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Inflammatory Pseudotumor Resembling a Malignant Pancreatic Disease Process

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Abstract. *Background/Aim: Inflammatory pseudotumors are complex entities given that they carry varying characteristics with a multitude of behaviors that can resemble a malignancy clinically, radiographically, and histologically. Patients and Methods: Our case report presents a 65-year-old-female with a history of fever, abdominal pain, and anemia with imaging suggestive of a malignant disease process involving an ill-defined soft tissue mass between the left adrenal gland and pancreatic tail. Results: Following diagnostic laparoscopy with abdominal washings and subsequent open resection of the mass, final pathology revealed multiple specimens demonstrating dense fibrosis with admixed spindled cells and inflammatory cells, an overarching morphology, and an immunohistochemical staining profile consistent with pancreatic inflammatory pseudotumor. Conclusion: Inflammatory pseudotumor is a challenging diagnosis and should be included in the differential diagnosis for a patient who presents with nonspecific symptoms and an ill-defined mass on imaging.*

Inflammatory pseudotumors are complex entities given that they carry varying characteristics with a multitude of behaviors that can resemble a malignancy clinically, radiographically, and histologically (1). These tumors comprise myofibroblastic spindle cells, infiltrates of inflammatory cells, as well as varying levels of necrosis and fibrosis (2). It is unclear what the etiology of inflammatory pseudotumors is, although it seems that they can be related to both acute and chronic inflammation, autoimmune processes, trauma, surgery, infection, another related malignancy, and IgG4-related disease processes (1, 2). The course of an inflammatory pseudotumor is variable and can range from benign and indolent, to spontaneously resolving, to locally recurring, to even aggressive and rapidly fatal in some cases (1). The treatment is usually surgical resection, if feasible. Inflammatory pseudotumor is a challenging diagnosis and thus, is quite important to keep in mind while making a differential diagnosis for a patient who presents with nonspecific symptoms and a mass on imaging. Within this case report, we present a case of an inflammatory pseudotumor in a 65-year-old female who presented with non-specific symptoms of fever, abdominal pain, and anemia with imaging indicating an ill-defined soft tissue mass involving the tail of the pancreas.

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Case Report

Our patient was a 65-year-old woman with no pertinent past medical history who presented to us with an ill-defined soft tissue mass between the left adrenal gland and pancreatic tail, with associated splenic artery occlusion (Figure 1). Her abdominal exam was normal. She underwent a full adrenal panel, to rule out a functional adrenal tumor, which was negative. Due to its location, the mass was not amenable to percutaneous biopsy or esophagogastroduodenoscopy/endoscopic ultrasound (EGD/EUS). Therefore, the patient underwent a diagnostic laparoscopy with abdominal washings, which showed a 2-3 cm mass intimately involved with the posterior body of the pancreas, portion of the adrenal gland, and stomach. We obtained washings of the mass for cytology, which was negative for malignancy.

Following diagnostic laparoscopy, there was interval enlargement of the left adrenal gland, as well as progressive left retroperitoneal adenopathy on follow-up imaging (Figure 2). Therefore, the patient underwent an open distal pancreatectomy, left adrenalectomy, and splenectomy to rule out malignancy. Intraoperatively, the mass measured approximately 4 cm × 3 cm × 3 cm. The peri-splenic and perigastric lymph nodes were dissected and sent for frozen section, which returned as reactive lymph nodes. Thus, a portion of the mass on the surface of pancreas was then removed and sent for frozen section, which returned as normal

pancreas tissue. With a lack of diagnosis from the frozen sections, a full resection was set forth, as planned. During dissection of the mass from the stomach, additional peri-gastric lymph nodes were removed and sent for frozen section, which returned as concerning for lymphoma versus neuroendocrine tumor, not pancreatic adenocarcinoma or adrenal cortical carcinoma. Following the operation, the patient recovered appropriately and was discharged on hospital day 5.

Final pathology report revealed multiple specimens demonstrating dense fibrosis with admixed spindled cells and inflammatory cells, with overarching morphology and immunohistochemical staining profile consistent with pancreatic inflammatory pseudotumor. Perigastric lymph nodes were negative for malignancy. There was no evidence of carcinoma or lymphoma. Leukemia/lymphoma immunophenotyping by flow cytometry of the pancreas specimen and perigastric lymph nodes did not detect monotypic B-cell population, phenotypically abnormal T-cell population, or blast cell population.

At the post-operative visit, her pre-operative symptoms (fevers, abdominal pain, and night sweats) resolved. Surveillance imaging with CT scan at six months will be obtained to ensure that the pseudotumor is not recurring.

Discussion

Inflammatory pseudotumors comprise a challenging diagnosis, and thus it is vital to keep this diagnosis in mind when a patient presents with a soft tissue tumor. However, inflammatory pseudotumors can be difficult to distinguish from other soft tissue lesions, and thus, the differential diagnosis can be rather extensive.

It is unclear what causes inflammatory pseudotumors, although it seems that they can be related to both acute and chronic inflammation, autoimmune processes, trauma, surgery, infection, another related malignancy, and IgG4-related disease processes (1, 2). Often, immunohistochemical staining involving T cells and B cells can aid in differentiating between the diagnosis of inflammatory pseudotumor and lymphoma. In an inflammatory pseudotumor, both T cells and B cells are present, compared to lymphoma, where either T cells or B cells will dominate the population of cells (1, 2). A multitude of organisms have been associated with inflammatory pseudotumors, such as Epstein-Barr virus, actinomycetes, mycoplasma, nocardiae, as well as many others (1, 2, 3). Some of the characteristics of inflammatory pseudotumors, such as fever, anemia, thrombocytosis, weight loss, among others, are associated with interleukins and cytokines, which produce the systemic effects seen throughout the body (1, 2).

Many studies have demonstrated that inflammatory pseudotumors with certain histology can predict how aggressively the tumor will behave. Anaplastic lymphoma kinase (ALK) is a receptor tyrosine kinase that has been found to be over-expressed in half of inflammatory pseudotumors, leading to a neoplastic process (2). A study by Coffin *et al*. showed that tumors lacking ALK positivity were associated with an older age and distant metastasis (not local recurrence); patients may die from the disease, thus advocating that ALK expression in these tumors may be a marker of a more favorable prognosis (2, 4). A study by Mariño-Enriquez *et al*. reported that a specific ALK staining pattern in the nuclear membrane of inflammatory myofibroblastic tumors was correlated to rapid local recurrence and decreased mortality, suggesting a more aggressive behavior and less favorable prognosis in this subset of patients (2, 5). Thus, testing for the presence of ALK may be beneficial in patients with inflammatory pseudotumors.

An inflammatory pseudotumor can present in practically any location in the body, although the most common sites involve the orbit or the lungs (1, 2). Inflammatory pseudotumors can involve the gastrointestinal tract, albeit rare, with gastric and ileocecal lesions being most commonly located in the gastrointestinal tract (2, 6). Radiographic imaging is a vital diagnostic component for these patients. These tumors can be difficult to be distinguished on radiographic imaging due to the variability and non-specific appearance. Inflammatory pseudotumors can be either hyperechoic or hypoechoic, have variable borders on ultrasound, show high to low attenuation in comparison to the surrounding structures on CT scan, demonstrate heterogeneous or homogeneous features, and variable signal intensity with T1-weighted and T2-weighted images on MR imaging (1, 2, 7-10). Inflammatory pseudotumors of the pancreas, liver, and stomach can reveal calcification on imaging as well. With identification of these imaging characteristics, it is critical for differential diagnosis (1).

As discussed previously, the treatment is usually surgical resection, if feasible. However, other treatment modalities include radiation, steroids, nonsteroidal anti-inflammatory drugs, and even in some cases, chemotherapy (1, 2, 6, 11). Recently, studies revealed that pediatric patients with inflammatory myofibroblastic tumors can have improved outcomes with treatment involving either neoadjuvant or adjuvant ALK inhibitors. Inflammatory myofibroblastic tumors, a subset of inflammatory pseudotumors, have the capacity of carrying *ALK* translocations that hold the ability to respond to these tyrosine kinase inhibitors. This therapy can be utilized as definitive therapy in certain cases, or as supplementation to surgical resection in others (12). A study by Brivio *et al*. in 2019, involving two separate cases of inflammatory myofibroblastic tumors, demonstrated utilization of and treatment response to Ceritinib, a second-generation tyrosine kinase inhibitor, for the treatment of inflammatory myofibroblastic tumors. One of the two patients underwent sole treatment with the ALK inhibitor, while the second patient underwent Ceritinib treatment leading to a 70%

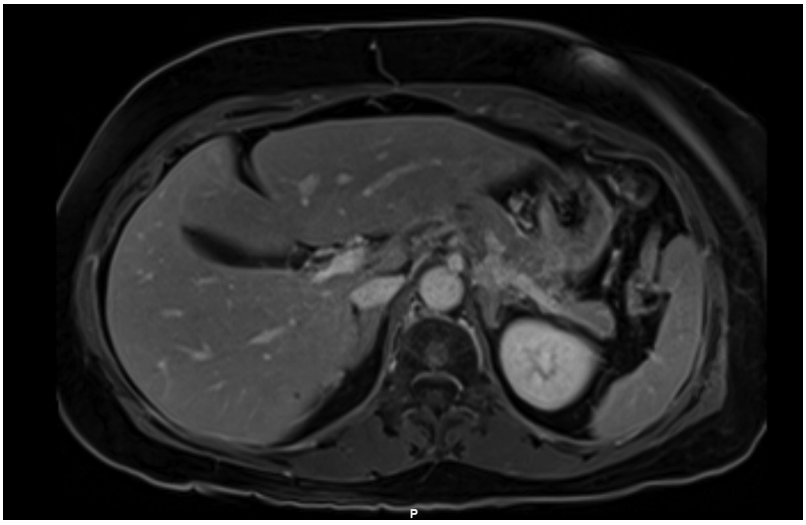

Figure 1. *Pre-operative MRI of the abdomen with and without IV contrast. Ill-defined, infiltrative soft tissue in the tail of the pancreas and left adrenal gland, measuring 1.5×1.5 cm (yellow arrow).*

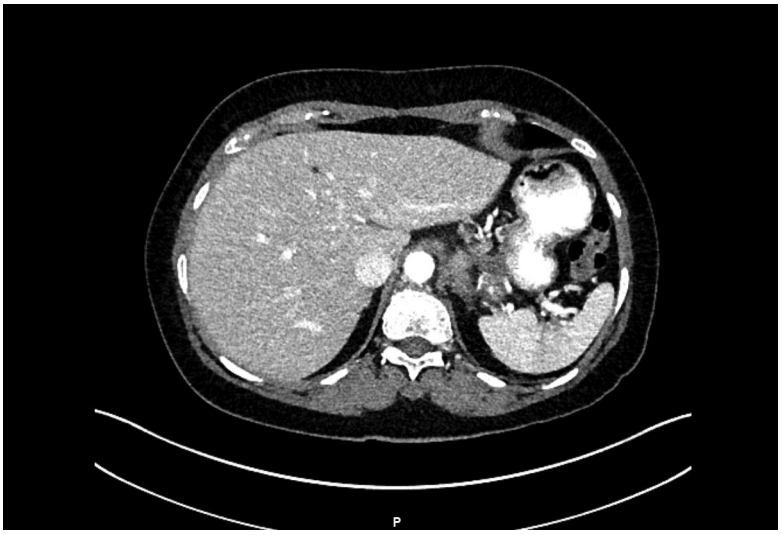

Figure 2. *Computed tomography scan of the abdomen and pelvis with IV contrast, following diagnostic laparoscopy with abdominal washings, prior to definitive operation. Progression of infiltrative, ill-defined soft tissue located in the retroperitoneum, measuring 3.4×1.7 cm, and worsening left retroperitoneal adenopathy (yellow arrow).*

reduction in the size of the tumor, and subsequent complete surgical resection (13). Again, this highlights the usefulness of testing for ALK in patients with inflammatory pseudotumors and may help direct treatment regimens. The estimated rate of recurrence for inflammatory pseudotumors is between 18-40% (2, 6). Upon recurrence, surgical resection may continue to be the treatment modality of choice given that transformation to a malignancy has been reported (6, 14).

Inflammatory pseudotumor is a challenging diagnosis and thus, is quite important to keep it in mind while making a differential diagnosis for a patient who presents with nonspecific symptoms and a mass on imaging. Clinically and radiographically, these tumors can mimic malignant disease processes (1). Therefore, surgeons should be knowledgeable on the necessary workup and treatment modalities for this patient population.

Conflicts of Interest

The Authors have no conflicts of interest to declare regarding this study.

Authors' Contributions

JK wrote the case report and contributed to the literature review, CM contributed to the literature review, MS contributed to the literature review, and EG provided the patient information, images and reviewed the final manuscript.

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