Hodgkin’s Lymphoma Presenting as a Protein-Losing Enteropathy

A Case Report

A. J. SILBERT, J. D. IRELAND, P. J. D. UYS, M. D. BOWIE

SUMMARY
A 10-year-old boy presented with oedema. Panhypoproteinaemia due to excessive enteric protein loss was demonstrated, and further investigation revealed the cause to be lymphocyte-depleted Hodgkin’s lymphoma. Appropriate chemotherapy resulted in a dramatic improvement in the serum protein level and resolution of the proptosis and lymphadenopathy.


Panhypoproteinaemia caused by protein-losing enteropathy (PLE) is well described. Many disorders have been reported which are characterized by excessive enteric protein loss, the single most common paediatric condition recorded being intestinal lymphangiectasis. Lymphomas, and particularly lymphosarcomas, are a well-recognized cause of PLE. Hodgkin’s disease is listed in some aetiological classifications but is not further described in the paediatric literature.1,4

We report a child with Hodgkin’s disease who initially presented with PLE and has shown signs of recovery on chemotherapy.

CASE REPORT
A 10-year-old boy was admitted with a 1-week history of malaise, complaints of intermittent left-sided abdominal pain and intermittent peri-orbital oedema. No history of pyrexia, anorexia, recent loss of weight, diarrhoea or steatorrhoea was obtained.

He was below the 3rd Boston percentile for weight and height. Small, shotty lymph nodes were palpable in the left axilla and mild pretibial and peri-orbital oedema was evident. The abdomen was mildly distended and had a ‘doughy’ consistency. No definite masses were palpable and no ascites was detectable. The rest of the clinical examination was non-contributory.

The haemoglobin concentration was 13.7 g/dl and the white cell count was 9,900/μl, with 18% lymphocytes. There was no eosinophilia. Repeated full blood counts subsequently revealed a persistent lymphopenia of less than 1,500/μl. The erythrocyte sedimentation rate was 60 mm/1st h. A chest radiograph revealed the lung fields to be clear, and there was no evidence of hilar or para-tracheal lymphadenopathy. An ECG was normal. Microscopical examination of the stool revealed the presence of Hymenolepis nana eggs, but no pathogens were found on stool culture. Mantoux and Candida skin tests were negative. The biochemical values were: total protein 46 g/l, albumin 19.7 g/l and globulin 27.8 g/l (α-globulin 3.5 g/l, α₁-globulin 9.7 g/l, β-globulin 6.6 g/l, fibrinogen 7.5 g/l, γ-globulin 8.0 g/l). There was no proteinuria.

A diagnosis of PLE was considered and confirmed by a ⁵¹Cr-labelled albumin study.² Twenty per cent of the intravenously administered dose was recovered during the 4-day stool collection (normal 0 - 0.7%). Barium meal and enema examinations were negative. A peroral intestinal biopsy revealed normal mucosa and a moderate infestation of Giardia lamblia.

Therapy consisting of a high-protein, low-fat diet supplemented by medium-chain triglycerides was instituted, and the H. nana and G. lamblia infestations were treated with niclosamide and metronidazole respectively. No clinical or biochemical improvement was noted.

Six weeks after admission an induration developed over the right zygoma and within a few days proptosis of the right eye was evident. This was associated with enlargement of the pre-auricular and submandibular lymph nodes. A biopsy of the former revealed lymphocyte-depleted Hodgkin’s lymphoma. While the patient was under general anaesthesia for the biopsy an ill-defined midline abdominal mass was palpated. Bone marrow aspiration and biopsy showed no infiltration, and a skeletal survey revealed no osseous involvement. Intravenous pyelography (IVP) demonstrated lateral displacement of the left kidney and ureter with dilatation of the caliceal system, suggestive of ureteric obstruction (Fig. 1).

The standard treatment of Hodgkin’s lymphoma utilizing the MOPP regimen (merchlorethamine, vincristine (Oncovin), prednisone and procarbazine) was instituted 54 days after admission—there was dramatic resolution of the proptosis, and the submandibular and axillary glands returned to their normal size. Serial determinations of the plasma protein level and the lymphocyte count show the response to treatment (Table 1).

DISCUSSION
This boy was admitted with hypoproteinaemia caused by PLE. Initial investigations revealed G. lamblia infestation...
Fig. 1. IVP at 10 minutes (before the introduction of chemotherapy). Lateral displacement of the left kidney and ureter, dilatation of the calyceal system suggestive of obstruction, and a double right ureter can be noted.

(a documented cause of PLE), but eradication of the parasite brought about no improvement. The institution of a high-protein, low-fat diet supplemented with medium-chain triglycerides was equally unsuccessful — this diet has been used in the management of PLE on the grounds that it limits intestinal lymphatic flow and diminishes chylous leakage into the lumen.

Several weeks after the patient's presentation with PLE the development of proptosis and associated lymphadenopathy gave the aetiological diagnosis. Hodgkin's lymphoma was diagnosed on lymph node biopsy, and at the same time, while the patient was under anaesthesia, a midline abdominal mass was palpated.

Two pathophysiological mechanisms may result in excessive enteric protein loss: 14 Altered gut permeability may be caused by primary involvement of the intestinal mucosa, as in the case of ulcerative colitis or acute infective enteritis. Lymph stasis is the second mechanism; as a result of obstructed lymphatic flow, excess chylous fluid drains into the intestinal lumen, for example in intestinal lymphangiectasias or tuberculous adenitis. Combinations of both mechanisms may be present in some cases of protein-losing enteropathy, as in Crohn's disease.

The second mechanism seems the most likely in this child. Hodgkin's lymphoma rarely infiltrates the small bowel, but when it does the terminal ileum is usually involved and the intestinal biopsy would have missed such a lesion. The midline mass and the displacement of the left kidney and ureter with caliceal changes suggestive of obstruction are more indicative of involvement of the abdominal lymphatics and lymph nodes.

Clinical improvement occurred with the administration of appropriate chemotherapy; within 10 days there was a significant rise in the serum albumin level (Table I). This has been sustained, and at present after the standard 6-course MOPP regimen the patient is in complete remission with no evidence of lymphadenopathy or hypoproteinaemia. A repeat IVP is now completely negative (Fig. 2). The response in the lymphocyte count lagged behind the rise in the serum protein level, but this was probably

<table>
<thead>
<tr>
<th>Day</th>
<th>Lymphocyte count (/μl)</th>
<th>Protein (g/l)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>Albumin</td>
</tr>
<tr>
<td>Admission</td>
<td>1 782</td>
<td>46</td>
<td>10.7</td>
</tr>
<tr>
<td>12</td>
<td>1 425</td>
<td>46</td>
<td>11.8</td>
</tr>
<tr>
<td>27</td>
<td>768</td>
<td>46</td>
<td>12.0</td>
</tr>
<tr>
<td>54</td>
<td>1 350</td>
<td>48</td>
<td>10.3</td>
</tr>
<tr>
<td>64</td>
<td>450</td>
<td>53</td>
<td>22.4</td>
</tr>
<tr>
<td>114</td>
<td>2 624</td>
<td>64</td>
<td>32.2</td>
</tr>
<tr>
<td>156</td>
<td>4 221</td>
<td>74</td>
<td>39.0</td>
</tr>
<tr>
<td>270</td>
<td>2 295</td>
<td>79</td>
<td>46.9</td>
</tr>
</tbody>
</table>

Fig. 2. IVP at 10 minutes (after the introduction of chemotherapy) is negative — there is no displacement of left kidney and ureter, and the calyceal system of left kidney is normal. The double right ureter can still be noted.
due to the cytotoxic effect of therapy. Serial determinations of serum protein levels have been found of use in evaluating the efficacy of lymphoma therapy in cases where PLE is a manifestation, and this has proved to be so in our patient with Hodgkin's disease.

REFERENCES

Cryptococcus neoformans Meningitis
A Case Report

S. B. YALABURGI, K. C. MOHAPATRA

SUMMARY
A 4-year-old Motswana boy suffered from cryptococcal meningitis; in addition to the signs of meningeal irritation, he had cortical blindness and seventh cranial nerve palsy. The child improved after treatment with amphotericin B and 5-fluorocytosine. It is suggested that this combination may be better than either drug used alone.


Cryptococcosis (European blastomycosis or torulosis) is a pulmonary infection with a special predilection for the central nervous system. The disease is found world-wide, occurring mostly after puberty and predominantly in males. Cryptococci form neither spores nor mycelia and reproduce entirely by budding. The capsular material, a polysaccharide, is responsible for serological typing, slimy colonies and glairy lesions in the body. Four serotypes are found, of which type A is the commonest. It is seen in patients who have undergone cardiac surgery and receive immunosuppressant or long-term corticosteroid therapy. The meningeal infection mimics tuberculous meningitis. This is the first case reported from Botswana.

Princess Marina Hospital, Gaborone, Botswana
S. B. YALABURGI, M.B. B.S., D.CH., M.D., Paediatrician
K. C. MOHAPATRA, M.B. B.S., M.D., Pathologist

CASE REPORT
A 4-year-old Motswana boy weighing 10 kg was referred to the paediatric department of Princess Marina Hospital, Gaborone, with a history of irregular fever, cough, vomiting, frontal headache and lethargy of 2 months’ duration. He had been treated for tuberculous meningitis at the district hospital but 4 weeks of therapy produced no improvement. On admission he lay in a curled-up position and resented disturbance. He was emaciated, had a high temperature and was photophobic. Neck stiffness was present and the patient had a left-sided upper motor neuron facial palsy. The pupils were widely dilated, equal and round. They did not react to light but did contract to third nerve stimuli such as squeezing the lids. No papilloedema was observed. Except for the cortical type of blindness no other neurological defect was found and no primary lesion was detected in the lung.

The CSF pressure was 250 mm H2O; protein 16 mg/100 ml; sugar 43 mg/100 ml, and chloride 122 mEq/l. During the cell count numerous round to ovoid organisms (5 - 20 μm) were seen, which were capsulated and single-budded on India ink preparations. Culture in Sabouraud’s agar, fermentation and sugar assimilation tests proved them to be cryptococci. Animal pathogenicity tests were not carried out. Gram staining, Ziehl-Neelsen staining and culture did not reveal any bacteria.

Treatment was started with an initial test dose of 1 mg amphotericin B in 100 ml 5% dextrose intravenously, which was raised to a 15 mg dose gradually given over