Bilateral adrenal non-Hodgkin’s lymphoma with adrenal insufficiency

R D Ellis, D Read

Abstract
A 74 year old women presented with lethargy and weight loss and was found to have profound adrenal insufficiency and bilateral adrenal mass lesions. Histological examination revealed non-Hodgkin’s lymphoma. There was no evidence of lymphoma outside the adrenal glands. Isolated bilateral adrenal masses may rarely be due to primary adrenal non-Hodgkin’s lymphoma, which is often associated with adrenal insufficiency.

Keywords: lymphoma; adrenal insufficiency

Case report
A 74 year old women presented with a three month history of general ill health with lethargy, weight loss, non-specific abdominal pains, and constipation. There was a past history of angina pectoris and hypertension. Treatment with methyldopa had been stopped one week before admission to hospital because of hypotension (blood pressure 110/80 mm Hg). There were no clinical signs of adrenal insufficiency apart from mild dehydration and moderate postural hypotension (blood pressure 140/80 mm Hg supine, 100/70 mm Hg erect).

Initial investigations revealed a normal full blood count, blood film, and erythrocyte sedimentation rate. Serum electrolyte estimation revealed a sodium concentration of 137 mmol/l (normal range 136–148) and potassium concentration of 5.0 mmol/l (3.8–5.0). There was a raised urea concentration of 13.7 mmol/l (2.8–6.5) and creatinine concentration of 170 mmol/l (60–120). The serum calcium concentration was raised at 2.97 mmol/l (2.20–2.60) with an albumin concentration of 44 g/l (35–52) and phosphate concentration of 1.17 mmol/l (0.80–1.40), but the serum calcium concentration quickly returned to normal after intravenous rehydration with normal saline.

Serum parathyroid hormone concentration was 15 pg/ml (10–65). Liver function tests, protein electrophoresis, and immunoglobulin concentrations were normal.

A short adrenocorticotropic hormone stimulation test revealed adrenal insufficiency with a baseline cortisol concentration of 5 nmol/l (150–680) with no rise at 30 and 60 minutes.

Computed tomography with intravenous enhancement of the abdomen and pelvis revealed bilateral, 10 cm adrenal mass lesions that were partially necrotic (fig 1). Histological examination of a percutaneous computed tomography guided biopsy specimen revealed a diffuse B-cell non-Hodgkin’s lymphoma of centrocytic/centroblastic type. Immunohistochemistry demonstrated expression of bcl-2 protein confirming follicle centre cell origin.

A bone marrow biopsy specimen and aspirate showed no morphological evidence of infiltration by lymphoma, although immunophenotyping by flow cytometry was not performed. A chest radiograph was normal and there was no lymphadenopathy on clinical examination.

Primary bilateral adrenal non-Hodgkin’s lymphoma with adrenal insufficiency was diagnosed. Treatment with glucocorticoid and mineralocorticoid hormone replacement therapy was started. Chemotherapy with intravenous cyclophosphamide, Adriamycin, vincristine, and prednisolone was administered.

The patient then became neutropenic and developed an Escherichia coli septicaemia. This was successfully treated but the general condition of the patient deteriorated and she died three weeks after starting chemotherapy. A request for postmortem examination was refused by the family.

Discussion
Adrenal masses are usually metastases from malignant tumours, most often from bronchial carcinomas. Non-Hodgkin’s lymphoma affecting the adrenal glands is usually associated with other sites of disease, most usually the
Table 1  Previously reported cases of bilateral primary adrenal non-Hodgkin’s lymphoma

<table>
<thead>
<tr>
<th>Paper</th>
<th>Age</th>
<th>Sex</th>
<th>Presentation</th>
<th>Diagnosis</th>
<th>Histology</th>
<th>hypoadrenal</th>
<th>Treatment</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feldberg et al</td>
<td>43</td>
<td>Male</td>
<td>Abdominal pain, fever, hypertension, hypocalcaemia</td>
<td>CT</td>
<td>Diffuse histiocytic lymphoma</td>
<td>No</td>
<td>Chemotherapy (reduction in size of masses on CT at 2 months)</td>
<td>?</td>
</tr>
<tr>
<td>Ito et al</td>
<td>47</td>
<td>Male</td>
<td>Transverse myelitis: incidental finding of lymphoma</td>
<td>CT</td>
<td>Diffuse large cell</td>
<td>No</td>
<td>Chemotherapy: MACOP-B* (reduction in size of mass on CT)</td>
<td>5 months</td>
</tr>
<tr>
<td>Aron et al</td>
<td>70</td>
<td>Male</td>
<td>Abdominal pain, lethargy, vomiting</td>
<td>Postmortem</td>
<td>Reticulum cell sarcoma</td>
<td>Yes</td>
<td>None</td>
<td>1 week</td>
</tr>
<tr>
<td>Pagliuca et al</td>
<td>59</td>
<td>Male</td>
<td>Vomiting, lethargy, weight loss, night sweats</td>
<td>CT</td>
<td>High grade B-cell lymphoblastic</td>
<td>Yes</td>
<td>Chemotherapy: CHOP†</td>
<td>1 month</td>
</tr>
<tr>
<td>Domenici et al</td>
<td>52</td>
<td>Female</td>
<td>Fever, weight loss</td>
<td>Postmortem</td>
<td>Immunoblastic lymphoma</td>
<td>Yes</td>
<td>None</td>
<td>2 months</td>
</tr>
<tr>
<td>Shea et al</td>
<td>81</td>
<td>Male</td>
<td>Back pain</td>
<td>CT</td>
<td>Reticulum cell sarcoma</td>
<td>Yes</td>
<td>None</td>
<td>1 week</td>
</tr>
<tr>
<td>Sparagana et al</td>
<td>71</td>
<td>Male</td>
<td>Nausea, weight loss, fever, weakness</td>
<td>Postmortem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alvarez-Costello et al</td>
<td>59</td>
<td>Female</td>
<td>Abdominal pain, weakness, weight loss</td>
<td>CT</td>
<td>Large cell pleomorphic</td>
<td>No</td>
<td>Chemotherapy (regression of masses on serial CT scans)</td>
<td>?</td>
</tr>
<tr>
<td>Alvarez-Costello et al</td>
<td>69</td>
<td>Male</td>
<td>Abdominal pain, weakness, weight loss</td>
<td>CT</td>
<td>Large cell</td>
<td>No</td>
<td>Chemotherapy (resolution of masses on CT)</td>
<td>?</td>
</tr>
</tbody>
</table>

*MACOP-B is a combination of methotrexate, Adriamycin, cyclophosphamide, prednisolone, and bleomycin.
†CHOP is a combination of cyclophosphamide, Adriamycin, vincristine, and prednisolone.

CT = computed tomography.

retroperitoneal lymph nodes and ipsilateral kidney. Adrenal involvement in widespread non-Hodgkin’s lymphoma occurs in 4% of cases as assessed by computed tomography and in 24% at postmortem examination. Disease arising in, and confined to, the adrenal glands is unusual and is termed primary adrenal lymphoma. The adrenal gland in man contains no lymphoid tissue, and the follicle-like cell origin of this lymphoma suggests the tumour may have arisen on a background of previous autoimmune adrenalitis, consistent with the finding of profound adrenal insufficiency. Bilateral primary adrenal non-Hodgkin’s lymphoma is rare, with only nine previous cases reported, all occurring in patients over 40 years of age. Five cases were treated with chemotherapy with decrease in adrenal mass size in four cases with maximum reported survival of five months (see table 1). In the present case, the patient died three weeks after starting combination chemotherapy. An alternative treatment strategy would be to administer an oral alkylating agent, or local radiotherapy.

Adrenal insufficiency due to adrenal involvement in widespread non-Hodgkin’s lymphoma was previously thought to be rare, but in a recent series there were four cases out of 127 patients. However, adrenal insufficiency is more common in bilateral primary adrenal non-Hodgkin’s lymphoma, occurring in half of the reported cases including this case.

Isolated bilateral adrenal masses may be due to primary adrenal non-Hodgkin’s lymphoma that is often associated with adrenal insufficiency and carries a poor prognosis.

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