The association of non-Hodgkin's lymphoma with glomerulonephritis

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Summary: Paraneoplastic glomerulonephritis is an infrequent complication in the course of non-Hodgkin's lymphoma (21 cases to date). We report a modality not previously described: mesangio-proliferative glomerulonephritis and mixed lymphocytic lymphoma, and review the literature on the subject. The onset of the two processes was simultaneous. Antitumour treatment induced simultaneous remission of the lymphoma and glomerulonephritis.

Introduction

The nephrotic syndrome is a paraneoplastic manifestation in 10% of all adult cases in some series (Lee et al., 1966; Eagen & Lewis, 1977). Hodgkin's disease has been the most commonly associated tumour, but cases have also been described in connection with other haematological diseases and carcinomas (Fer et al., 1981; Richmond et al., 1962).

There are only a few publications which associate glomerulonephritis (GN) with non-Hodgkin's lymphomas (NHL). We report a case of NHL presenting with nephrotic syndrome and renal failure due to mesangio-proliferative GN.

Case report

A 67 year old white woman was admitted to our hospital because of generalized oedema for 8 months.

On physical examination, the only positive findings were inguinal lymphadenopathy and anasarca. Laboratory data showed a normal haemogram; erythrocyte sedimentation rate, 110 mm in the first hour; urine protein excretion, 6.60 g/24 h; hyaline-cellular and granular casts; 9 to 10 erythrocytes and 15 to 20 leucocytes per high power field; serum total proteins, 41 g/l; albumin, 21 g/l; creatinine clearance, 15 ml/minute. The following results were either normal or negative: urine culture, immunoelectrophoresis, antistreptolysin titre, hepatitis B virus serology, VDRL, antinuclear antibodies, complement, cryoglobulin and circulating immune complexes.

Lymph gland biopsy showed mixed diffuse lymphocytic lymphoma (Figure 1). Chest X-ray, pedal lymphogram and hepatic and bone marrow biopsies were normal.

Kidney biopsy was performed from which eight glomeruli were obtained, some of them augmented in size and with an elevated number of nuclei. Deposits of fuchsinophilic material were detected in the basement membrane and the mesangium. No signs of amyloidosis, vasculitis or infiltration by lymphoma were observed (Figure 2). Granular deposits of IgM and C3 were detected by immunological techniques in mesangium and capillaries.

The patient was treated with CVP (cyclophosphamide, vincristine and prednisone) and diuretics. The treatment was continued for a total of 12 months.

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manifestations in cases are the other two

We have found 22 described cases of GN, including 7-74 nephropathy which was detected as shown in Table I. In cases 12 and 13, besides GN, renal infiltration by lymphoma was observed. It is not possible to establish a relationship between the histological types of NHL and GN.

In ten cases the evolution of both processes is mentioned explicitly. Eight of them (cases 2, 7, 8, 9, 10, 11, 12 and 15) presented parallel courses in that the progression or remission of the tumour was accompanied by a similar course in the kidney disease. The clinical course was independent in cases 6 and 13. In the case described by Hyman et al. (1973) (case 6), GN appeared 4 months after the appearance of the lymphoma, which was at that time in complete remission. Banks et al. (1984) (case 13) describe the onset of focal proliferative GN in a patient who had been diagnosed as having a lymphoma 13 years earlier. Partial remission of the nephropathy was achieved and maintained by means of a specific treatment, despite the progression of the lymphoma.

Minimal change glomerulonephritis has been the most common histological type of nephropathy associated with Hodgkin's disease (Eagen & Lewis, 1977). However, proliferative (Lowry et al., 1971), membranous (Row et al., 1975) and focal segmental sclerosis (Powderly et al., 1985) glomerular lesions have been described. There is, however, no predominant histological type associated with non-Hodgkin's lymphoma.

Glomerulonephritis can appear before, simultaneously or after the appearance of the lymphoma, whether it be Hodgkin's or non-Hodgkin's. When glomerular disease occurs at the same time as lymphoma, treatment of the neoplasia may suppress associated nephropathy. Although the antineoplastic drugs might act directly on the glomerulus, the regression after radiation therapy to extrarenal areas suggests that a direct effect of therapy on the glomerulus is not always the cause of the therapeutic response of the nephropathy.

The pathogenesis of GN in this type of patient is not clear. Alteration of T lymphocytes in patients with neoplasms (Shalhoub, 1974; Moorthy et al., 1976) has been mentioned as the disorder responsible for minimal-change nephropathy. In other histological types, the occasional finding of tumoral antigens and antibodies and of antigen-antibody complexes in serum and renal eluate (Costanza et al., 1973; Mendes Da Costa et al., 1974; Couser et al., 1974; Sutherland et

Discussion

We have found 22 cases of NHL and different types of GN, including our own. We have excluded the six cases described by Gupta (1973) and one of those described by Muggia & Ulmann (1971) given the absence of precise histological data. The remaining 15 cases are shown in Table I.

The average age of the patients was 47 years, range 7-74 years and the male: female ratio was 10:4. The patient's sex is not mentioned in one case (Gluck et al., 1973).

The presentation of GN and NHL was simultaneous in seven cases. Four cases presented with clinical manifestations of nephropathy (nephrotic syndrome in two and nephrotic syndrome plus kidney failure in the other two). Lymphadenopathy was the first manifestation in the three cases. There is no information regarding the presentation sequence in the remaining case.

The pathology of NHL is difficult to compare due to the diversity of the nomenclature employed in the classification. The majority (9 cases) were in stage IV, according to the Ann Arbor staging system (Carbone et al., 1971), at the time of diagnosis.

A wide range of histological glomerular lesions was shown

Figure 2 Glomerulus with augmented mesangial matrix, occupying the entire capsular area. (a) Haematoxylin-eosin x 400 and (b) haematoxylin-eosin and silver stain x 800.

There was complete remission of tumour and nephropathy which continued 7 years after presentation.
<table>
<thead>
<tr>
<th>Case</th>
<th>Histological types</th>
<th>GN</th>
<th>Mode of onset of nephropathy</th>
<th>Presentation sequence</th>
<th>Response of GN to treatment of NHL</th>
<th>Reference</th>
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<tbody>
<tr>
<td>1</td>
<td>Lymphosarcoma</td>
<td>Minimal-change</td>
<td>+</td>
<td>Onset of NHL 12 months later</td>
<td>No treatment of NHL</td>
<td>Ghosh &amp; Muehrcke (1970)</td>
</tr>
<tr>
<td>2</td>
<td>Reticulum-cell</td>
<td>Membrano-proliferative</td>
<td>+</td>
<td>Simultaneous</td>
<td>PR initial recurrence of NHL: no response</td>
<td>Muggia &amp; Ultmann (1971)</td>
</tr>
<tr>
<td>3</td>
<td>Well differentiated diffuse lymphocytic Lymphosarcoma</td>
<td>Diffuse proliferative with crescents</td>
<td>+</td>
<td>Onset of NHL 8 months later</td>
<td>No treatment of NHL</td>
<td>Rabkin et al. (1973)</td>
</tr>
<tr>
<td>4</td>
<td>Lymphosarcoma</td>
<td>Membranous</td>
<td>+</td>
<td>ND</td>
<td>ND</td>
<td>Gluck et al. (1973)</td>
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<tr>
<td>5</td>
<td>Burkitt</td>
<td>Membrano-proliferative</td>
<td>+</td>
<td>Onset of GN 4 months later</td>
<td>No relation</td>
<td>Hyman et al. (1973)</td>
</tr>
<tr>
<td>7</td>
<td>Well differentiated diffuse lymphocytic</td>
<td>Minimal-change</td>
<td>+</td>
<td>Simultaneous</td>
<td>CR</td>
<td>Gagliano et al. (1976)</td>
</tr>
<tr>
<td>8</td>
<td>Well differentiated diffuse lymphocytic</td>
<td>Diffuse proliferative with crescents</td>
<td>+</td>
<td>Simultaneous</td>
<td>PR</td>
<td>Petzel et al. (1979)</td>
</tr>
<tr>
<td>9</td>
<td>Well differentiated diffuse lymphocytic</td>
<td>Diffuse proliferative with crescents</td>
<td>+</td>
<td>Simultaneous</td>
<td>Death 3 days after diagnosis</td>
<td>Petzel et al. (1979)</td>
</tr>
<tr>
<td>10</td>
<td>Lymphoma T</td>
<td>Segmentary and focal sclerosis</td>
<td>+</td>
<td>Simultaneous</td>
<td>PR</td>
<td>Belghiti et al. (1981)</td>
</tr>
<tr>
<td>11</td>
<td>Diffuse convoluted T cell lymphocytic</td>
<td>Segmentary and focal sclerosis</td>
<td>+</td>
<td>Onset of NHL several weeks later</td>
<td>CR</td>
<td>Herskovitz et al. (1982)</td>
</tr>
<tr>
<td>12</td>
<td>Well differentiated diffuse lymphocytic</td>
<td>Focal proliferative with crescents; invasion by lymphoma</td>
<td>+</td>
<td>Onset of NHL 18 months later</td>
<td>PR</td>
<td>Banks et al. (1984)</td>
</tr>
<tr>
<td>13</td>
<td>Well differentiated diffuse lymphocytic</td>
<td>Focal proliferative with crescents; invasion by lymphoma</td>
<td>+</td>
<td>Onset of GN 13 years later</td>
<td>No relation</td>
<td>Banks et al. (1984)</td>
</tr>
<tr>
<td>14</td>
<td>Lymphocytic</td>
<td>Rapidly progressive (Type III)</td>
<td>+</td>
<td>Onset of GN 1 year later</td>
<td>PR</td>
<td>Biava et al. (1984)</td>
</tr>
<tr>
<td>15</td>
<td>Mixed diffuse lymphocytic</td>
<td>Mesangial</td>
<td>+</td>
<td>Simultaneous</td>
<td>CR</td>
<td>Present case</td>
</tr>
</tbody>
</table>

NHL: non-Hodgkin's lymphoma; GN: glomerulonephritis; NS: nephrotic syndrome; RF: renal failure; CR: complete remission; PR: partial remission; ND: no data.
al., 1974; Pascal et al., 1976), suggests an immune complex-mediated mechanism. Helin et al. (1980), in a study of 24 patients with different types of neoplasms without clinically manifested kidney disorder, demonstrated the existence of glomerular electron-dense complexes in 11 of them and a significant correlation with the presence of circulating antibodies. From the group of patients dealt with in our review, only one had circulating immune complexes and cryoglobulins were detected in two. Finally, it is possible that the association between neoplasms and GN is a coincidence, with independent evolution presented in some cases (Hyman et al., 1973: Banks et al., 1984). However, the discovery of a greater incidence of neoplasms in some types of GN (Lee et al., 1966; Gluck et al., 1973; Biava et al., 1984; Row et al., 1975) would lend support to a causal relationship.

In conclusion, we have presented a case of non-Hodgkin's lymphoma associated with nephrotic syndrome and kidney failure which widens the spectrum of glomerulonephritis in connection with this type of lymphoma, extending it to include mesangio proliferative glomerulonephritis, an association which had not been described previously.

References


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doi: 10.1136/pgmj.62.734.1141

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