**New Frontiers in Pathology 2024**

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**Diagnosis: Inflammatory well-differentiated liposarcoma**

**Clinical history:** 45-year-old male with a large mass in the retroperitoneum. The tumor was excised.

**Microscopic findings:**The sections show areas with a diffuse background of chronic lymphocytes and plasma cells. There is some background fibrosis. At higher power, there are rare, atypical cells with conspicuous nucleoli.

MDM2 immunohistochemistry highlighted the atypical cells. Further confirmation was found by positive MDM2 gene amplification by FISH.

**Discussion:**

Well-differentiated liposarcoma typically arises in middle aged to older adults in deep anatomic locations such as the proximal extremities, abdomen, retroperitoneum, or mediastinum. Histologically, these tumors are often associated with adipocytic tissue traversed by fibrous septa which contain atypical cells with enlarged and hyperchromatic nuclei. However, these tumors can have many morphologic variations, including sclerosing, myxoid or hibernoma-like changes.

Well-differentiated liposarcoma can also exhibit an “inflammatory” type of appearance that can be difficult to recognize. This variation contains sheets of lymphocytes which can cloak identifiable morphologic the usual features associated with liposarcoma. Follicles with germinal centers can be identified. Alternatively, inflammatory well-differentiated can also exhibit sheets of acute inflammatory cells. The atypical tumor cells in these tumors can exhibit vesicular nuclei with conspicuous nucleoli which mimic Reed-Sternberg cells seen in Hodgkin lymphoma.

In addition to lymphoma, the differential diagnosis of inflammatory well-differentiated liposarcoma can include infection or a fibroinflammatory type of process (that can be IgG4-mediated). MDM2 immunohistochemistry can sometimes be helpful in highlighting the tumor cells but MDM2 fluorescence in situ hybridization (for MDM2 gene amplification) is most definitive in confirming or excluding the diagnosis.

Inflammatory well-differentiated liposarcoma is a prominent example of soft tissue tumor with prominent inflammation. This “inflammatory” morphology can be particularly treacherous to the surgical pathologist as the inflammation can belie a tumor’s actual mesenchymal differentiation. Other soft tissue tumors which can have an inflammatory appearance include angiomatoid fibrous histiocytoma, inflammatory myofibroblastic tumor, myxoinflammatory fibroblastic sarcoma, pseudomyogenic hemangioendothelioma, among others. When considering an inflammatory soft tissue tumor in the diagnosis, a pathologist should also assess for infection, lymphoma, and sampling error in the differential diagnosis.

**References:**

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