Light Chain Disease and Massive Proteinuria

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We describe the case of a 64-year-old man with lambda type light chain disease, in whom panhypogammaglobulinemia was associated with anemia, massive Bence Jones proteinuria (24.6 g/L), and renal failure. Lambda type light chains were present in the serum.

Additional Keyphrases: cancer · Bence Jones protein · gammopathies · immunoglobulins

Light chain disease, which accounts for 16 to 19% of all myelomas (1), is characterized by hypogammaglobulinemia, Bence Jones proteinuria of either the kappa or lambda type (2), short life expectancy (30 months for the kappa type, 10 months for the lambda type) (3), and a high incidence of lytic bone lesions, hypercalcemia, and renal failure (2, 4). It occurs with equal frequency in men and women (3), and the mean age at which it is diagnosed is 59 to 61 years (2, 3). The reason for the impressive difference between the survival rate for the two types of light chain disease is unknown. It cannot be explained by differences in serum urea nitrogen, calcium, or albumin concentrations, or by degree of anemia or Bence Jones proteinuria, none of which differ significantly (3) between the two types of disease.

We report here a case of a lambda type light chain disease, characterized by hypogammaglobulinemia, anemia, and decreased renal function, but with unusual features of normocalcemia, absence of lytic bone lesions, and extremely intense proteinuria.

Case History

A 64-year-old man was admitted to our hospital for investigation of anemia and fatigue. His medical history was notable only for adult-onset diabetes mellitus controlled by insulin. Physical examination revealed no abnormalities.

At the time of admission, the patient's leucocyte count was 3500 cells per mm$^3$, hemoglobin concentration 58 g/L, hematocrit 15.9%, and platelet count 147 × 10$^3$ cells per mm$^3$. Blood viscosity was normal. The serum creatinine concentration was 265 mmol/L, urea nitrogen 15.6 mmol/L, calcium 2.3 mmol/L, uric acid 0.45 mmol/L, total protein 59 g/L, and albumin 35 g/L. Activities of liver enzymes were within normal limits. Two 24-h urine specimens contained 24.6 and 34.7 g of protein, as determined by precipitation with trichloroacetic acid.

A bone-marrow biopsy on the second day of hospitalization demonstrated 58% of the cells to be anaplastic plasma cells. Electrophoresis of serum protein (Figure 1) showed an M-component migrating in the gamma globulin region, with suppression of the normal gamma globulin bands. Immunoelectrophoresis of serum (Figure 2) showed only a small IgG arc reacting against the polyvalent antiserum in the gamma region. The trivalent and monospecific antisera confirm the suppression of the IgA and IgM components. The kappa arc against the anti-kappa antiserum was small; the lambda arc was thickened and bowed and also slightly displaced.

Electrophoresis and immunoelectrophoresis of urinary protein (Figures 1 and 2, respectively) showed the massive proteinuria to be almost exclusively from excreted free lambda light chains (Bence Jones protein), with only minor contributions from albumin and other proteins. The immunoglobulin concentrations (g/L) in serum were: IgG 4.0 (normal 6.4–13.5), IgA 0.12 (0.70 to 3.1), and IgM 0.22 (0.56 to 3.5). No lytic bone lesion was apparent on bone scan.

Materials and Methods

For electrophoresis of serum protein we used cellulose polyanilic membranes (Sephaphore III; Gelman Instruments (Canada) Ltd., Montreal, Quebec). For immunoelectrophoresis we used Titan Gel IEP plates (Helena Laboratories, Beaumont, TX 77704) with antisera from Hoechst-Behring (Canada) Inc., Montreal, Quebec, and normal human serum from a pool of normal patients.

We quantified IgG, IgA, and IgM in serum by rate nephelometry with the Immunochemistry Analyzer II (Beckman Instruments Inc., Brea, CA 92621).

Discussion

Multiple myeloma, a plasma-cell malignant disease, accounts for nearly 1% of all malignancies recorded in North America (5). It is characterized by the proliferation of a single clone of plasma cells, which produce a specific protein, generally (75–90% of cases) a complete immunoglobulin composed of a pair of heavy chains (γ, α, δ, or e) and a pair of light chains (κ or λ). In 16 to 19% (1) of all monoclonal gammopathies, however, only free light chains, either of the kappa or the lambda type, are produced. These cases form the subclass of multiple myelomas known as "light chain disease."

Although the clinical presentation of light chain disease may mimic renal failure, primary amyloidosis, or solitary bone tumor (2) or be associated with bone pain (as are 68% of all myelomas (5)), laboratory findings are often misleading. The Westgreen erythrocyte sedimentation rate (ESR) is lower than the rate usually seen in multiple myeloma, only 33% of all light chain disease being associated with an ESR exceeding 50 mm/h, as compared with 70% for all cases of multiple myelomas (5). Also, light chains are present in the serum of 80% of light chain disease cases (2, 6), but routine protein electrophoresis shows panhypop-
Fig. 1. Electrophoregrams of serum protein (left) and urinary protein (right) on cellulose acetate at pH 8.6

Left: Lane 2: quality-control serum. Lane 3: patient's serum with monoclonal protein spike. Lanes 1, 4, 5, 6: serum from patients with unrelated disorders.

Right: Lane 2: serum from a patient with multiple myeloma. Lane 3: quality-control serum. Lane 8: Patient's urine with Bence Jones proteinuria. Lanes 1, 4, 5, 6, 7: serum from patients with unrelated disorders

Fig. 2. Immunoelectrophoresis of serum proteins (left) and urinary proteins (right) on agarose gel

P: patient's serum or urine; NHS, normal human serum; triv, trivalent antiserum
gammaglobulinemia in two thirds of these cases (2) rather than the usual M-component spike that is seen in 76% of all myelomas (5). In addition to these special features, the diagnosis is made difficult because routine tests fail to detect the characteristic proteinuria of light chain disease: dipsticks, and sometimes the sulfosalicylic acid test as well, fail to react with Bence Jones proteins (2, 7, 8). Immuneelectrophoresis, electrophoresis, or immunofixation electrophoresis of urine are the only sure ways to establish their presence (7, 9).

Our case report is an example of the 5–12% of all multiple myelomas (10) that are lambda type light chain disease, as illustrated by the presence of hypogammaglobulinemia on electrophoresis and immunoelectrophoresis of the serum, and the evidence of free lambda light chain on immunoelectrophoresis of the serum and urine. We were impressed by the massive proteinuria (24.6 g/L), which was almost exclusively ascribable to lambda light chains as shown by immunoelectrophoresis of the urine. This degree of proteinuria is quite unusual (2, 3, 5, 11), and is the result not only of increased light chain synthesis but also of the high rate of renal excretion of this particular component, 2.5 times that for the excretion of kappa light chains (2).

The renal failure in this case, although moderate (the serum creatinine concentration was 265 μmol/L), is probably related to the high concentration of Bence Jones proteins in the circulating blood. The nephrotoxicity of these proteins is well known (2).

The role assigned to the laboratory in the diagnosis of a monoclonal gamopathy is unique, and requires an effective approach. Serum protein electrophoresis should be done on all patients suspected of having multiple myeloma, macroglobulinemia, or amyloidosis. It should also be part of the work-up of unexplained fatigue or weakness, anemia, high E.S.R., back pain, osteoporosis, osteolytic lesion or fracture, hypogammaglobulinemia, hypercalcemia, Bence Jones proteinuria, renal failure, or recurrent infection (8). If a monoclonal spike is seen on the serum electrophotogram, then serum immunoelectrophoresis, urine electrophoresis, and immunoelectrophoresis of a concentrated urine specimen, plus quantification of serum immunoglobulins and of protein in a 24-h specimen, should confirm the presence of a monoclonal protein and identify the immunoglobulin class and the light chain type (8, 12).

The presence of a normal serum electrophotogram together with a high index of suspicion based on clinical presentation should lead to immunoelectrophoresis and (or) immunofixation of serum and urine and a quantification of serum immunoglobulins (8, 9, 12). This strategy will allow detection of small amounts of monoclonal protein that otherwise would be undetected by serum electrophoresis, or the identification of a beta-migrating monoclonal protein, of a heavy chain disease, or of a light chain disease (2, 8, 9).

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References