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Case Report

Castleman disease of the renal hilum: A rare case report ☆

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ABSTRACT

Castleman's disease is a rare benign lymphangioproliferative disorder. The hyaline vascular subtype has a better outcome and is curable after surgical resection. Typically, Castleman disease manifests in the thorax, with rare reports of a renal hilum location. We present a 42-year-old male patient who had an incidentally detected right hilar hyaline vascular type of Castleman's disease, which we managed with surgical excision. Cross-sectional imaging modalities help in suggesting the diagnosis based on enhancement patterns and, more importantly, define the extent of the tumor pre-operatively. Although the renal hilum is a rare location for Castleman disease, it needs to be considered when imaging features suggest it.

Introduction

Castleman disease (CD), also called angiofollicular lymph node hyperplasia, is a rare type of benign proliferative lymphoid tissue disease first described by Dr. Benjamin Castleman in 1956 [1,2]. The disease has 4 major histologic types, with the commonest being the hyaline vascular (HV) type [2]. IL-6, a pro-inflammatory cytokine, plays a major role in the pathogenesis, although the etiology remains not definitively established. The human herpes virus-8 (HHV-8)-associated type is firmly associated with multicentric CD in immunocompromised patients [1,3]. The disease can occur either in a single lymph node station or can be systemic, affecting multi-

Abbreviations: CD, Castleman disease; HV, hyaline vascular; PC, plasma cell; HHV-8, human herpes virus-8; IL-6, Interleukin-6; MRI, magnetic resonance imaging; CT, computed tomography.

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ple lymph node locations. The former is called localized or unicentric CD and is largely asymptomatic with an excellent prognosis after complete surgical resection. On the other hand, multicentric type disease carries a poor prognosis with no effective treatment options to date. CD typically occurs in the thorax and chest [4]. Abdominopelvic disease, particularly in pararenal areas, is extremely rare [5–7]. Preoperative diagnosis of retroperitoneal CD is difficult as both imaging and clinical features are non-pathognomonic.

Case presentation

A 42-year-old, a known type 2 diabetic on an oral hypoglycemic agent, presented to our university hospital following detection of an asymptomatic right renal hilar mass on an ultrasound (done in an outside setup) during a routine medical checkup. He did not complain about headaches, palpitations, fever, or weight loss. On physical examination, he had stable vital signs, with no swelling or tenderness on his right flank. The complete blood count and renal function tests were normal. The human immunodeficiency virus (HIV) test was negative. Subsequently, abdominal magnetic resonance imaging (MRI) showed a 4.3 × 3.8 cm right renal hilar region non-fatty and non-necrotic mass with intermediate signal intensity on T1 and T2 weighted sequences (Fig. 1). The tumor was intimately related to the right renal vein. Computed tomography (CT) showed an enhancement with perilesional fat stranding (Fig. 2). Subsequently, surgery was decided. The patient was informed about the possibility of a right nephrectomy due to the close proximity of the right renal vein to the mass. An approach through the right subcostal incision was made. The mass was found adherent to the right renal vein and encircled it by about 270 degrees. It was also very close to the inferior vena cava and right renal artery. It was gently dissected and completely resected. There was a small right renal vein tear, which was repaired with Prolene suture 5-0. The patient's recovery was uneventful, and he was discharged on the third post-operative day.

Pathologic examination revealed grey-white to grey-brown encapsulated tissue (5 × 4 × 4 cm) with a firm grey-white cut surface. Microscopic examination of multiple sections of tissue displayed expanded mantle zones with characteristic onion skin multilayering, transversed by sclerosed blood vessels, and fusion of follicles displaying more than one atretic germinal centers (Fig. 3). All these macroscopic and microscopic findings are consistent with the HV type of CD.

Discussion

CD, also known as angiofollicular lymph node hyperplasia, is a non-clonal lymphoproliferative disorder and one of the causes of benign lymphadenopathy [1–3]. Histopathologic classification is preferred and categorizes the disease into hyaline vascular (HV), plasma cell (PC), human herpes virus-8 (HHV-8)-associated, and multicentric Castleman disease, not otherwise specified. Morphologically, they are classified based on the extent of lymph node involvement into unicentric and multicentric diseases. Among localized CD, HV accounts for 76%–91% and PC type for 9%–24% [2]. The latter is much more common with the multicentric disease. Both the HV and PC variants have no sex preference. The median age of presentation is between the second and third decades for localized HV and PC forms and in the fifth decade for multicentric disease [3].

The etiology of CD is not settled. HV-CD is a lymphoid proliferation where follicles are depleted of germinal cells and have expanded mantle zones with lymphocytes arranged concentrically in an onion-skin manner. The interfollicular zone is expanded by prominent hyalinized blood vessels and myloid and lymphoid cells. Frequently, follicular dendritic cell dysplasia is observed with additional features to support its association with HV-CD, such as strong expression of the epidermal growth factor receptor and the development of follicular cell dysplasia sarcomas in some HV-CD patients. Rich vasculature is a recognized characteristic, and in some cases, it is due to vascular endothelial growth factor expression. In contrast to HV-CD, PC-CD has preserved and hyperplastic follicles with increased interfollicular non-monoclonal plasma cells. Follicular cell dysplasia is not present. However, these features can also occur with reactive lymphadenopathies secondary to infections, autoimmune and collagen vascular diseases, and immunodeficiency-related lymphadenopathies, so it is necessary to rule out these disorders before confidently diagnosing PC-CD. The HHV-8-associated CD is multicentric and has a poor prognosis and usually occurs in immunocompromised patients, mostly HIV-infected, and can progress to large B-cell lymphoma. It is also associated with Kaposi sarcoma [1–3].

Unlike PC-CD, which takes on an aggressive course and is associated with a wide variety of extra-lymphoid diseases, HV-CD is considered benign, with 100% 5-year survival after complete resection, and is only rarely complicated by additional neoplasms such as lymphoma and vascular tumors [8].

Interleukin-6 (IL-6) assumes a central role in the pathogenesis of CD. Its serum level is high in CD patients and falls after IL-6 therapy or surgical resection of nodal disease. It also induces systemic inflammation by raising acute-phase proteins, which give rise to constitutional symptoms in CD patients. It is also a vascular endothelial growth factor inducer that causes vascular lymph nodes commonly observed in CD. While the trigger for IL-6 in HIV-negative CD remains unknown, the IL-6 homolog encoded by HHV-8 is responsible in HHV-8-associated CD [1,3].

CD occurs in the thoracic cavity (70%), neck (15%), and abdominopelvic cavity (15%) [4]. Within the abdominal cavity, CD predominates in the retroperitoneum [9,10]. Bucher et al. [5] supported this by reviewing 195 cases of CD arising from the abdomen and retroperitoneum. They discovered that the majority rose from the retroperitoneum, accounting for 122 (63%), and the rest, 73 (37%), came from the abdomen. Perirenal disease is rare, with only 24 cases. Other isolated reports have also described peri-renal CD [11–13].

Clinical manifestation, treatment options, and prognosis all depend on the centricity and histological type of CD [1,8,14]. As mentioned above, localized CD is mainly due to HV type and less commonly due to PC. It predominantly affects a sin-

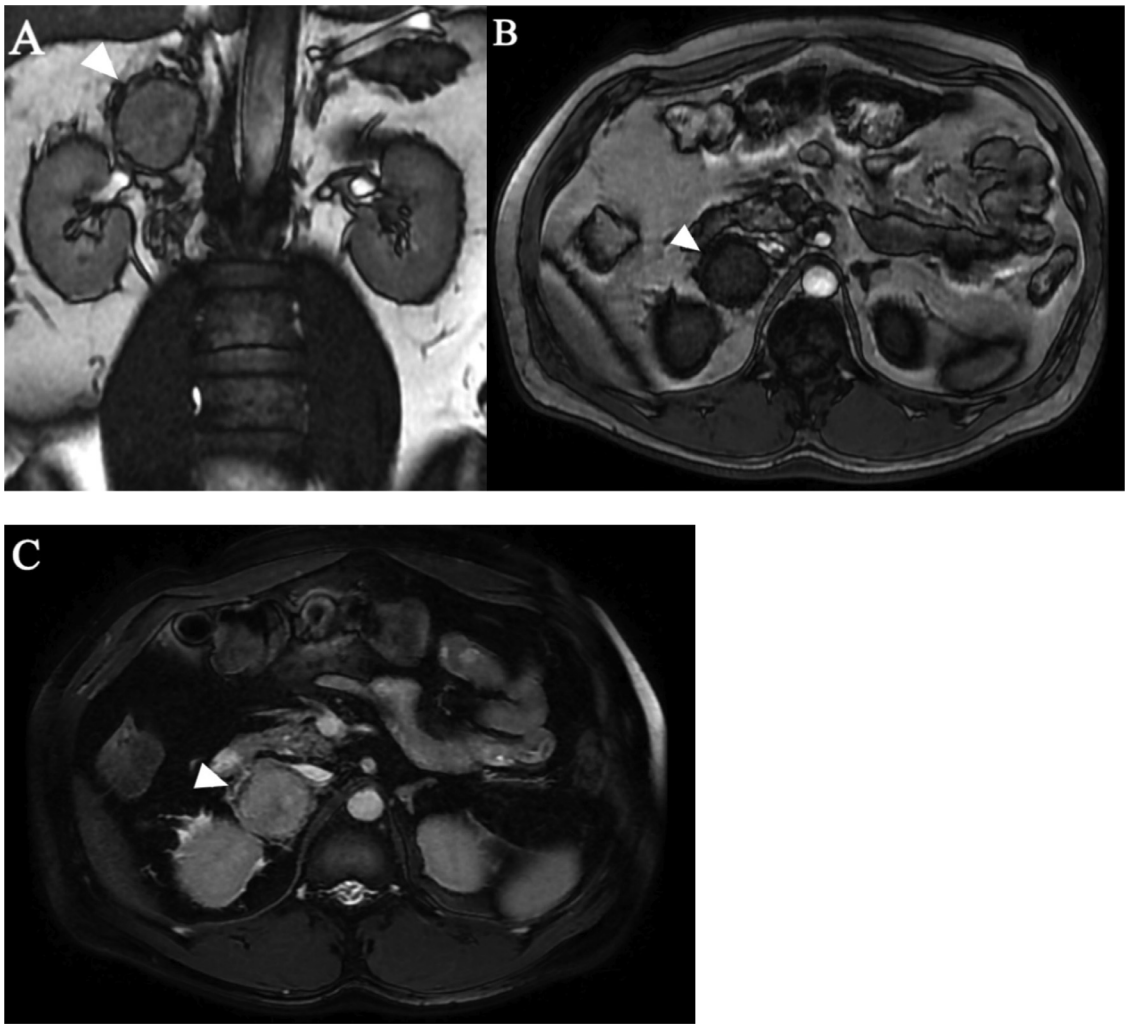

Fig. 1 – Multisequential abdominal MRI in Coronal T2W (A), axial out-of-phase T1W (B), and axial fat suppressed T2W (C) planes: The mass is isointense on both T1 out-of-phase and T2W images. It does not show fat suppression (white arrowhead in A-C).

gle lymph node station. The symptoms are secondary to the local mass effect. It can also be an incidental discovery in imaging studies. Conversely, PC-CD patients with either localized or multisystemic disease will be sicker, presenting with fever, excess sweating, weight loss, anorexia, multiple lymphadenopathies, hepatosplenomegaly, effusions, and a raised erythrocyte sedimentation rate. These features mimic other illnesses like infection and malignancy [4,7,10,15].

Radiologically, abdominopelvic CD has no pathognomonic features; thus, imaging mainly plays an adjunct role by visualizing affected lymphoid regions and, more notably, defining their relation to adjacent organs, in particular, vascular structures, which are paramount for surgical planning [16]. On ultrasound, localized CDs are usually well delineated and hypoechoic. CT and MRI are better for radiologic description, but they lack specificity. On CT, localized CD appears as well-defined, rounded, homogeneous lesions with strong to moderate enhancement. Larger than 5cm lesions can have central, non/weakly enhancing regions that correspond to fibrosis histologically [7]. Another distinguishing feature is the rarity of cystic or necrotic changes, given CD's high vascularity and lymphatic follicle resistance to necrosis [10]. One-third of cases exhibit intralesional calcification, with a central radiating or star-like pattern suggesting a more characteristic feature of CD. Ultrasound will show these as central shadowing foci [5,9,10]. MRI has better soft tissue resolution and shows hypointense mass on the T1W study, hyperintense lesions on the T2W image, and centripetal enhancement after gadolinium injection [4,17,18]. On angiography, CD has early centripetal enhancement, which persists into the delayed stage. Angiography (and multidetector CT) also reveal hypertrophied perilesional vessels, which can serve as additional clues to CD. Hypertrophied vessels are also important to search for, as pre-surgical embolization can be used to decrease intraoperative bleeding risk [16,17].

Zheng et al. [16] reported three left peri-renal CDs and proposed 3 new CT imaging features after observing their cases and reviewing the literature. The first one is rim enhancement seen in the arterial and portal phases of post-contrast CT. This appearance had been previously reported in an extremely rare

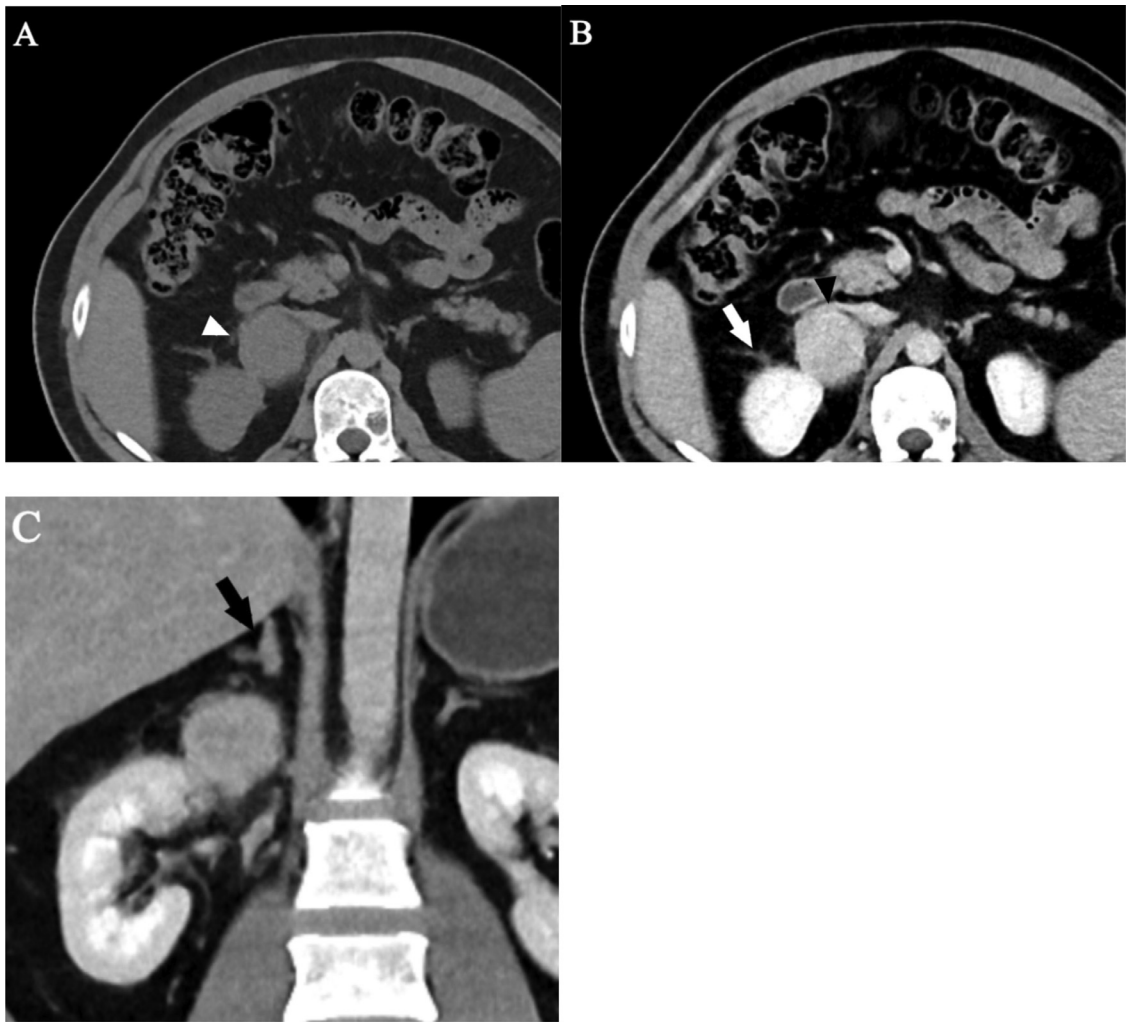

Fig. 2 – Axial pre-contrast (A) and portal venous phase (B) as well as coronal delayed phase (C) abdominal CT: There is a non-calcified round mass in the right hilar region (white arrowhead in A). It shows homogeneous enhancement with surrounding and right perihilar fat stranding (white arrow in B). On the delayed phase, the mass maintains its enhancement. It is clearly separate from the right adrenal gland (black arrow in C).

location of CD in the pancreatic body and tail (pancreas) during the delayed phase. The second finding is interesting as the authors, after a literature review, noticed an overwhelming majority of peri-renal CDs occurring on the left side, similar to all their cases, with a striking ratio of 13:4. They hypothesized increased lymphatic glands and vessels in the left retroperitoneum to account for this difference. The third finding is the presence of perilesional peritoneal thickening, which is surgically correlated with reactive hyperplasia. In our case, there is definite fat stranding surrounding the edge of the tumor and extending to the right perirenal region, consistent with perilesional reactive changes. The disturbed fat blurs the exact margins of the lesion in our case, but areas of increased peripheral enhancement are still seen in the portal venous phase.

In light of the relative rarity of CD in the abdomen and non-specific imaging features, presurgical suspicion of CD is uncommon. Radiologically, lymphoma is the prime consideration for homogeneously enhancing CD [10]. Additionally, lesions that are not primarily fat in consistency, such as ectopic pheochromocytoma or paraganglioma, neurogenic tumors, retroperitoneal metastases, and various forms of sarcomas, can also be confused with CD [4,7,10]. Moreover, retroperitoneal CD can extend to nearby structures and obliterate fat planes, and, when heterogeneously enhanced, can mimic a malignant lesion [15]. Surgical resection in such cases also carries a higher complication rate [18]. At such junctures, a decision needs to be made about the appropriateness of a pre-operative biopsy. Ordinarily, for retroperitoneal tumors, if imaging is non-specific or if neo-adjuvant therapy is a consideration, biopsy is indicated [19]. But the core needle is inadequate for CD, as a preserved surgical sample is required to confirm the diagnosis [3,4,18].

The preferred treatment for localized CD is complete surgical resection, which is associated with a high cure rate. A systemic review by Talat et al. [14] looked at 404 published CD cases that were surgically managed (surgery) and found that a significant amount of unicentric CD underwent resection surgery when compared to multicentric disease. Fur-

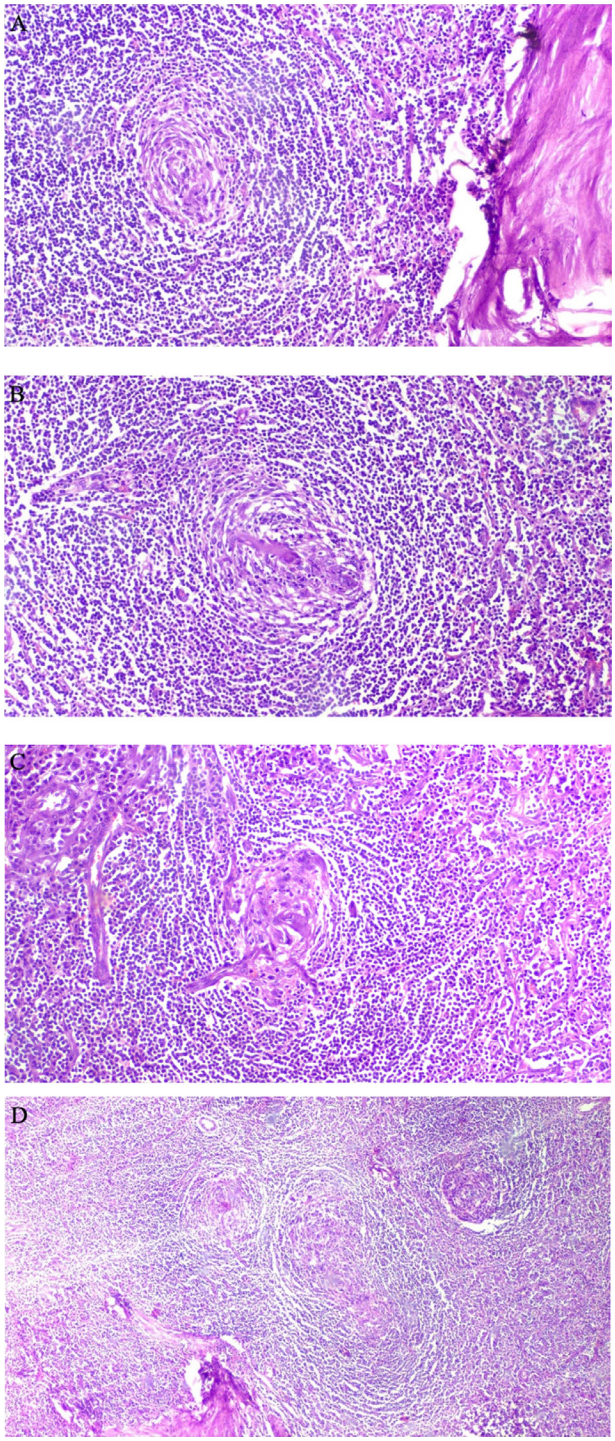

Fig. 3 – H & E stain of the resected mass in 10X (A-C) and 4X (D) magnifications: A and B show an atretic germinal center with a thickened mantle zone displaying onion skin layering. C depicts the atretic germinal center and thickened mantle zone traversed by the penetrating vessel (Lollipop sign). Fused mantle zones containing more than one germinal center are visible in D. The pathologic appearance is best represented by the HV type of CD.

ther analysis revealed that unicentric disease had a significantly better outcome than multicentric disease. Death due to unicentric CD in ten years was significantly more common when it was located in the retroperitoneum, mediastinum, abdomen, and pelvis. Overall, the review showed the prognosis is mainly based on the centricity of the disease rather than the histopathological type. Other studies also support the satisfactory outcome of localized CD [1–3,8].

No established follow-up schedule exists after resection of localized CD, but some advice prudence as associated tumors and rarely late recurrences, despite their low risk, can occur [1,2]. One proposal is an annual CT for the first three years, and another at 5 years postoperatively [18].

In conclusion, CD is rare, and localized renal hilar location is even rarer but needs to be considered when imaging features suggestive of the diagnosis are present.

Patient consent

Complete written informed consent was obtained from the patient for the publication of this study and accompanying images.

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