Case report

Synchronous retroperitoneal Castleman's disease with clear cell renal cell carcinoma

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SUMMARY

Castleman's disease is a rare non-clonal lymphoproliferative disorder and known to be associated with a number of disorders such as polyneuropathy, organomegaly, endocrinopathy, monoclonal protein and skin changes syndrome, Kaposi sarcoma, paraneoplastic pemphigus and plasma cell dyscrasias. The association of Castleman's disease with epithelial malignancy is not clear and limited to few case reports. We describe a case of synchronous Castleman's disease with renal cell carcinoma in a 53-year-old woman. She presented with right abdominal lump with feeling of heaviness. She also presented with vague discomfort in left hypochondrium for 15 years. The CT imaging of abdomen revealed two masses—one in right kidney and another in left anterior pararenal space of retroperitoneum. The patient underwent right radical nephrectomy with excision of left retroperitoneal mass. Histological examination revealed clear cell renal cell carcinoma and Castleman's disease, respectively. Role of interleukin-6 has been postulated as an important factor in association of Castleman's disease and epithelial malignancy.

BACKGROUND

Castleman's disease (CD) is a rare lymphoproliferative disorder with uncertain aetiopathogenesis and heterogeneous clinicopathological forms. It was first described by Castleman in 1954.¹ This entity is also known as giant lymph node hyperplasia and angiofollicular lymph node hyperplasia. Its association with haematolymphoid lesions has well been documented, however, its association with epithelial malignancy is limited to a few case reports. Here, we present a case report of an unusual case of concomitant hyaline vascular type of CD of retroperitoneum and clear cell renal cell carcinoma (RCC).

CASE PRESENTATION

A 53-year-old female patient, resident of Punjab, presented with right abdominal lump for 5 months associated with feeling of heaviness. She had also presented with vague discomfort in left hypochondrium for 15 years and it was associated with muscular cramps in same location. There was loss of weight and appetite, however no fever, pain, haematuria or altered bowel movements were noted. She had associated comorbidities in the form of hypothyroidism and insomnia and was on medication. On examination, the patient was conscious, cooperative, alert and oriented. Pulse rate and blood

pressure were normal. No pallor, icterus, clubbing, cyanosis, lymphadenopathy or oedema was noticed. Cardiovascular and chest examination was normal. Abdominal examination showed a large 10×10 cm mass in right lumbar region which was non-tender, firm, mobile and moving with smooth respiration. Another 6 cm mass in the left hypochondrium was identified which was non-tender and firm, however, it was non-mobile and upper margin was not reachable.

INVESTIGATIONS

On investigation, haemogram, renal function tests and liver function tests were normal. On CT imaging, the renal mass in right side was 11.2×13.2×10.9 cm. The mass was multilobulated and solid–cystic. It was heterogeneously enhancing, hypervascular with central necrosis. Fat planes were lost with liver and abdominal wall ([figure 1A](#)). The left retroperitoneal mass was in anterior pararenal space and measured 11.8×10.2×12.5 cm. It was well defined, lobulated, heterogeneous with punctate and arborising pattern of calcifications. Fat planes with adjacent organs were maintained ([figure 1B](#)).

DIFFERENTIAL DIAGNOSIS

Two possibilities, retroperitoneal gastrointestinal stromal tumour and metastasis from the RCC were considered as differential diagnosis preoperatively.

TREATMENT

She underwent right radical nephrectomy with excision of left retroperitoneal mass. Intraoperative findings were 10×11 cm right renal mass with multiple pararenal parasitic vessels supplying the mass and an 11×10 cm left retroperitoneal mass lifting pancreatic tail anteriorly, displacing left kidney posteroinferiorly and pushing spleen cranially and posteriorly. Multiple feeding parasitic vessels were noted all over the mass.

Grossly, right renal mass was 10×11 cm and had a yellow-tan cut surface with areas of necrosis and haemorrhage giving a variegated appearance ([figure 2A](#)). The left retroperitoneal mass was encapsulated and cut surface was stony hard and homogeneous tannish orange with attached fat at the periphery ([figure 2B](#)). Histology of the renal mass showed characteristic features of clear cell RCC with nests and tubules of tumour cells separated by thin intricate vascular channels. The tumour cells had abundant clear cytoplasm with

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Figure 1 (A) CT scan shows right renal mass which is multilobulated and solid–cystic showing heterogeneous enhancement with hypervascularity and central necrosis. (B) CT scan shows left retroperitoneal mass which is well defined, lobulated, heterogeneous with punctate and arborising pattern of calcifications.

International Society of Urologic Pathology nuclear grade II (figure 3A,B). No capsular breach was identified and the renal sinus was free of tumour. Microscopic examination of left retroperitoneal mass revealed lymphoid follicles with burnt out and hyalinised germinal centres, which were rimmed by a cuff of small lymphocytes arranged in concentric layers. Some of these follicles showed capillaries penetrating into it, giving a lollipop appearance. Interfollicular areas revealed high endothelial venule proliferation, hyaline material deposition along with lymphoplasmacytic cells. The left retroperitoneal mass was diagnosed as a hyaline-vascular type of CD (figure 3C,D).

OUTCOME AND FOLLOW-UP

Postoperative course was uneventful and the patient was discharged on postoperative day 11. She had not received any chemotherapy. After 1½ years, the patient is doing well and is on follow-up.

DISCUSSION

CD was first described by Castleman in 1954 as a case report and subsequently as case series in 1956.^{1,2} It has two forms—unicentric form, when it is localised to single lymph node and multicentric form when it occurs systematically. The unicentric forms include hyalinevascular type and plasma cell variant. Mixed form is also described. Hyaline vascular type is the most common variant of CD and accounts for 76%–91% of total unicentric CD.³ Histologically, this variant shows increased numbers of small, hyalinised blood vessels within the regressed follicles with onion-skin arrangement of expanded mantle zones around these follicles. Hyaline-vascular CDs mainly involve mediastinum or pulmonary hilum and head and neck region. Infrequent locations include mesenteric, retroperitoneal and abdominal locations.⁴

Figure 2 (A) The gross picture of right renal mass shows a tumour in the lower pole which is yellow tan in colour with areas of necrosis and haemorrhage. (B) Cut surface of left retroperitoneal mass is homogeneous tannish orange with attached fat at the periphery.

Figure 3 (A) Low power photomicrograph of the renal mass shows nests and tubules of tumour cells separated by thin intricate vascular channels (H&E; ×100). (B) High power photomicrograph shows tumour cells with low nuclear grade with abundant clear cytoplasm (H&E; ×400). (C) Low power microphotograph from left retroperitoneal mass reveals many lymphoid follicles with burnt out and hyalinised germinal centres. Interfollicular areas show proliferation of high endothelial venules (H&E; ×40). (D) High power microphotograph shows a lymphoid follicle with atretic germinal centre and penetrating capillaries. Prominent rimming by cuff of small lymphocytes is also noted (H&E; ×400).

CD is known to be associated with various conditions such as Kaposi sarcoma, lymphoma, amyloidosis, polyneuropathy, organomegaly, endocrinopathy, monoclonal protein and skin changes syndrome and follicular dendritic cell sarcoma.³ Its association with epithelial malignancy is also known, but is very rare and limited to case reports only. Chen *et al* reported a solitary case of mesenteric CD with left RCC and stomach leiomyoma in a 57-year-old man.⁵ Single case reports of association with other epithelial malignancies such as gallbladder carcinoma, thymic carcinoma, pulmonary squamous cell carcinoma and squamous cell carcinoma of tongue have been reported in literature.^{6–9}

The exact association of CD with epithelial malignancy is not yet elucidated. Various hypotheses have been proposed. One of the proposed hypotheses is involvement of interleukin-6 (IL-6) in synchronous occurrence of RCC as well as CD. IL-6 has already been known to have an aetiopathogenetic role in development of CD. Yoshizaki *et al* found normalisation of IL-6 in a patient with unicentric CD following excision of involved lymph node.¹⁰ Role of IL-6 in human carcinogenesis has been revealed. Heikkilä *et al* in an excellent review pointed out the role of IL-6 in human carcinogenesis.¹¹ In this review, they found increased concentration of IL-6 in patients with cancer when compared with healthy controls. Another mechanism that may be suggested is the association of vascular endothelial growth factor (VEGF) with CD. The prominent vascular proliferation seen in this variant of CD might be attributed to VEGF.¹² The role of VEGF in RCC has already been studied. Nicol *et al* show an increased VEGF expression in RCC and proposed its paracrine effect in stimulating angiogenesis.¹³ It can be proposed that some mediators such as IL-6 or VEGF or unknown factors might be involved in the crosstalk of these two pathologically distinct and unrelated entities. However, it remains open whether the

simultaneous occurrence of CD and epithelial malignancy is just a mere incidence or much more.

Learning points

- Castleman's disease is a rare lymphoproliferative disorder with uncertain aetiopathogenesis and heterogeneous clinicopathological forms.
- Castleman's disease can be associated with epithelial malignancy, although this phenomenon is very uncommon and limited to case reports.
- Retroperitoneum is an uncommon site of Castleman's disease and is an important differential diagnosis of retroperitoneal mass lesions.
- Castleman's disease may not be overtly symptomatic and may mimic metastatic disease in the presence of epithelial malignancy.
- This uncommon association of epithelial malignancies with Castleman's disease requires further research to elucidate its significance.

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