Unicentric Castleman’s Disease as a Localized Retroperitoneal Mass: A Case Report and Review of Literature

Abstract
Castleman’s disease (CD) is a rare disorder characterized by proliferation of the lymphoid tissue. Clinically, it presents in two forms either a unicentric (UC) or multicentric. Mediastinum is the most common location. UC retroperitoneal presentation is rare. We report a case of 29-year-old female who presented with left loin pain, and on abdominal imaging, evaluation identified a retroperitoneal mass in the left hypochondrium in the pararenal space. Mass was surgically excised entirely. Histopathological examination demonstrated hyaline vascular type of CD. CD should be considered in differential diagnosis of retroperitoneal mass, especially in equivocal cases. We also reviewed literature of 134 cases of retroperitoneal CD to analyze the presentation, management, and outcome.

Keywords: Castleman’s disease, hyaline type, retroperitoneum, unicentric

Introduction
Castleman’s disease (CD), angiofollicular lymph node hyperplasia, is an autoimmune disorder which involves hyperactivation of the immune system with multiple organ system dysfunctions. Two forms are unicentric (UC) and multicentric (MC), subclassified into a hyaline vascular (HV) type and a plasma cell (PC) type based on histology. UC disease affects mainly mediastinum and retroperitoneal location is rare; only 7% of all 400 cases reported so far. We report a case of female who presented with a pararenal mass and was diagnosed as unicentric hyaline form of CD after the complete excision. Due to the lack of specific markers or imaging features, CD is misdiagnosed. We analyzed 134 cases of retroperitoneal UC lesions reported in the literature to identify the clinical presentations, management, and outcome.

Case Report
A 29-year-old female presented with left-sided loin pain of 1-month duration. Pain was dull aching, intermittent, and nonradiating in nature. No other associated urological, gastrointestinal, or systemic symptoms were present. She was asthmatic and had a history of drug allergy. Her general examination and vitals were in normal limits.

Routine blood and urine parameters were normal. Chest X-ray did not reveal any mediastinal mass. Initial ultrasound imaging showed a retroperitoneal mass on the left hypochondrium suggestive of adrenal lesion. Further investigations including serum cortisol, serum aldosterone, and serum dehydroepiandrosterone and urine metanephrine were normal. Computed tomography (CT) imaging showed well-circumscribed homogenously enhancing lesion in the left hypochondrium in the pararenal space of size 3.5 cm × 2.7 cm × 4.2 cm abutting the loops of the jejunum [Figure 1]. No significant lymphadenopathy noted.

Since the mass was small and retroperitoneal in location, we decided to proceed for a left retroperitoneal flank approach and mass excised entirely. Intraoperatively, we identified a well-encapsulated soft-tissue mass of size 6 cm × 5 cm, firm in consistency, deriving blood supply from multiple sources associated with few enlarged lymph nodes largest measuring 1 cm in size. Mass was excised in toto and sent for pathological examination. Blood loss was minimal and no blood transfusion was required.

Cut surface was dark red with a central white zone of fibrosis and calcification.

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Microscopic examination showed lymphoid follicle of varying size with characteristic “onion skin” layering of lymphocytes in the mantle zone [Figure 2]. We also noticed regressed and hyalinized germinal center with a vessel entering it giving “lollipop” appearance. High vascular proliferation was demonstrated with reticulin staining.

Discussion

CD, angiofollicular lymph node hyperplasia, first described by Benjamin Castleman in the mid-1950s[2] is an autoimmune disorder which involves hyperactivation of the immune system with multiple organ system dysfunctions. The etiology remains unclear and it is benign in nature and presented in forms (UC) or generalized form (MCD disease [MCD]). CD is classified into a HV type and a PC type based on their histologic features.[1] UC disease affects mainly mediastinum, and retroperitoneal location is rare; only 7% of all 400 cases reported so far.[3] The average age of diagnosis of UC CD is around 30s and 40s, while MCD patients are in the age group of 50s and 60s.

The UC disease commonly affects mediastinum, peripheral lymph nodes, and abdomen. Abdominal lesions consist of 10%–17%, of which the majority of cases are retroperitoneal, whereas retroperitoneal lesion in MCD is rare.[1,5] UC disease is usually asymptomatic; however, when the mass enlarges and compresses adjacent organs, it results in mass effect symptoms. MCD is associated with systemic disturbances and constitutional symptoms, asthenia, fever, weight loss, generalized lymphadenopathy, and hepatosplenomegaly. Infection by human herpesvirus-8 and HIV is associated with CD, especially in MCD. This usually occurs in the younger patient group, and the prognosis is very poor.[6]

Histological variants include HV, PC, mixed variant, and a plasmablastic variant of multicentric CD.[1,7,8] The HV type is mostly unifocal and asymptomatic and diagnosed incidentally, and PC type presents in multifocal form associated with systemic diseases. Histologically, HV consists lymph follicles with hyalinization of its wall and concentric whirls of mantle lymphocytes giving an onion skin pattern.[6] PC contains polyclonal PCs with a less marked hyalinization and vascularization.[2]

Laboratory tests show rise in acute-phase reactants such as C-reactive protein and interleukin (IL)-6. On ultrasonography (USG), CD is seen as a homogeneously hypoechoic mass. In contrast-enhanced CT, CD manifests as homogeneous or heterogeneous mass of soft-tissue density with rim enhancement and slow washout. In magnetic resonance imaging, lesions are heterogeneous with increased signal on T2 and T1. In positron emission tomography scan, fluorodexoyglucose shows avidity to CD lesion and can be useful in follow-up to detect recurrence. In equivocal retroperitoneal hypervascular mass, CT or USG-guided core biopsy or open biopsy can confirm the diagnosis.

UC disease is treated by the radical surgical resection. Managing hypervascular retroperitoneal mass surgically is challenging due to its proximity with vital structures either by direct involvement by tumor or desmoplastic and inflammatory response with adjacent structures. In our case, the lesion was harboring multiple vessels from different sources and individual ligation was required for complete resection. Role of neoadjuvant radiotherapy has been described by de Vries et al.[9] for an unresectable abdominal UC lesion involving the iliac vessels to downsize the tumor, followed by complete resection. Neoadjuvant rituximab (CD20 monoclonal antibody) has successfully used in mediastinal UC disease involving pulmonary artery and superior vena cava.[9] For unresectable cases, partial resection or observation with long-term follow-up may be useful. If the resection is successful, prognosis is excellent with recurrence-free survival.[10]

In MCD disease, surgical role includes in obtaining tissue biopsy and to debulk the tumor to address...
specific problems such as bowel obstruction, vascular or airway compromise, and massive organomegaly.[10] Treatment options include antiviral, antiretroviral agents, chemotherapeutic agents (doxorubicin, vincristine, cyclophosphamide, melphalan, and chlorambucil), and monoclonal antibodies to IL-6 and suramin.[2] Successful role of immunomodulatory agents (cyclosporine-A and thalidomide) has been documented. In failure of chemotherapy, azathioprine and bone marrow suppression have been tried. An accepted follow-up regimen is not established. Patients with UC disease should receive radiological follow-up every 6–12 months for 3 years and again at 5 years postoperatively. Further evaluation is required if recurrence is suspected.

A literature review of retroperitoneal unicentric CD has been done. Systematic research was done for literature on retroperitoneal CD in Medline and Cochrane database, and totally 134 cases were included in the study. The mean age of patients was 40.2 years with equal sex predilection, male: female (1:1.03) [Table 1]. Common locations were retroperitoneal space (53%), pararenal (15%), and peripancreatic (9.7%) [Table 2]. Rare locations of lesions in ureteral, duodenal, and paravertebral were also reported. Average size of the lesion was 6.4 cm. Abdominal pain was the common presentation (42%), and incidental cases were identified in 26% [Table 2]. HV variety was observed in majority (88%) of cases [Table 1]. Other associations such as paraneoplastic pemphigus, myasthenia gravis, weight loss, and B symptoms were reported. Complete resection was possible in 115 cases of HV, and radiotherapy was required for one case for recurrence. In PC type, steroids were initiated in three cases as adjuvant therapy. Follow-up period includes from 4 to 34 months, and in 23 cases, follow-up status was not reported. We noticed that 77% of patients were alive without recurrence with available data [Table 3].

### Table 1: Overview of sex, age, and histological variants of localized retroperitoneal Castleman’s disease

| Parameters | Values |
|------------|--------|
| Total patients | 134 |
| Male:female | 66:68 |
| Mean age (years) | 40.2 |
| Average size (cm) | 6.4 |
| Histologic variants (%) | |
| HV | 118 (88) |
| PC | 12 (0.9) |
| Mixed | 1 (0.07) |
| NK | 3 |

HV: Hyaline vascular; PC: Plasma cell; NK: Not known

### Table 2: Different locations and presentations of retroperitoneal Castleman’s disease lesions

| Location of lesion | n (%) | Clinical presentation | n (%) |
|--------------------|-------|-----------------------|-------|
| Retroperitoneal space | 72 (53) | Abdominal pain | 57 (42) |
| Pararenal | 20 (15) | Incidental | 35 (26) |
| Peripancreatic | 13 (9.7) | NK | 14 (10) |
| Adrenal | 11 (8.2) | Backache | 7 (5.2) |
| Pelvic | 9 (6.7) | Abdominal mass | 6 (4.4) |
| Perivesical | 4 (2.9) | Gastric symptoms | 4 (2.9) |
| Ureteral | 4 (2.9) | Weight loss | 4 (2.9) |
| Paravertebral | 2 (1.4) | Hematuria | 4 (2.9) |
| Duodenal | 1 (0.7) | B symptoms | 3 (2.2) |

NK: Not known

### Table 3: Treatment modalities and outcome of localized retroperitoneal Castleman’s disease

| Histologic variants | Surgical resection | Adjuvant therapy | Biopsy | Outcome |
|---------------------|-------------------|-----------------|--------|---------|
|                     | CR | PR | Steroids | RT | Biopsy | NRE | RE | Dead | NK |
| HV | 115 | 1 | - | 1 | 1 | 89 | 1 | 5 | 23 |
| PC | 7 | 1 | 3 | - | 1 | 10 | - | 1 | 1 |
| Mixed | 1 | - | - | - | - | 1 | - | - | - |
| NK | 2 | 1 | - | - | - | - | - | - | - |

HV: Hyaline vascular; PC: Plasma cell; NK: Not known; CR: Complete resection; PR: Partial resection; RT: Radiotherapy; NRE: No recurrence; RE: Recurrence

### Conclusion

CD is a rare disorder that remains a diagnostic challenge. In our case, we report a rare presentation of UC retroperitoneal CD. Due to its rarity, lack of specific markers, and definitive diagnostic radiologic features, preoperative diagnosis is difficult and surgeons may encounter intraoperative difficulty due to its hypervascular nature. For UC disease, complete resection is the gold standard of treatment and has good prognosis. In the current era, improved radiologic criteria, intervention techniques, and newer adjuvant therapies may be helpful in diagnosis and management of this rare entity. Hence, CD should be included in diagnosis of solitary, heterogeneous, and hypervascular retroperitoneal mass.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initial will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.
Conflicts of interest

There are no conflicts of interest.

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