Unicentric Castleman disease disguised as a pancreatic neoplasm

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Castleman disease or angiofollicular lymph node hyperplasia is an uncommon cause of an incidental abdominal mass found on imaging. The etiology of Castleman disease is relatively unknown, however, it is thought to be primarily associated with an oversecretion of interleukin-6. The oversecretion of this pro-inflammatory cytokine leads to lymph node hyperplasia. Castleman disease can be classified into 2 categories: unicentric or multicentric. Most cases of unicentric Castleman disease are asymptomatic and are found on routine imaging. It is found predominately in middle-aged persons of equal sex and is managed primarily by surgical resection. We present here a case of a peri-pancreatic mass diagnosed by surgical excision as Castleman disease, hyaline vascular type.

Case presentation and summary

A 40-year-old woman transferred to our hospital from a rural community hospital with a diagnosis of possible acute cholecystitis. A computed-tomography (CT) scan of her abdomen and pelvis showed she had a large mass measuring 6.0 x 4.0 cm abutting the gallbladder, pancreas, liver, and duodenum. The diagnosis of acute cholecystitis was ruled out with a negative ultrasound finding, however, with sono-graphic imaging this mass was able to be visualized. The patient was referred for a gastroenterology consultation and she underwent magnetic resonance imaging (MRI) of the abdomen to better visualize the mass and characterize its features. The MRI revealed a large hypervascular mass of roughly 6.0 cm abutting the aforementioned structures seen with the CT scan. A CT angiography of the abdomen and pelvis was ordered because of the hypervascular nature of the mass, and the mass was wedged off the pancreas and sent to the pathology lab (Figure 2). A frozen section of the mass intraoperatively revealed possible lymphoma. After the final pathology was reported, the woman was diagnosed with Castleman disease, hyaline vascular type. The patient’s HIV and human herpesvirus-8 (HHV-8) serology was negative. The patient was referred to the hematology department at our institution. Their recommendations included no further treatment and recommended follow up imaging in 6 months.

Discussion

Castleman disease is a rare but unique pathology associated with malproduction of interleukin-6 (IL-6). It was first reported in 1956 by Dr Benjamin Castleman and has gained attention from medical and surgical specialties as an important differential diagnosis to consider in the work-up of enlarged lymph nodes and incidental masses. The disease’s underlying physiology has not been completely elucidated, but the majority consensus is that there is an underlying mechanism of hypersecretion of...
IL-6 that induces changes in the lymph nodes and leads to hyperplasia, growth, and neovascularization.²

The histologic variants of Castleman disease can be divided into 3 classes: hyaline vascular type; HHV-8-positive or -negative type plasma cell type; and mixed cell variant.³ The hyaline vascular type is the most common variant of the disease. The histopathologic findings associated with hyaline vascular type are concentric whorls around the lymph nodes with fibrosis that leads to typical “onion skinning” formation of the lymph nodes (Figure 3). Because of the highly vascular nature of the disease, neovascularization is seen on the periphery of histological specimens and can demonstrate “lollipop” lesions (Figure 4) where blood vessels penetrate the stereotypical onion skinning lesions as a result of the increased levels of vascular endothelial growth factor (VEGF) secondary from increased IL-6 production.

Castleman disease can be classified as either unicentric and multicentric. Unicentric Castleman disease (UCD) is found usually as an incidental mass either on physical exam or imaging study. It occurs equally in men and women without a gender predominance, and the mean age of presentation is 35-45 years. UCD is most often asymptomatic until discovered incidentally. Clinical presentations of UCD usually involve abdominal pain or can lead to compression of structures that causes symptomatic disease such as in the airway. The most common site of UCD is the thoracic cavity followed by axilla, pelvis, and retorperitoneum. Mesenteric and abdominal cases of UCD are less common sites of disease. Imaging modalities such as ultrasound, CT, and MRI will be able to find lesions. Typically, there is a calcified appearance of the mass on imaging and can display evidence of hypervascularity because of the increased VEGF levels from IL-6 production.²

The treatment for UCD is primarily surgical resection. Either open or laparoscopic excision has been described. Czeka and colleagues have reported a case of pancreatic Castleman disease treated with a laparoscopic distal pancreatectomy in which the lesion was present in the tail of the pancreas.⁴ For our case, the possibility of malignancy with no tissue diagnosis necessitated an open approach. There is usually no medical treatment that is needed for UCD unless the size of the mass is compressing vital structures such as the airway and for which neoadjuvant monoclonal antibodies are given to shrink the tumor preoperatively. Resection is usually curative of UCD, and patients are followed with serially imaging studies. There has been scant data to suggest a risk of non-Hodgkin lymphoma (NHL) in UCD patients postoperatively, however, the
development of NHL after resection of UCD was present in small cohort patients from 1 case series.\textsuperscript{4,5} Multicentric Castleman disease (MCD) presents more systemic symptoms including fever, chills, and weight loss. HHV-8 is associated with the production of IL-6 that subsequently leads to MCD. Virally encoded proteins stimulate latency-associated nuclear antigen and viral FLICE-inhibitory proteins, or FLIPs, which in turn activate IL-6 production through nuclear factor kappa beta and activator protein-1.\textsuperscript{6,7} Increased VEGF levels have also been found in patients with MCD.\textsuperscript{2}

MCD has a more complicated clinical course than UCD. Surgical excision is the definitive treatment for UCD, but MCD usually is treated with monoclonal antibody therapy and chemotherapy. Situlixmab, an anti-IL-6 antibody, and tocilizumab, an IL-6R monoclonal antibody, make up the current IL-6 treatment therapy for patients with MCD. Untreated MCD carries a high mortality if left untreated. In regard to differential diagnoses, MCD is found in 2 unique clinical entities: POEMS syndrome and paraneoplastic pemphigus.\textsuperscript{9,10} A recent case report on a patient with MCD who developed limbic encephalitis raised the question of autoimmunity and its role in MCD.\textsuperscript{11}

UCD of the abdomen, especially in the pancreas, has been a rare finding. Fu and colleagues comprised a global review of literature from 2013 that demonstrated 19 cases worldwide of UCD of the pancreas. Most of the patients underwent complete surgical excision at that time. Presentation was either with symptomatic abdominal pain or asymptomatic found on routine imaging. Most of the patients were treated with surgical resection and with no recurrent disease.\textsuperscript{3} Since 2014, there have been 3 additional cases of Castleman disease of the pancreas: Shety and colleagues have described 2 cases similar to our patient, in which UCD was a peripancreatic mass, and Matsumoto and colleagues have described a case of UCD arising from the main pancreatic duct.\textsuperscript{12,13}

In conclusion, pancreatic Castleman disease remains a rare clinical phenomenon. Differential diagnosis of Castleman disease should be included for work-up of either symptomatic or incidental mass found on imaging unexplained by other causes.

References