

# Bilateral adrenal lymphoma presenting as Addison's disease

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**Summary:** We describe an unusual case of non-Hodgkin's lymphoma of the adrenals which presented as Addison's disease. Examination of tissue taken by computed tomography guided biopsy revealed a high grade B cell centroblastic lymphoma. The patient was treated with chemotherapy but died from invasive aspergillosis. Autopsy confirmed bilateral adrenal involvement by lymphoma.

## Introduction

Non-Hodgkin's lymphoma has an extranodal origin in approximately 10–25% of cases.<sup>1</sup> Adrenal involvement at the time of presentation is rare and may be difficult to establish. Surprisingly, adrenal involvement by lymphoma at post-mortem occurs in up to 35% of cases, usually associated with retroperitoneal lymph node involvement.<sup>2,3</sup>

It is generally believed that at least 90% of adrenal cortical tissue must be destroyed before the clinical features of adrenal dysfunction ensue.<sup>4</sup> We present an unusual case of Addison's disease in whom large bilateral adrenal masses proved to be centroblastic lymphoma on biopsy.

## Case report

A 59 year old man presented with a 6-month history of nausea, vomiting and lethargy associated with night sweats and weight loss. On examination he was noted to have increased palmar crease pigmentation. His blood pressure was 110/70 mmHg. Abdominal examination revealed two large abdominal masses which moved with respiration. Both the liver and spleen were palpable just below the costal margin.

The patient had a normocytic normochromic anaemia with a haemoglobin of 10.4 g/l. Serum sodium and potassium were normal but the urea was raised at 15.3 mmol/l. Blood glucose was 7.1 mmol/l. Alkaline phosphatase was raised at 336 IU/l with a raised bone isoenzyme, otherwise the liver function tests were normal.

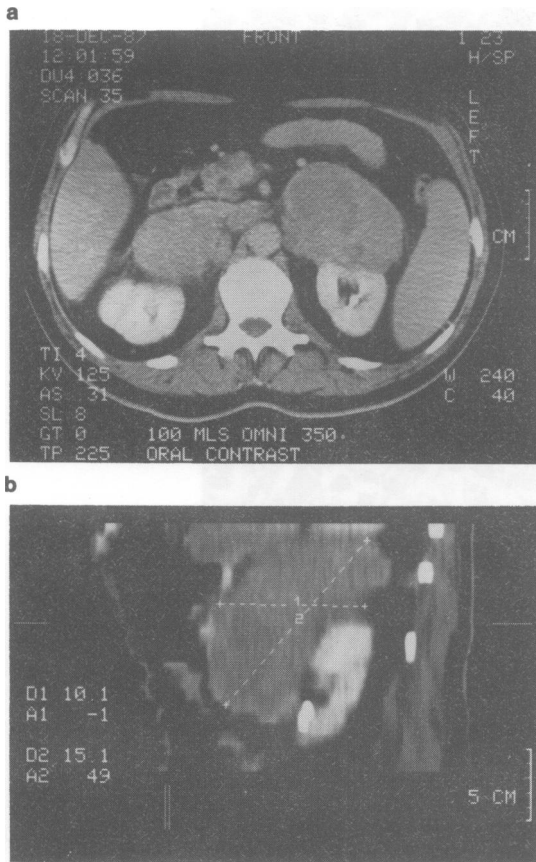
Thyroid function was normal. A short Synacthen test (Ciba, UK) was carried out (250 µg of tetracosactin intramuscularly) which showed a baseline cortisol of 300 nmol/l, 20 minute cortisol of 340 nmol/l and a 60 minute cortisol of 340 nmol/l. Corticotrophin (ACTH) was raised at 98 ng/l confirming Addison's disease. Adrenal autoantibodies were not assessed.

Abdominal ultrasound revealed bilateral adrenal masses with enlargement of both liver and spleen. These findings were confirmed on abdominal computed tomographic (CT) scanning (Figure 1a,b). There was no evidence of lymphadenopathy elsewhere. The left adrenal was biopsied under CT guidance. Histology showed complete replacement of adrenal tissue by a population of large malignant cells with rounded nuclei and multiple nucleoli (Figure 2), which precluded any histological assessment of a pre-existing autoimmune process. Immunohistochemistry showed these cells to express leucocyte common antigen (CD45) and the B cell marker MB1 (CD45R). T cell markers UCHL1 and MT1 were both negative. A diagnosis of a high grade B cell centroblastic non-Hodgkin's lymphoma was made. The bone marrow aspirate and trephine were normal with no evidence of infiltration by centroblasts.

He was rehydrated and started on fludrocortisone 100 µg daily with improvement in his symptoms and normalization of his renal function. Once stabilized he was started on combination chemotherapy with MACOP-B,<sup>5</sup> which includes methotrexate, adriamycin, cyclophosphamide, vincristine, bleomycin and daily prednisolone (50 mg) and was discharged home after the first week of therapy.

Five days after his first dose of methotrexate (700 mg) he developed severe mucositis and hypotension (BP 70/50 mmHg) and was readmitted requiring intravenous fluids and hydrocortisone. Despite these

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**Figure 1** (a) Contrast enhanced scan at the mid renal level. Large masses are seen lying anterior to both kidneys. Further scans and sagittal reconstruction (b) confirmed that the masses arose from the adrenals.

measures his clinical condition deteriorated and he developed a profound pancytopenia with bone marrow aspiration confirming a drug-induced aplasia. Ten days after admission he developed invasive aspergillosis of the lungs from which he succumbed.

Post-mortem examination revealed markedly enlarged and necrotic adrenals which were completely

replaced by lymphoma. Liver and spleen were both enlarged but there was no intra-abdominal lymphadenopathy. Both kidneys showed patchy mononuclear cell infiltrates but no lymphomatous infiltration. The lungs showed haemorrhagic infarction with thrombosis of pulmonary vessels and extensive infiltration by septate, dichotomously branching fungal hyphae with the appearance of *Aspergillus*.

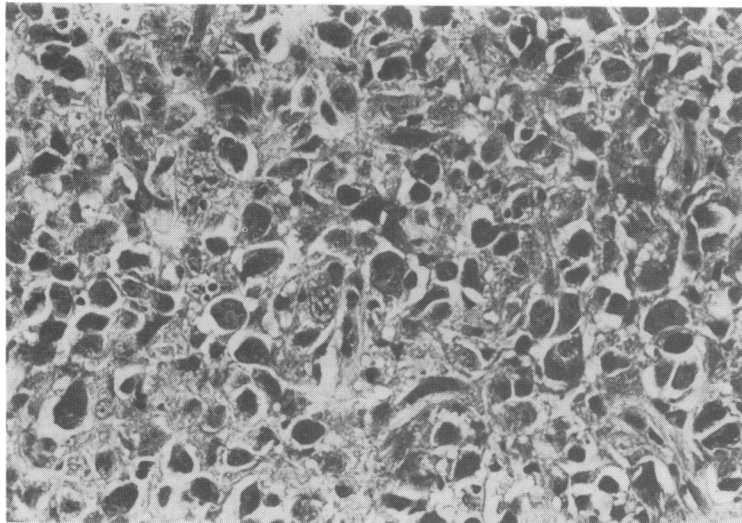
### Discussion

Bilateral adrenal masses are rare and in the absence of clinical manifestations it is often difficult to distinguish primary adrenal neoplasms from infiltration by metastases and reticuloses. Assessment by conventional radiological methods may be difficult; however, computed tomography<sup>6</sup> and magnetic resonance imaging<sup>7</sup> have proved to be useful non-invasive techniques which may help to characterize the cause of adrenal enlargement.

Enlargement of both liver and spleen in our case was suggestive of non-Hodgkin's lymphoma and this was confirmed by CT guided needle biopsy of the left adrenal mass. Surprisingly there was no enlargement of lymph nodes elsewhere.

Unlike the thyroid gland, involvement of the adrenals as the presenting manifestation of lymphoma is unusual with only five cases<sup>8-12</sup> reported in the literature, of which only one had bilateral involvement.<sup>12</sup> Furthermore, presentation of lymphoma with the clinical and biochemical features of Addison's disease as illustrated by our case has only been reported once.<sup>13</sup> In the absence of any evidence of non-Hodgkin's lymphoma in other lymph glands we postulate that the primary site of lymphoma in this case was the adrenal gland. In common with other endocrine lymphomas one might speculate that transformation may have occurred secondary to a pre-existing autoimmune state;<sup>14</sup> however, we were not able to prove this.

In conclusion, despite the rarity of this presentation primary adrenal lymphoma should be excluded in the evaluation of adrenal masses presenting with Addison's disease.



**Figure 2** Needle biopsy specimen of left adrenal showing large malignant cells with rounded nuclei and prominent nucleoli (H & E  $\times$  288).

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