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ORIGINAL RESEARCH

BIOPSY IS NOT THE END, EFFICACY OF IHC AIDED DIAGNOSIS IN DETERMINING THE MODALITY OF TREATMENT IN LIPOSARCOMA

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INTRODUCTION
Liposarcoma are malignant tumour of fatty tissue and are the malignant counterpart to benign lipoma. They are the second most common type of soft tissue sarcoma. There are 3 groups of liposarcoma well-differentiated (WDL) and dedifferentiated liposarcoma (DDL), myxoid/round cell liposarcoma, and pleomorphic liposarcoma. In all 3 groups, complete surgical resection is central in treatment aimed at cure and is based on grade. Radiation can reduce risk of local recurrence in high-grade lesions like dedifferentiated liposarcoma or minimize surgical morbidity in the myxoid/round cell liposarcoma group. Classification based on histological appearance is not always precise, especially because of the partial overlap of histological features of well-differentiated liposarcoma and Pleomorphic liposarcoma that may be better differentiated based on MDM2 expression on Immunohistochemistry. Detection of *MDM2* and CDK*4* amplification serves to determine the treatment modality. The differential diagnosis between well-differentiated liposarcoma and dedifferentiated liposarcoma from their morphologic counterparts is challenging.

METHODOLOGY
This study is a retrospective study done in post graduate medical college in Puducherry from January 2022 to august 2022. Patient who presented with soft tissue swelling over upper extremity who underwent surgery was included. 20 liposarcoma cases were taken in which 10 cases were of dedifferentiated liposarcoma, rest 10 cases were of pleomorphic liposarcoma.

RESULT
Out of 20 cases, 10 cases were pleomorphic liposarcoma, 5 were dedifferentiated liposarcoma and 5 well differentiated liposarcoma which was confirmed by Immunohistochemistry. Wide local excision was done in well differentiated liposarcoma, radiation therapy was given to dedifferentiated liposarcoma and pleomorphic sarcoma which subsequently showed improvement in the prognosis of patient.

CONCLUSION
The spectrum of pathological variations of liposarcoma directly impacts prognosis. Differentiation of subtypes of liposarcoma therefore has a high significance for prognosis and therapeutical approach. Even though the pathology is same the subtype decides the therapeutic conduct of patient. This study is emphasized that histopathological examination is not final modality but IHC is the final modality in management.

KEY WORDS: Soft tissue tumour, liposarcomas, histopathology, immunohistochemistry

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Introduction

In the esophagus, retroperitoneum, and popliteal fossa, liposarcoma, a tumor of lipoblasts, can appear. At various sites in the body, liposarcoma is more prevalent in certain subtypes than others. It is still unknown what causes liposarcoma [1]. Many patients with soft tissue sarcomas do not meet these risk factors, as documented by the American Cancer Society. This malignancy is caused by a genetic mutation that is still being investigated. Among soft tissue sarcomas worldwide, liposarcoma is the most common. It is not known if there is any other predisposition to liposarcoma. Neither race nor gender are significantly associated. According to some studies, males predominate slightly. Liposarcomas can be classified into three types: well-differentiated (WDL), dedifferentiated liposarcomas (DDL), myxoid/round cell liposarcomas, and pleomorphic liposarcomas. Liposarcoma presents differently based on where the tumor is located. Liposarcoma has a greater chance of developing in the extremities, the retroperitoneum, and, least often, in the esophagus. Lower extremity myxoid liposarcomas present as deep masses. Treatment consists primarily of surgical excision. High-grade lesions may require surgical excision, adjuvant radiation, and/or chemotherapy. Nevertheless, the response of liposarcoma to chemotherapy is not well documented. As a result, chemotherapy does not yet have a proven track record in treating liposarcomas. Myxoid subtypes may benefit from radiation therapy, especially in conjunction with surgery [3].

A well-differentiated liposarcoma characterized by mature adipocytes with fibrous stroma with atypical nuclei is the most common type. Idiopathic liposarcomas (MLS), which include low-grades and high-grades, are the second most common type of esophageal liposarcoma [4]. A chicken-wire pattern of curving capillaries appears in low-grade MLS. These tumors have low cellularity, bland nuclei, and prominent capillaries. There is a distinctive hypercellularity in high-grade MLS with at least 5% of the tumor composed of solid sheets of round cells. Pléomorphic liposarcoma, which occupies at least 65% of the tumor and at least focal areas of typical liposarcoma, is the least common type of esophageal liposarcoma. Histological classification is not always accurate, especially because of partial overlap between well-differentiated liposarcomas and pleomorphic liposarcomas, which may be better differentiated on Immunohistochemistry based on MDM2 expression [6]. Liposarcoma and other benign and neoplastic lesions of the esophagus may appear very similar from a clinical and microscopical perspective. In order to determine treatment modality, the MDM2 and CDK4 amplifications are detected [7]. Liposarcomas are difficult to distinguish from dedifferentiated liposarcomas based on their morphology.

Methodology

This study is a retrospective study done in post graduate medical college in Puducherry from January 2022 to august 2022. Patient who presented with soft tissue swelling over upper extremity who underwent surgery was included. 20 liposarcoma cases were taken in which 10 cases were of dedifferentiated liposarcoma, rest 10 cases were of pleomorphic liposarcoma. Hematoxylin and eosin-stained sections were used to identify morphological patterns and to make differential diagnoses. According to the morphological pattern observed in H&E-stained sections, similar unstained sections were taken for immunohistochemistry with different antibodies

Results

The mean age for benign tumors was 40 ± 28.2 years, for intermediate tumors it was 57.50 ± 28.2 years, and for malignant tumors it was 65 ± 28.2 years. The overall male to female ratio for total soft tissue tumors was 55.5 ± 12.0. The overall ratio of male to female in tumor was 1:1 to 1:0. The overall ratio of benign to malignant was 100:1. The most cases of benign soft tissue tumors 45% occurred in the extremities and the most common site for malignant tumor was trunk with 45%. Out of 20 cases, 10 cases were pleomorphic liposarcoma, 5 were dedifferentiated liposarcoma and 5 well differentiated liposarcoma which was confirmed by Immunohistochemistry. Wide local excision was done in well differentiated liposarcoma, radiation therapy was given to dedifferentiated liposarcoma and pleomorphic sarcoma which subsequently showed improvement in the prognosis of patient.

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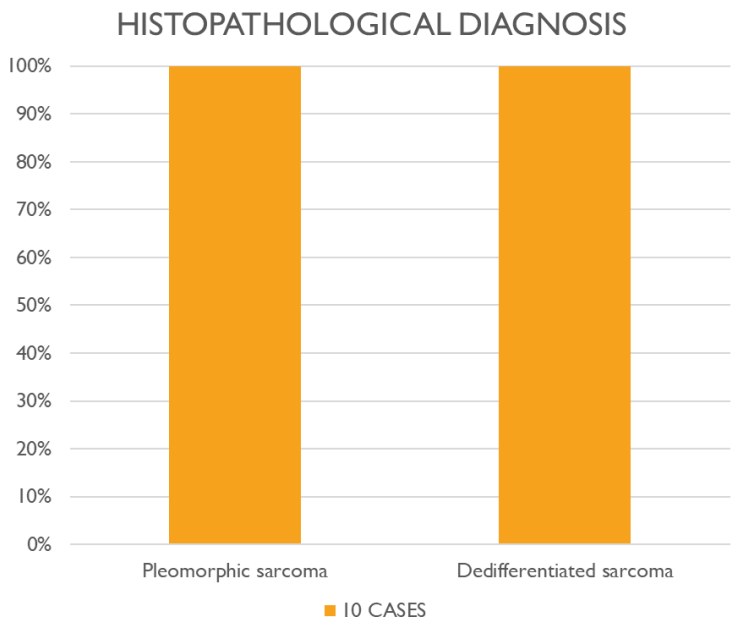

Figure 1 – Histopathological diagnosis

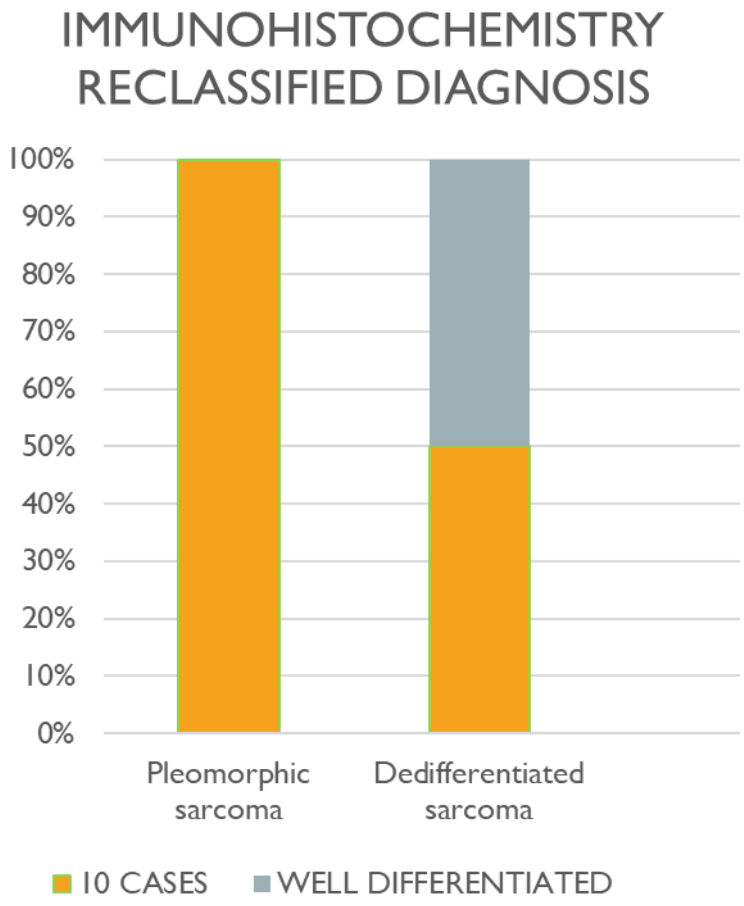

Figure 2 - Immunohistochemistry reclassified diagnosis

Discussion

Myxoid pleomorphic liposarcoma is uncommon in young patients, and it shows mixed histological features of

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conventional myxoid liposarcoma and pleomorphic liposarcoma. Upon histological examination, all cases had relatively bland, abundantly myxoid areas with a prominent capillary vasculature, admixed with cellular foci and lesser myxoid foci, containing numerous pleomorphic lipoblasts and markedly pleomorphic spindled cells. As myxoid pleomorphic liposarcoma presents unique morphologic, genetic, and epigenetic characteristics, its classification as a separate entity should be maintained for now [8].

According to Kojima et al., 2022, 16 liposarcomas were studied clinicopathologically, and the histology of them tumor cells closely resembled hibernoma, with brown fat-like, finely multivacuolated-to-eosinophilic cells with little or no nuclear atypia. There was evidence of DDIT3 rearrangements in the hibernoma-like components of MLS, but only negligible or equivocal expression of UCP1 in the tested cases. MLSs and well-differentiated liposarcoma often display hibernoma-like histology. Based on the expression of UCP1, some of these elements are neoplastic in WDLS. For an accurate diagnosis, an examination of classic liposarcoma histology and additional tests for MDM2/CDK4 or DDIT3 status are recommended [9].

According to Song et al., 2017, differentiating dedifferentiated liposarcoma (DDLPS) from other high-grade spindle and pleomorphic sarcomas is important for a better outcome. There is evidence that MDM2 amplification is present in some other sarcomas as well as in DDLPS. Among 85 cases (48.2%), 41 showed MDM2 amplification and expression. On the basis of histology, immunophenotype, and clinical data, MDM2 amplifications were reclassified. Among 41 cases, 39 were reclassified as DDLPS, including 30 diagnosed originally as DDLPS, 7 as undifferentiated pleomorphic sarcomas, 1 as myxofibrosarcomas, and 1 as pleomorphic liposarcomas. Additionally, immunohistochemistry and fluorescence in situ hybridization of MDM2 showed an excellent correlation (P0.001, sensitivity 92.7%, specificity 100%). In spite of the fact that a few other sarcomas also show MDM2 amplification and expression, MDM2 amplification and expression may be very useful to distinguish DDLPS from other undifferentiated high-grade spindle sarcomas [10].

To confirm the diagnosis, cytogenetic or molecular genetic techniques are often used. Recent studies have demonstrated the utility of DDIT3 immunohistochemistry (IHC) in the differential diagnosis of soft tissue tumors containing adipocytic cells and myxoid cells. In 50 cases of high-grade MLPS, mice monoclonal antibodies directed against the N-terminus of DDIT3 were used for IHC. DDIT3 was strongly stained by IHC in 48 of the 48 (96%) high-grade MLPS. In summary, DDIT3 IHC shows 96% sensitivity and 98% specificity for high-grade MLPS; strong, diffuse staining shows 96% sensitivity, but 100% specificity. Molecular genetic testing may be replaced in many cases with immunohistochemistry using an antibody directed against the N-terminus of DDIT3 [11].

The diagnosis of dedifferentiated liposarcoma (DDL) can sometimes be challenging given a wide range of histological features, according to Usman Tariq et al., 2020. It is not uncommon for DDL to contain "meningothelial-like" whorls, which can also be found in follicular dendritic cell sarcomas and neural tumors. The formation of metaplastic bones is frequently accompanied by this feature. DDL most likely represents an early stage of dedifferentiation as it contains meningothelial-like whorls. In addition to the presence of well-differentiated liposarcoma areas, metaplastic bone formation, positive expressions for p16 and -SMA on immunohistochemistry, and MDM2 gene amplification, diagnostic clues include the presence of well-differentiated liposarcoma areas. There is a possibility that these tumors will behave aggressively [12].

A patient with stage IV metastatic liposarcoma presented with a rapidly growing nodule on the scalp, according to Yu et al., 2016. In order to characterize the neoplasm further, MDM-2 immunostaining was also performed and was found to be negative. There is a great deal of difficulty in diagnosing pleomorphic liposarcoma. The histological characteristics of this tumor often make it difficult to differentiate from myxofibrosarcoma and other high-grade pleomorphic sarcomas. However, bizarre lipoblasts and negative MDM-2 staining can help distinguish this neoplasm from the histological mimics [13].

Kammerer et al., 2017 report that it is difficult to distinguish atypical lipomatous tumor/well-differentiated liposarcoma from dedifferentiated liposarcoma (DDLPS). Recent studies have suggested that p16 IHC is a useful diagnostic biomarker. A false-positive lipoma with secondary changes, especially in biopsy results, impaired p16's specificity of 68.2% in the differential diagnosis of ALT-WDLPS. ALT-WDLPS/DDLPS could be distinguished with p16 combined with MDM2 and CDK4 immunohistochemistry, which may allow it to be used as a single immunohistochemical marker [14].

Conclusion

Immunohistochemistry plays a key role in the diagnosis of soft tissue tumors. IHC is an important modality for diagnosing the management of liposarcoma. The spectrum of pathological variations of liposarcoma directly impacts prognosis. Differentiation of subtypes of liposarcoma therefore has a high significance for prognosis and therapeutical approach. Even though the pathology is same the subtype decides the therapeutic conduct of patient. This study is emphasized that histopathological examination is not final modality but IHC is the final modality in management.

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