Case history

51 year-old woman presented with abdominal discomfort in 2016; imaging revealed a small bowel mass and liver lesions. Biopsy of a liver lesion in 2016 demonstrated gastrointestinal stromal tumor; immunohistochemical profile at the time showed positive staining for KIT, DOG1, and CD34 and negative staining for pan-keratin, desmin, and smooth muscle actin.

She was started on imatinib 400 mg and continued on it for 2 years. Surveillance imaging 2/28/2018 showed evidence of disease progression. At our institution, she was started on an experimental agent. A protocol biopsy was obtained on 4/26/2018.

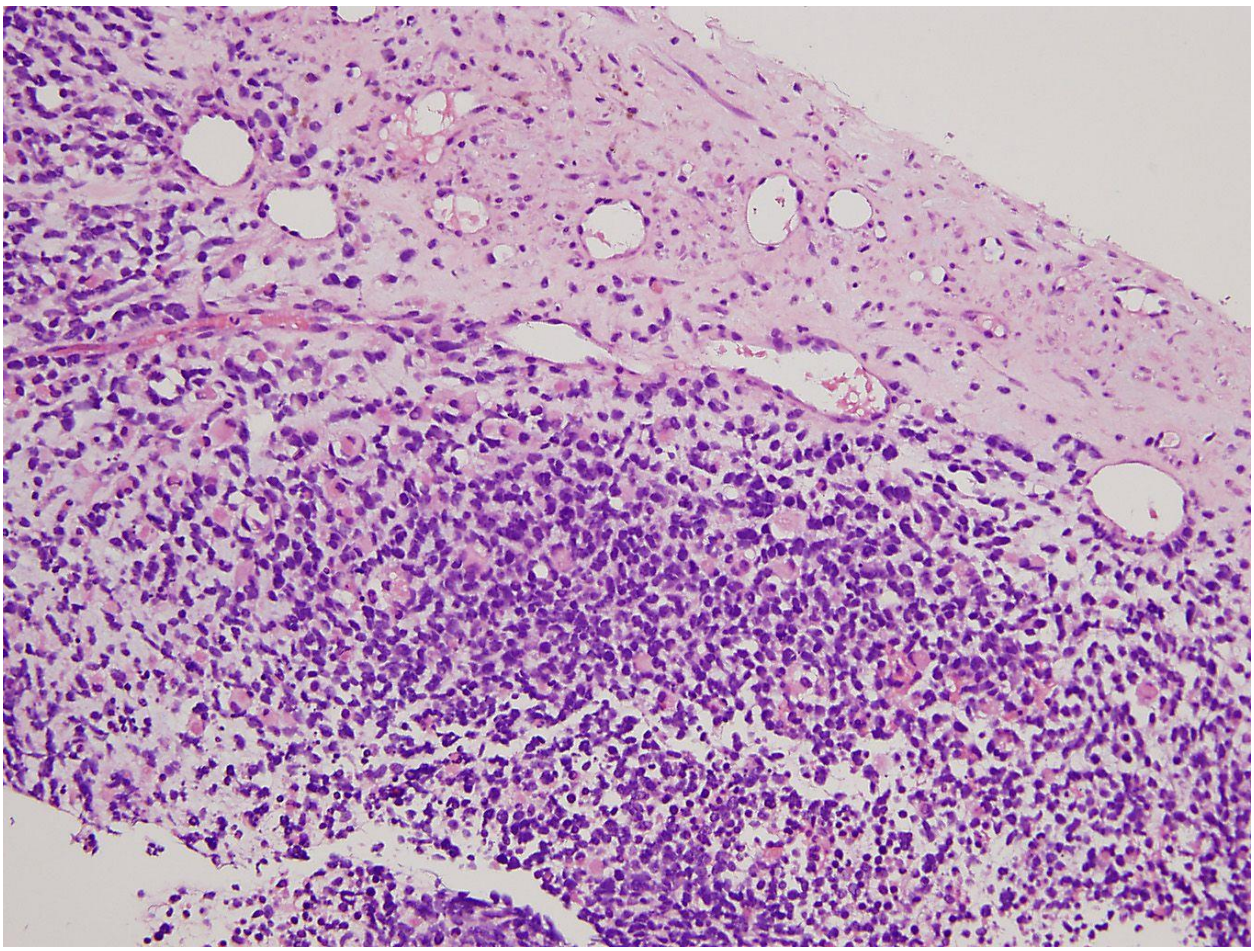

Figure 1. H&E stain

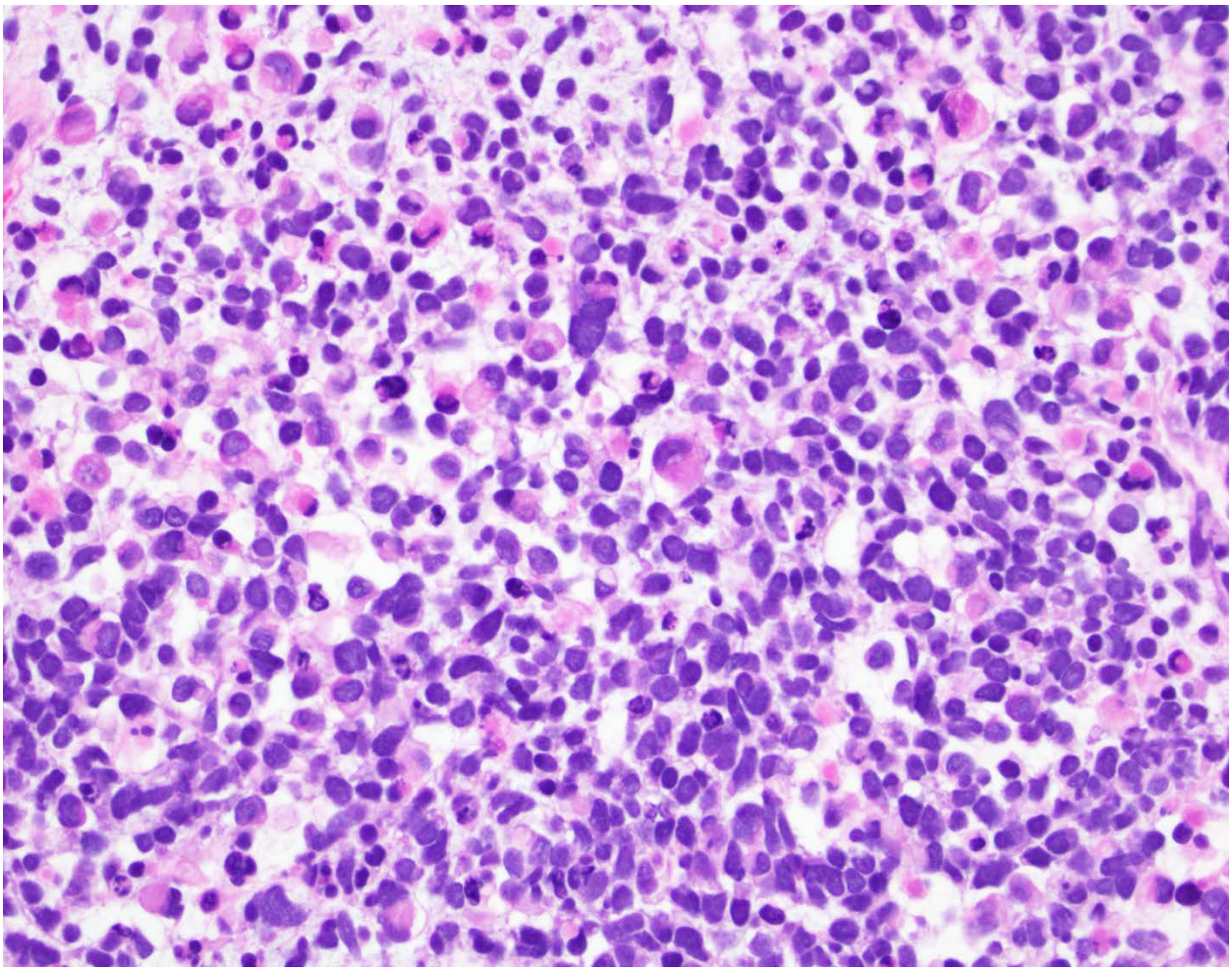

Figure 2. H&E stain

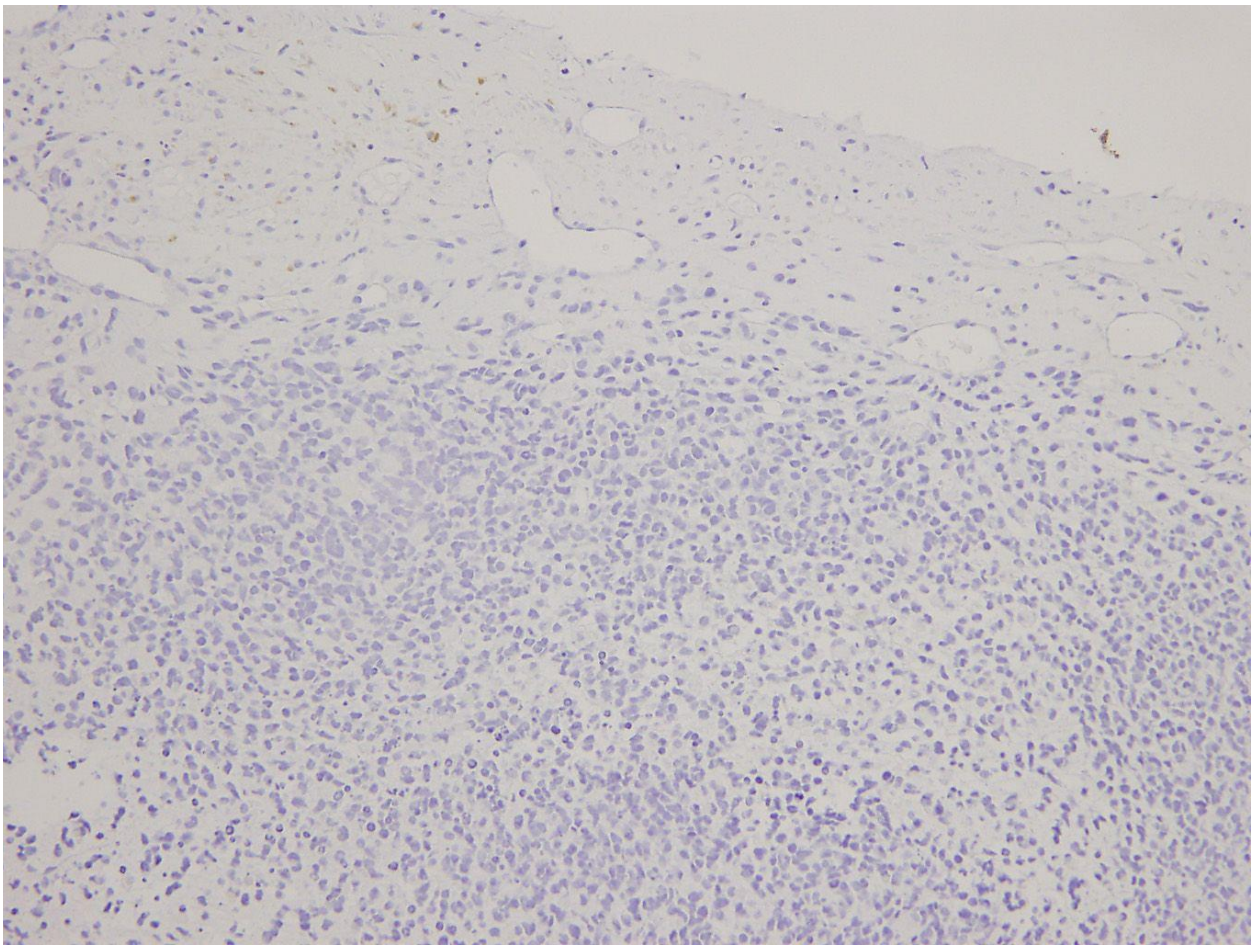

Figure 3. C-KIT immunohistochemistry

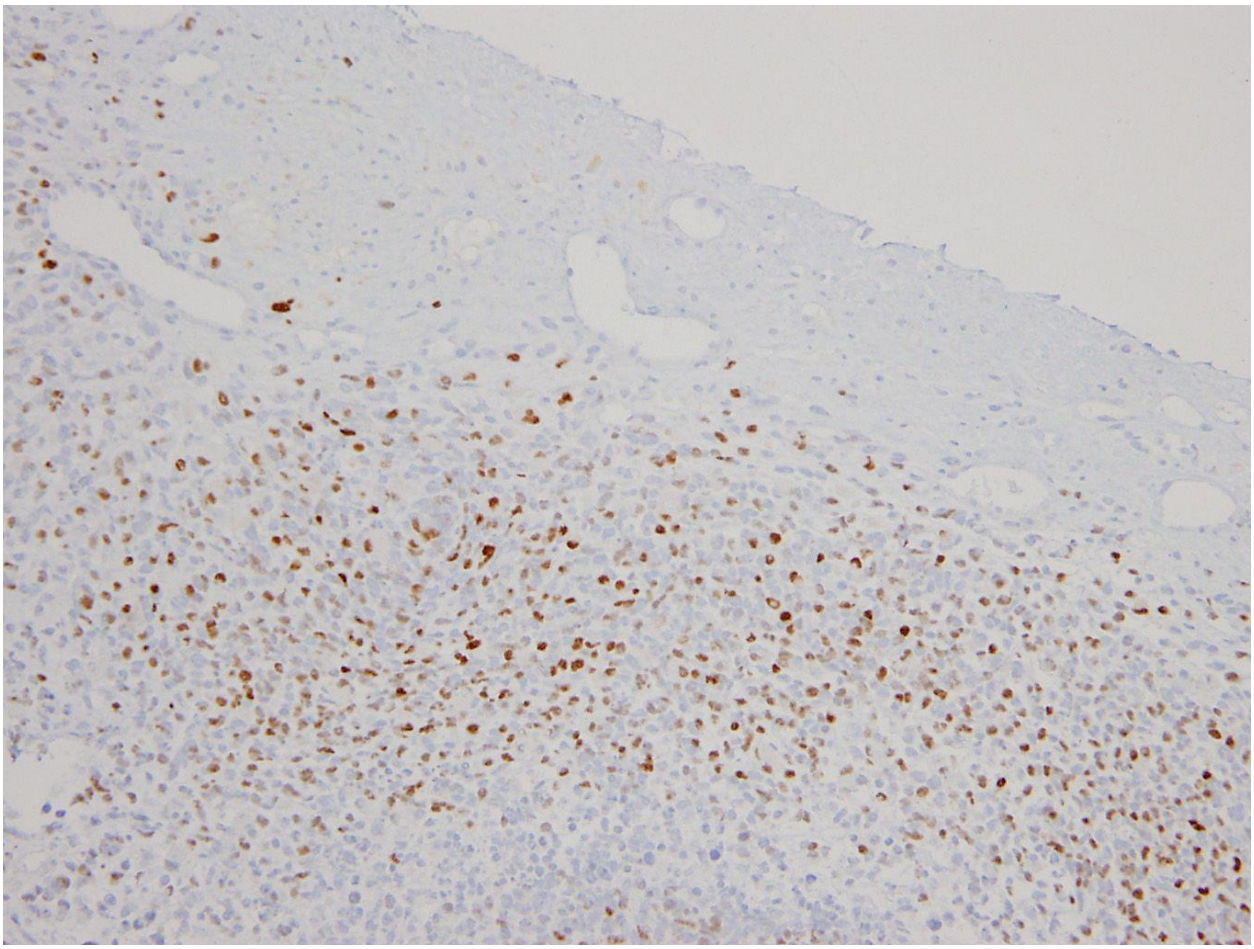

Figure 4. Myf4 immunohistochemistry

What is the most likely diagnosis?

a. Dedifferentiated gastrointestinal stromal tumor with heterologous rhabdomyoblastic differentiation

b. Malignant Triton tumor (malignant peripheral nerve sheath tumor, high-grade, with heterologous rhabdomyoblastic differentiation)

c. Dedifferentiated liposarcoma with heterologous rhabdomyoblastic differentiation

d. Embryonal rhabdomyosarcoma

e. Poorly differentiated carcinoma with focal signet-ring-cell features

Correct diagnosis

a. Dedifferentiated gastrointestinal stromal tumor with heterologous rhabdomyoblastic differentiation.

Description of findings and differential diagnosis

Biopsy of the liver mass shows a primitive small round blue cell neoplasm with abundant necrosis and brisk mitoses. Cytologically, the majority of tumor cells are monomorphic with scant cytoplasm and nuclei with fine chromatin. Scattered cells have eccentric nuclei and abundant bright eosinophilic cytoplasm (Figures 1, 2)

Immunohistochemical stains performed on this biopsy demonstrated negative staining for KIT (Figure 3), DOG1 and pan-keratin. Myf-4 highlights rhabdomyoblasts (Figures 4). H3K27Me3 was retained, and immunohistochemical stains for MDM2 and CDK4 showed weak and multifocal staining.

Of soft tissue tumors most likely to occur in the peritoneal cavities, those most likely to show rhabdomyoblastic differentiation include malignant peripheral nerve sheath tumor and dedifferentiated liposarcoma. However, retained nuclear expression of H3K27Me3 makes a diagnosis of high-grade malignant peripheral nerve sheath tumor less likely given the relatively high sensitivity of H3K27Me3 loss in the sporadic setting. In addition, a diagnosis of dedifferentiated liposarcoma is also unlikely given the nonspecific staining for MDM2 and CDK4. Although the tumor morphologically resembles embryonal rhabdomyosarcoma, this diagnosis would be extremely unusual in a middle-aged woman. Despite the higher prevalence of carcinomas over soft tissue neoplasms, the morphologic and immunophenotypic features are not compatible with a poorly differentiated carcinoma, and signet-ring-cells would not be positive for Myf-4 (a marker of skeletal muscle differentiation).

Dedifferentiated GIST with rhabdomyoblastic differentiation is rare, but is an important diagnostic consideration, particularly in patients with a prior history of GIST who have been treated with long term tyrosine kinase inhibitor therapy. Dedifferentiated GIST can happen without treatment (tumors previously called malignant fibrous histiocytoma of stomach in literature are most likely examples of dedifferentiated GIST), but they are incredibly rare. Most cases of dedifferentiated GIST are post-treatment.

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