Inflammatory Pseudotumor-like Follicular/Fibroblastic Dendritic Cell Sarcoma of the Liver, Epstein-Barr Positive, in a 35-year-old Female: A Case Study

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Background Information:

- Inflammatory pseudotumor-like follicular/fibroblastic dendritic cell sarcoma is a rare neoplasm of lymphatic tissue (<1%) that tends to arise in the spleen or liver of predominantly female patients[1].
- It most commonly affects women who are young to middle age[1].
- Patients most commonly present with abdominal pain (with or without a palpable mass), which can also be associated with systemic symptoms, such as fever or weight loss[1].
- Grossly, tumors generally present as solitary, ovoid to round, circumscribed, rubbery or soft, with pushing borders, and a tan cut surface with disperse areas of hemorrhage and necrosis[2].
- Histologically, tumors present with spindle or ovoid shaped cells admixed with an abundance of lymphocytes and plasma cells, the presence of eosinophils, and nuclear atypia[2].
- Neoplastic cells are commonly positive for one or more immunohistochemistical (IHC) follicular dendritic cell markers such as CD21, CD23, and CD35[1,2].
- Neoplastic cells are consistently correlated with a positive result for in situ hybridization for Epstein-Barr Virus (EBER)[1,2].
- Follicular dendritic cells (FDCs) are stationary antigen presenting cells, located in germinal centers of lymphoid follicles in lymphatic organs[3].
- FDCs bind immune complexes composed of antigens and antibodies and present them to B cells[3].
- FDCs are stromal in origin and develop from the mesenchymal stem cell line. Thus, these tumors are classified as sarcomas[1].
- The exact mechanism of neoplastic proliferation of FDCs remains unknown. However, there is some evidence that suggests a recurrent loss-of-function alteration in the genes *NFKBIA* and *CYLD*, involved in the regulation of tumor suppressor gene NF-kappaB, as well as alterations in genes *CD274* and *PDCD1LG2*, involving immune evasion and in genes *CDKN2A* and *RB1*, involving cell cycle progression[1,4].

Pertinent Positive and Negative Immunohistochemical and Molecular Testing Results:

Table 1. Chart indicating the results for specific IHC and molecular tests, which helped to determine the final diagnosis.

Test	Positive Result	Negative Result
CD21 Follicular Dendritic Cell Marker[5]	✔	
CD23 Follicular Dendritic Cell Marker[5]	✔	
CD35 Follicular Dendritic Cell Marker[5]	✔	
ALK1 T cell Marker[5]		✔
EBER Most Sensitive Marker for EBV-infected B cells[5]	✔	

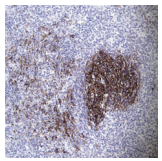

Figure 1. H&E of spindle cells within the tumor with positive CD21 IHC stain.

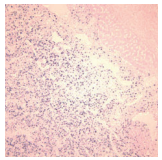

Figure 2. H&E of spindle cells within the tumor with positive in-situ hybridization for EBERS.

Pertinent Patient History:

- The patient is a 35-year-old Asian female with no previous medical history, who reported to the hospital with complaints of fatigue, fever, weight loss greater than 10 pounds, night sweats, persistent epigastric pain and a self-palpable mass in the right upper abdomen.
- The patient had an ultrasound and MRI performed, which noted a large mass in the left lobe of the liver. The patient then underwent IR guided biopsy, with subsequent immunohistochemical testing.
- The patient was taken into surgery, where a lobectomy of the left lobe of the liver was performed.
- The specimen was received in the pathology lab for prosection.

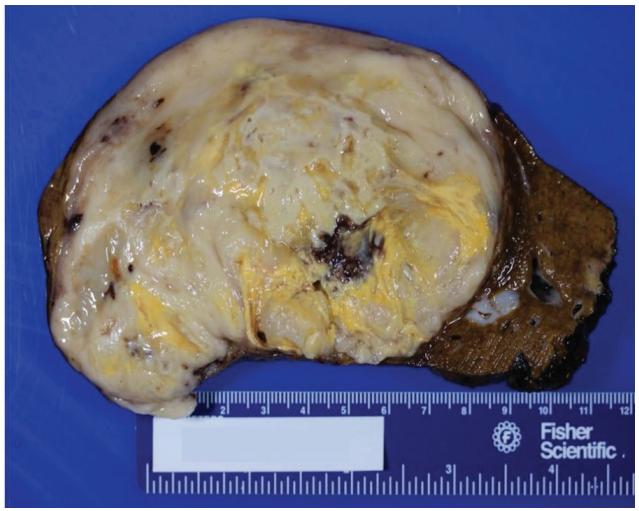

Figure 3. Lobectomy specimen revealing a 20.0 x 11.5 x 8.6 cm tan, fleshy mass with multiple areas of hemorrhage and yellow necrosis. The tumor abuts the capsule, approximately 2.0 cm from the nearest inked margin. Normal liver parenchyma is tan-yellow and rubbery.

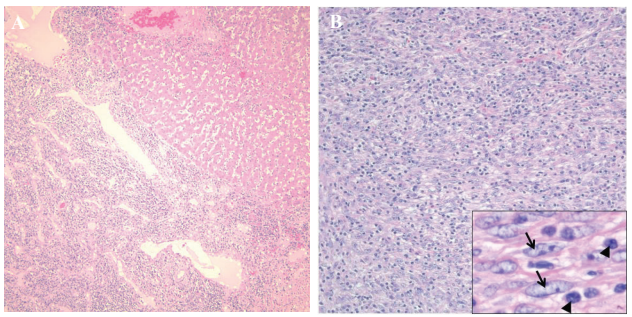

Figure 4. A) H&E of normal liver parenchyma with transition to tumor. **B)** The tumor is composed of spindle cells dispersed within a prominent lymphoplasmacytic infiltrate. Inset demonstrates high power view of the elongated spindle cells (arrows) with several lymphocyte nuclei (arrow heads).

Discussion:

- Inflammatory pseudotumor-like follicular/fibroblastic dendritic cell sarcoma is an intriguing malignancy, as the tumor demonstrates both malignant and benign characteristics simultaneously. The tumor displays hemorrhage and necrosis, but at the same time exhibits a low rate of metastasis with indolent behavior and has a good prognosis after complete removal.
- Another interesting aspect is the oncogenesis of the tumor in the liver. Normally, follicular dendritic cells are found in germinal centers of lymphatic organs, to which the liver is not generally considered to be a lymphatic organ. Therefore, the development of these types of tumors in the liver, as seen with this case, is intriguing. The exact mechanism is unknown, but the presence of Epstein-Barr virus in the neoplastic spindle cells almost certainly plays a major role[2].
- The oncogenesis of these tumors may be a combination of the expression of viral oncogene latent membrane protein 1 (LMP1) of Epstein-Barr virus, which allows the virus to inhibit apoptosis[2,5] and the persistent presence of Epstein-Barr virus as an antigen, which can contribute to the development of the liver as tertiary lymphatic tissue consisting of germinal centers containing follicular dendritic cells[3]. Tissue reorganization into tertiary lymphoid tissue is shown to occur anywhere in the body, as a result of the constant presence of an antigen[3].

Conclusion:

Narrowing down the diagnosis for Inflammatory pseudotumor-like follicular/fibroblastic dendritic cell sarcoma can be challenging due to its rarity and the similarities with other differential diagnoses. In order to reach the diagnosis, there needs to be a strong index of suspicion based on gross presentation, microscopic presentation, and specific IHC and molecular testing results.

The Role of the Pathologists' Assistant:

- Pathologists determine the final diagnosis after considering other alternatives. However, the role of the Pathologists' Assistant is integral.
- It is the Pathologists' Assistant who acts as an extension of the Pathologist, when receiving specimens in the pathology lab. Choosing which section to submit for processing is of utmost importance. For this case, important sections include sections demonstrating the tumor to the margin of resection, tumor to capsule, tumor and non-neoplastic liver, sections of tumor demonstrating hemorrhage and necrosis, and a section of normal liver parenchyma.
- The Pathologist base their decision of the final diagnosis on processed tissue sections. Therefore, optimal tissue selection made by the Pathologists' Assistant is crucial.
- Ultimately, the decision of which sections to submit made by the Pathologists' Assistant directly enhances or diminishes the Pathologists ability to make a diagnosis, which directly impacts the outcome of patient care.
- Every cut made by the scalpel and decision made by the Pathologists' Assistant has a direct impact on patient care.

References:

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