

Complete manuscript title:

Autoimmunity due to unicentric Castleman's disease cured by resection of a hepatic mass

Short title for a running head:

A case of autoimmunity cured by resection of a hepatic mass

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A 60-year-old man presented with night sweats in 2008. Investigations identified persistently raised inflammatory markers (CRP 80 mg/l, ESR 75 mm/hour), iron-deficiency anaemia and a 5.3 cm (width) x 3.8 cm (length) hepatic hilar mass. Laparoscopy revealed an abscess adjacent to a necrotic lymph node. Open surgery to remove the mass was considered to be too high-risk; instead, he was treated with antibiotics. The patient was lost to follow-up, but continued to have night sweats.

He re-presented in 2018 with polyarthralgia. Investigations again revealed anaemia and elevated inflammatory markers (Hb 10.8 g/dl, CRP 97 mg/l, ESR 79 mm/hour). Serological testing revealed a polyclonal increase in IgG (17.65 g/l; normal: 6-16.00 g/l) and IgA (6.50 g/l; normal: 0.80-4.00 g/l) and the presence of multiple autoantibodies: ANA (5.1 units; normal: 0.0-9 units), CCP (12 iu/ml; normal: 0-7 iu/ml) and low-grade elevation of MPO-ANCA (4.1 iu/ml; normal: 0.0-3.4 iu/ml) and PR3-ANCA (3.5 iu/ml; normal: 0.0-1.9 iu/ml). ACE levels were normal. No infectious cause was identified. A repeat CT abdominal scan showed a homogenous hypoattenuating hepatic mass adjacent to the head of the pancreas (figure 1), which had increased in size to 6 cm (width) x 4.5 cm (length).

The differential diagnosis included an inflammatory pseudo-tumour, an atypical infection or a paraneoplastic syndrome, although the latter two seemed unlikely given the duration of his illness. After multi-disciplinary discussion, the decision to surgically resect the lesion was made in order to establish a diagnosis and to reduce the risk of AA amyloidosis and accelerated atherosclerosis associated with persistent inflammation. The resected mass was 8 cm (width) x 6 cm (length) and located deep in the lesser sac, encasing the left gastric artery. Two adjacent enlarged lymph nodes

were also identified and resected. Histological examination of the hilar mass and gastric lymph nodes revealed follicular hyperplasia (Figure 2A-B) and medullary plasmacytosis (Figure 2C-D). There was no malignancy or granulomatous inflammation.

Following surgery, the patient's symptoms completely resolved. One month post-operatively, CRP, ESR and IgG levels had normalised (CRP <4 mg/l, ESR 2 mm/hour, IgG 11.10 g/l). CCP, ANA, MPO and PR3 ANCA autoantibodies had disappeared. In light of the clinico-pathological picture, the diagnosis was revised to unicentric Castleman's disease of the plasmacytic variant.

Castleman's disease (CD) is a rare lymphoproliferative disorder. The main histopathological types are hyaline-vascular, plasmacytic and mixed [1]. CD is classified clinically into unicentric (UCD) and multicentric (MCD) according to whether one or multiple lymph node groups are involved. UCD is usually of the hyaline-vascular type, whereas MCD is more commonly associated with the plasmacytic variant. MCD is more frequently associated with a systemic inflammatory response and has a poorer prognosis [2]. Treatment differs for the two types of Castleman's disease: UCD is usually by resection of the affected lymph node, whereas MCD is treated with immunosuppression [3].

Our case highlights that autoimmunity and systemic inflammation can be driven by unicentric Castleman's, and cured with surgical resection. There have been reports of single lymph node resections curing UCD, including a paediatric case with hypergammaglobulinaemia and autoantibodies [4]. UCD is a rare but potentially reversible cause of AA amyloidosis; Lachmann *et al* described resolution of inflammation and regression of AA amyloidosis following surgery [5].

References:

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Figure 1:

CT scan abdomen and pelvis with intravenous contrast, 6 months prior to surgery.

The mass (arrow) adjacent to the head of the pancreas and porta hepatis measured 6 x 4.5 cm. The left gastric lymph node had undergone interval size reduction, now measuring 9 mm (previously 14 mm).

Figure 2, A-D:

Histology of surgical specimen showing lymph node with follicular hyperplasia (arrow) and relatively abundant interfollicular plasma cells (asterisks), highlighted by CD138 immunohistochemistry.

2A: 20X, haematoxylin and eosin

2B: 200X, haematoxylin and eosin; higher-power view of the interfollicular area marked with a box in figure 2A

2C: 20X, immunohistochemistry with CD138 antibody

2D: 200X, immunohistochemistry with CD138 antibody; higher-power view of plasma cell infiltrate marked with a box in figure 2C



