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Other full case

# Retroperitoneal unicentric Castleman's disease with multiple lymph node involvement

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## Summary

A 78-year-old woman with B-symptoms was referred for a left adrenal incidentaloma of 5 cm. Imaging revealed features compatible with adrenal cancer. The authors excluded excess production of catecholamines or adrenal steroids. The tumour was removed by en bloc radical left retroperitonectomy with adrenalectomy, nephrectomy, interaortocaval lymphadenectomy and splenectomy. Histology demonstrated periadrenal hyaline vascular Castleman's disease with local infiltration and 14 positive lymph nodes. The lymphoid infiltrate spilled into the adjacent renal cortex. HHV8 was negative. The Ki67 proliferative index was 30–40% in germinal centres. There was no syn- or metachronous disease on extended imaging including fluorodeoxyglucose positron emission tomography-CT and narrow follow-up at 3 years. This is a rare case of unicentric hyaline vascular Castleman's disease with documented locoregional lymph node involvement. The case exemplifies the transition from unifocal unicentric disease into disseminated disease with involvement of multiple lymph node stations (multicentric disease). The authors demonstrate surgical cure by oncological resection.

## BACKGROUND

Castleman's disease is a rare lymph node disease. Current classification differentiates unicentric disease with a single lesion from multicentric disease with lymph node involvement in multiple lymphatic stations. Both have a significantly different outcome.[1] The condition is caused by human herpesvirus infection and is best understood as a model of virus driven disease propagation in an expanding B cell pool and diseased endovascular endothelium.[2] We demonstrate the rare case of unicentric disease with locoregional lymph node involvement and surgical cure achieved by oncological resection alone. Radical surgery rather than excisional biopsy may be indicated in patients with unicentric disease.

## CASE PRESENTATION

This generally well 78-year-old woman was initially referred for primary hyperparathyroidism and a 4.5 cm left adrenal lesion infiltrating the left kidney reported by an external MRI. Medical history includes arterial hypertension. She had fatigue and joint aches. Family and social history were unremarkable and clinical examination found no lymphadenopathy or any other suspicious finding.

## INVESTIGATIONS

Full blood count and blood biochemistry were normal but for eucalcaemic hyperparathyroidism with parathyroid hormone elevated to 113 ng/l (n:15–70) and an estimated glomerular filtration rate of 60–70 ml/min. Endocrine testing revealed normal urine catecholamines, renin-aldosterone ratio and morning cortisol. The iodine-131-meta-iodobenzylguanidine adrenal scan did not reveal any uptake.

A preoperative CT scan did not reveal any focal lesions beyond the known left retroperitoneal lesion and multiple small liver cysts. Chest x-ray was clear.

The preoperative dedicated adrenal CT showed a 4.5 cm low attenuation mass lesion at the inferior aspect of the left adrenal with fairly ill-defined borders and extending into the left renal hilum. There is inflammatory stranding in the retroperitoneal fat. The renal artery and vein course through the mass lesion which extends into the hilum abutting the left renal pelvis is shown in figure 1.

Pathological examination of the surgical specimen showed free resection margins. Fourteen retroperitoneal lymph nodes were positive for Castleman's disease, while four interaortocaval nodes were free of disease. Left kidney and adrenal tumour: the specimen weighs 363 g and consists of left kidney and adrenal along with perinephric fat and hilum. The surface of the specimen was painted black. The specimen measures 190 mm superior to inferior, 110 mm medial to lateral and 55 mm anterior to posterior. The cut surface of the specimen shows a periadrenal mass which appears ill-defined and brown in colour. There is some identifiable residual normal looking adrenal tissue within the lesion. The tumour extends very close to the upper pole of the kidney and into the hilar fat. Due to the poorly circumscribed nature of the tumour, it is difficult to measure the size accurately; however, it is approximately 45×35×25 mm. In addition, there is a small simple cyst noted at the lower pole measuring 14×15×5 mm. The remaining renal parenchyma appears unremarkable. Microscopy: sections of the adrenal appear normal. The capsule is intact and there is normal cortical to medullary ratio. The periadrenal tissue shows an extensive infiltrate of small lymphocytes intimately associated with dilated, and occasionally thick-walled hyaline blood vessels. There

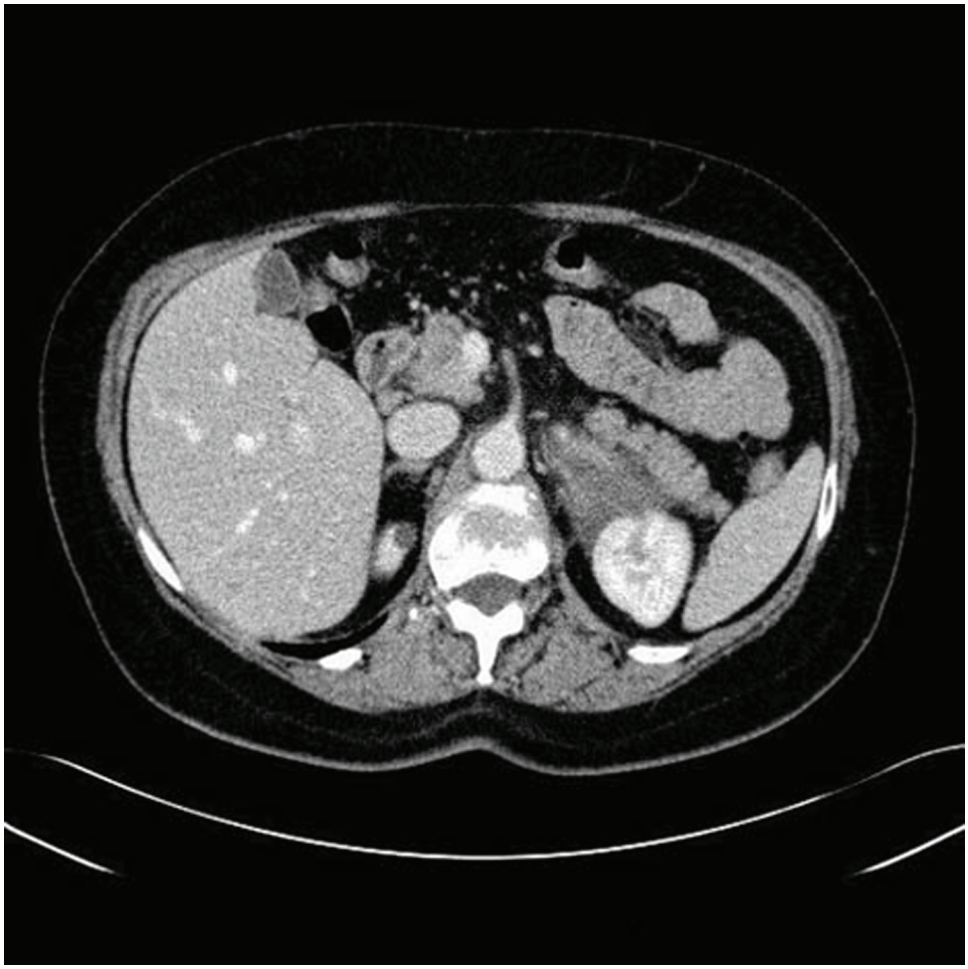

**Figure 1** CT showing a 4.5 cm low attenuation mass lesion at the inferior aspect of the left adrenal.

is also marked surrounding stromal oedema and fibrosis. The lymphoid infiltrate spills into the adjacent renal cortex and there is associated focal global and segmental sclerosed glomeruli together with interstitial involvement in this area. The renal medulla is unremarkable. There are also three incidental simple renal cysts. Fourteen lymph nodes show similar features. There is diffuse nodular expansion with regressive germinal centres composed of large cells with vesicular nuclei. Some of the follicles show vascular proliferation and hyalinisation of the germinal centre. There is 'onion-skinning' appearance to the lymphocytes at the periphery of the follicles. Immunohistochemical stains show that the nodules are strongly CD20, BCL2 and CD10 positive, while CD3 and CD5 highlight the perifollicular T cells. CD21 and CD23 are strongly positive in the follicular dendritic cells in the germinal centres. HHV8 is negative. Ki67 shows the germinal centres have a proliferative index of 30–40%, the rest of the lymph node is very low.[2] The diagnosis is localised retroperitoneal Castleman's disease (stromal rich, hyaline vascular type) (figures 2 and 3).

## DIFFERENTIAL DIAGNOSIS

The differential diagnosis of the CT-imaging findings include

- An adrenal adenoma (unlikely due to malignant features and washout criteria)
- A malignant retroperitoneal process was considered and felt to most likely be a primary adrenal lesion
- Tuberculosis
- Retroperitoneal sarcoma or retroperitoneal lymphoma
- Adrenal metastasis.

## TREATMENT

We performed open radical surgery as en bloc retroperitonectomy with adrenalectomy and nephrectomy, interaortocaval lymphadenectomy and splenectomy. A liver biopsy, done to stage an eventual lymphoma, showed only steatosis hepatis.

## OUTCOME AND FOLLOW-UP

Follow-up after 3 years (36 months) did not reveal local recurrence. The patient is free of symptoms. A postoperative whole-body fluorine-18 fluorodeoxyglucose positron emission tomography-CT did not reveal any specific uptake beyond a left colon lesion. This was endoscopically removed and demonstrated to be a high-risk colon polyp.

## DISCUSSION

This case is a presentation of a rare disease. Its importance relates to the fact that we demonstrate lymphadenopathy in 14 surrounding lymph nodes localised in the retroperitoneal fat and renal hilum. The tumour is clearly shown


*BMJ Case Reports* 2011; doi:10.1136/bcr.03.2011.3938

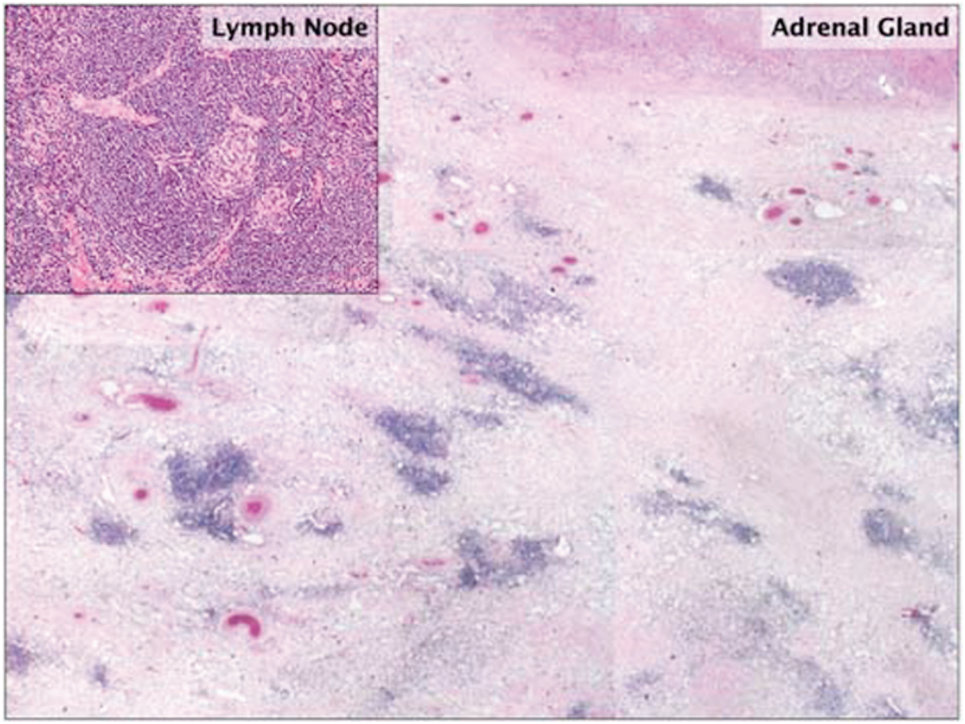


**Figure 2** The periadrenal soft tissue shows a multifocal nodular lymphocytic infiltrate with perivascular and interstitial patterns embedded in a hyalinised stroma-rich background (H&E 12.5×). The surrounding lymph nodes reveal classical picture of hyalin-vascular Castleman disease (inset, H&E 100×).

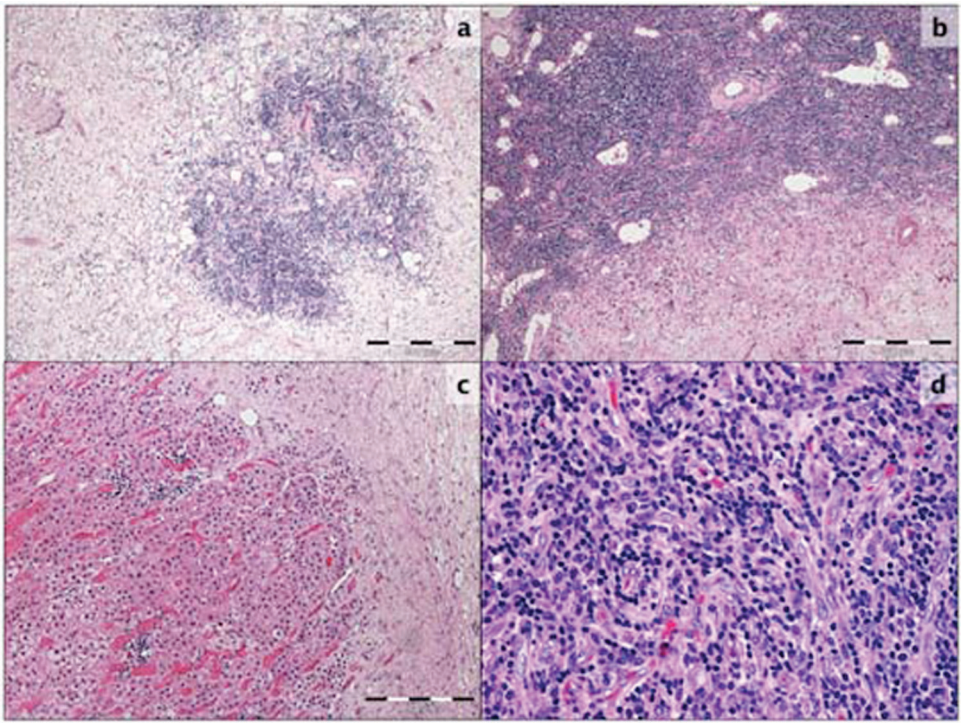


**Figure 3** The interstitial lymphocytic infiltrate reveals perivascular aggregates, dilated hyalinised vessel walls (panels A and B, H&E 40×) and extends to the sinusoidal spaces of the adrenal cortex (panel C, H&E 100×). A polymorphous infiltrate contains mature lymphocytes and scattered plasma cells without atypia, along with prominent endothelial network (panel D, H&E 200×).

to originate from the retroperitoneal fat, not the adrenal gland itself, as likely erroneously claimed by some former authors reporting on retroperitoneal Castleman's.[3–6]

There are only a few former reports describing locoregional lymph node seeding in CD.[7–10] The rarity of this observation relates to the fact that less than 10% of all

patients operated for Castleman's disease had systematic lymphadenectomy.[1]

We provide a strong argument for surgery aligned with oncological principles. In our patient this is highly likely to have enabled cure. Excision of the mass alone would have left the patient at risk for early recurrence due to expansion of the persistent lymph node disease. At the same time removal of the adjacent regional lymph node station (the interaortocaval nodes) has greatly contributed to inform the prognosis. In the absence of disease,[11] we have withheld highly toxic systemic chemotherapy and local radiation. Long-term results for surgery in unicentric Castleman's disease show excellent but imperfect results.[1] We propose that local recurrence and eventually death are consequences of incomplete removal of the locoregional disease caused by confusion between unifocal and unicentric disease.

## Learning points

- Retroperitoneal Castleman's disease originates from retroperitoneal lymph nodes rather than solid organs.
- Surgical cure can be achieved by oncological resection aiming at free margins and complete lymphadenectomy.
- Unicentric disease may present with locoregional lymphatic spread. The prognosis is still sharply different from that of multicentric disease.
- Locoregional lymphatic spread may constitute a transition stage between unifocal unicentric disease and multicentric disease.
- The present case provides clinical evidence for the theoretically based proposal of lymphatic propagation of Castleman's disease.

**Competing interests** None.

**Patient consent** Obtained.

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