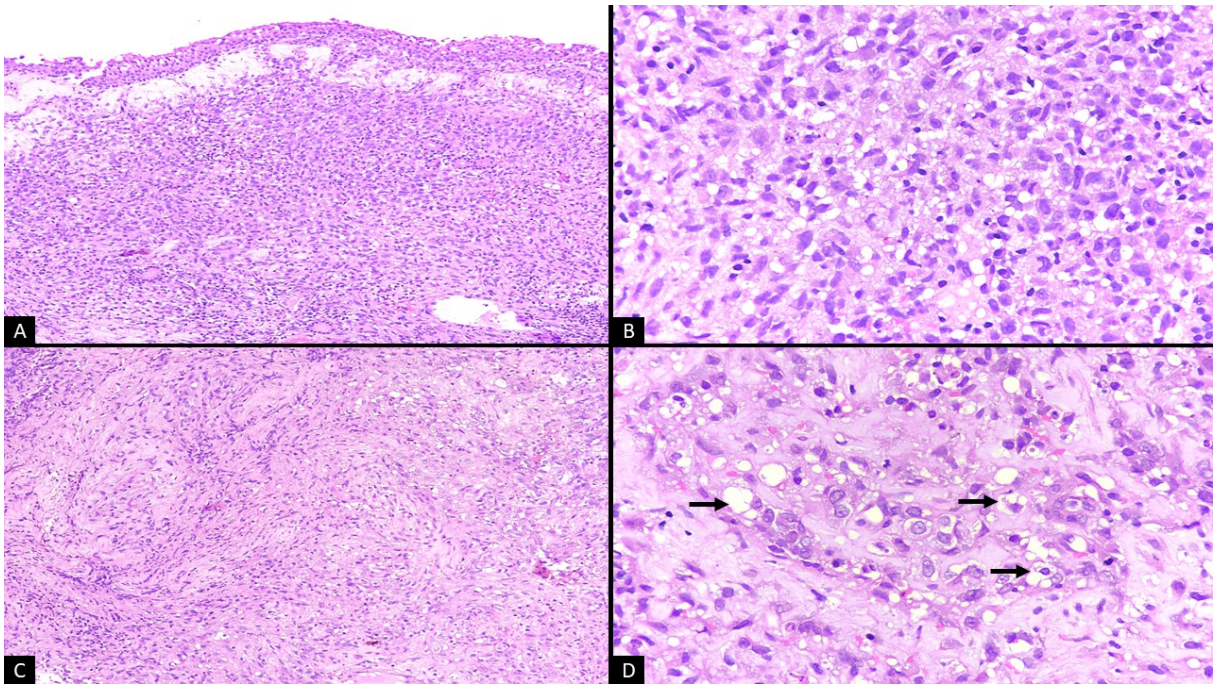

Figure 3. Histological images of the presented case
A. Subepithelial infiltrating tumor disposed in sheets and nests, intimately admixed with lymphocytes and plasma cells (H&E, 100X); **B.** Tumor cells displaying varied morphology ranging from spindle to ovoid shape (H&E, 400X); **C.** Tumor cells with lipoblast-like morphology embedded in the fibrous stroma (H&E, 100X); **D.** Lipoblast-like tumor cells (black arrow) (H&E, 400X).

measuring 40x28x41mm, SUVmax 8.99 (**Figure 1** and **Figure 2**). Based on the radiological findings, he was clinically diagnosed with nasopharyngeal carcinoma and a biopsy was undertaken for confirmation. Microscopic examination showed multiple tissue bits focally lined by respiratory epithelium. The subepithelium showed an infiltrating tumor disposed in sheets and nests, intimately admixed with lymphocytes and plasma cells. The tumor cells displayed varied morphology ranging from spindle, and ovoid to lipoblast-like cells. These cells had moderately pleomorphic nuclei, dispersed to vesicular chromatin, conspicuous nucleoli, irregular nuclear contour, and a variable amount of cytoplasm (**Figure 3**). Marked nuclear atypia and brisk mitosis were not evident. Considering histomorphology, a wide range of differential diagnoses were contemplated. Immunostaining showed positivity for MDM-2, p16, and CD34 (**Figure 4**), while immuno-negativity for pan-cytokeratin, p40, CD45, CD30, ALK-1, CD4, CD68, S-100, smooth muscle actin (SMA), desmin, and NKX2.2 was noted. INI-1 expression was retained by the tumor cells. A final diagnosis of low-grade DDL was rendered based on histomorphological and immunohistochemical (IHC) findings. Currently, the patient is on radiotherapy and is planned for concurrent chemotherapy.

DISCUSSION

Liposarcoma is the second most common soft tissue sarcoma, accounting for approximately 20% of all malignant mesenchymal neoplasms[5]. WDL and DDL represent a histologic and behavioural spectrum of a single disease entity. Nonetheless, diagnosis of the dedifferentiated subtype of liposarcoma becomes particularly challenging at non-retroperitoneal sites because of the wide morphologic spectrum and absence of the WDL component[6,7].

DDL is usually seen among middle-aged and elderly individuals with a nearly equal gender distribution. The retroperitoneum is the most common site and can seldom occur in the thorax, mediastinum, and within the head and neck[7,8].

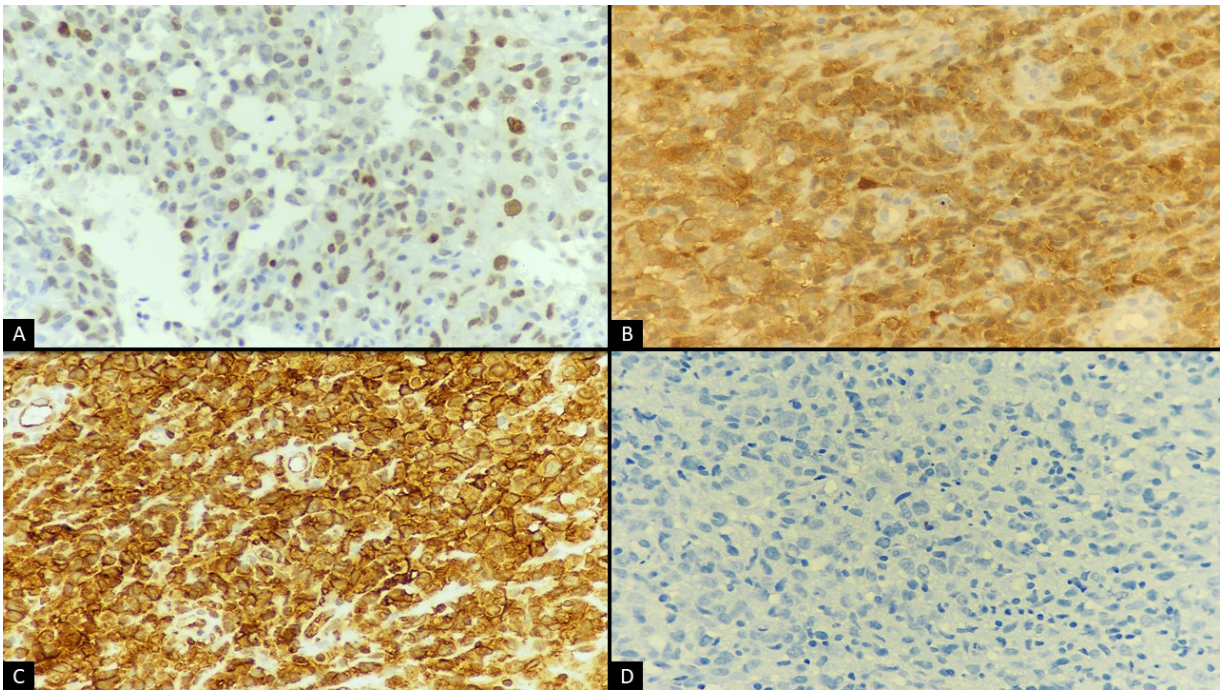

Figure 4. Immunohistochemical panel for the presented case: tumor cells are exhibiting
A. nuclear positivity for MDM2 (H&E, 400X); **B.** positivity for p16 (H&E, 400X); **C.** membranous positivity for CD34 (H&E, 400X); **D.** immuno-negativity for pan-cytokeratin (H&E, 400X).

Nasopharyngeal liposarcoma is exceedingly rare, with merely four cases reported in the current literature[1,3-5]. DDL exhibits a varied morphological spectrum but most often mimics undifferentiated pleomorphic sarcoma (UPS) or high-grade myxofibrosarcoma (HG-MFS). Additionally, cases with low-grade dedifferentiation have also been recognized, which pose a major diagnostic challenge for the pathologist. Nearly 5-10% of DDL display heterologous differentiation towards other mesenchymal lines such as myogenic, osteosarcomatous, or chondrosarcomatous lineages[7,8].

In the present case, initial clinico-radiological work-up favoured the diagnosis of nasopharyngeal carcinoma. However, the histopathological examination completely turned the table. The biopsy revealed an infiltrating tumor composed of cells that displayed varied morphology ranging from spindle, and ovoid to lipoblast-like cells. Hence, in addition to nasopharyngeal carcinoma, Lymphoma, especially Anaplastic large cell lymphoma (histiocytic variant), Ewing sarcoma, Histiocytic sarcoma, Malignant melanoma, Spindle cell rhabdomyosarcoma, Epithelioid sarcoma, and DDL were also considered in the differential diagnosis. Subsequently, an array of IHC markers were directed to exclude each of them. Finally, a diagnosis of low-grade DDL was rendered based on distinct histomorphology and immuno-reactivity of MDM2, p16, and CD34. The absence of a component of WDL and predominance of low-grade dedifferentiation may further compound the diagnostic dilemma as was with our case. However, one of the important histological clues that lead us to consider DDL in our differential diagnosis was the presence of lipoblast-like cells (depicting lipogenic differentiation). Therefore, we advocate a diligent search for such cells, especially at unusual sites. The diagnosis of DDL at a rare site entails a comprehensive approach. We should consider all the possible differential diagnoses that correlate with the designated site and histology to reach an appropriate diagnosis. Also, immunohistochemistry and molecular studies play a decisive role in narrowing down the differential diagnosis. Thway et al. documented that 93% of DDL express at least two among the immunohistochemical trio of CDK4, MDM2, and p16. They also highlighted that the combined use of CDK4 and p16 has better

discriminatory value than with MDM2[9]. More recently, fluorescence in situ hybridization (FISH) has emerged as a more sensitive and specific tool than MDM2 IHC for detecting MDM2 gene amplification. It is particularly useful in small biopsies or when the component of WDL is absent or obscure[7,10]. In the present case, the immunostaining pattern was similar to the one recorded by Thway et al. However, interphase FISH analysis for MDM2 could not be undertaken due to a lack of MDM2 amplification probes at our institute.

Data on the clinical behaviour of DDL indicate that the anatomical site is the most important adverse prognostic factor, with retroperitoneal lesions displaying worst outcome than those at other locations[8,11]. Davis et al. analysed the survival of patients with liposarcoma of the head and neck. They concluded that cases diagnosed with liposarcoma of the upper aerodigestive tract have better crude disease-specific survival rates when compared to other sites of the head and neck[12]. Also, among the four prior case reports of nasopharyngeal liposarcoma, two patients are alive and disease-free after appropriate treatment. While one patient died of the disease, the status of the other patient as well as the follow-up period has not been specified in the case report authored by Chakraborty et al[1,3-5]. In our case, the patient is receiving radiotherapy and is showing signs of improvement in three months. Given that nasopharyngeal liposarcomas are exceptionally rare and very few cases have been reported to date, a definite comment upon the site-specific prognostic implication of such malignancies is not possible. However, taking into account the statistics provided by Davis et al. and the status of the patient following adequate treatment in the former case reports, it may be extrapolated that liposarcomas of the nasopharynx have a better outcome in comparison to other sites.

CONCLUSION

Given the paucity of data, we intend to report and add another case of low-grade dedifferentiated nasopharyngeal liposarcoma. The recognition of this rare entity can prove to be a diagnostic challenge for the pathologist on biopsy samples obtained from such a site, as it exhibits a wide morphological spectrum, and less commonly shows an absence of a component of WDL, with low-grade dedifferentiation. Therefore, we advocate a conscientious search for lipoblast-like cells along with a comprehensive approach to the diagnosis of DDL at a non-retroperitoneal site. Accurate identification of DDL is foremost owing to the differences in management of the enlisted differential diagnosis.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgements

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