Brief Report

Two Bence Jones Proteins of Different Immunologic Types in the Same Patient with Multiple Myeloma

By Ralph L. Engle, Jr. and Ralph L. Nachman

IMMUNOLOGIC and biochemical studies of the abnormal proteins found in the blood and urine of patients with multiple myeloma are increasing our understanding of the immunoglobulins. If, as commonly believed, multiple myeloma is a disease of a single clone of plasma cells, such studies also shed light on the protein synthesizing capabilities of single clones. While normal immunoglobulins have both type K and type L immunologic specificity, serum myeloma proteins and the derived Bence Jones proteins of the same patient ordinarily have either type K or type L specificity but not both. These observations have led to the concept that myeloma cells from a single patient or single clones of plasma cells are capable of producing only one type of immunoglobulin. Immunofluorescence studies of plasma cells from patients with multiple myeloma have been consistent with this theory. We are presenting a patient with multiple myeloma who had a type L myeloma protein in the serum and two Bence Jones proteins in the urine, one of type K and the other type L.

The patient was a 52-year-old woman who was found to have proteinuria. During hospitalization for a respiratory infection large amounts of Bence Jones protein were found in the urine by the heat test. Further study revealed a serum protein of 10.9 Gm. per cent with 9.8 Gm. per cent globulin. Serum calcium was elevated to 13.8 mg. per cent and uric acid to 10 mg. per cent. There was a marked anemia. X-ray studies showed punched-out osteolytic lesions in the skull and in several of the vertebral bodies. Bone marrow aspiration revealed the marrow to be infiltrated with 31 per cent abnormal plasma cells. In doing the Mazzini test for syphilis, it was discovered that a pyroglobulin was present in the serum. Boundary electrophoresis of serum and urinary proteins showed a gamma spike in the serum pattern with marked reduction of all other components and a double gamma peak in the urine pattern. Ultracentrifugation of the urinary proteins revealed the principal component to have a sedimentation constant of 2.6 Svedberg units, typical of Bence Jones protein. The patient died within 5 months of the first signs of disease, and the diagnosis of multiple myeloma was confirmed at autopsy.

The serum myeloma protein and the two Bence Jones proteins were separated by zone electrophoresis in Pevikon. The two Bence Jones proteins

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were well separated by this method (fig. 1). Fractions from each peak, shown in figure 1 as A and B, were eluted from the block, dialyzed against water, and lyophilized. Immuno-electrophoretic analysis using antihuman serum revealed complete separation of peak A and peak B (fig. 2). Neither of these proteins gave a reaction with an antiserum prepared against heavy chains. Peak B reacted with rabbit antiserum against a type K Bence Jones protein but not with an antiserum against a type L Bence Jones protein, whereas peak A reacted with the type L antiserum and not with the type K antiserum (fig. 3). These antisera were absorbed with normal serum and in some experiments with normal urine to remove any contaminants which might be present and were shown to be type specific. Both Bence Jones proteins were Inv(a) negative. The serum myeloma protein was shown to be a \( \gamma \)-globulin of type L.

The finding in the same patient of two Bence Jones proteins of different electrophoretic mobility, one of type K and the other type L specificity, is to our knowledge unique. Observations of similar significance, however, have been made. For example, Mannik and Kunkel\(^4\) have reported a patient with a type K serum myeloma protein and a type L Bence Jones protein. Also, a patient has been studied with two separate myeloma proteins in the serum, one a \( \gamma \)-A and the other a \( \gamma \)-globulin.\(^5\)

It is possible that under certain circumstances single clones of plasma cells may produce proteins of both type K and type L specificity. Pernis and Chiappino,\(^6\) using immunofluorescence technics, found that single cells in the germinal centers of lymphoid follicles in the spleen and lymph node of human beings appear to contain both type K and type L \( \gamma \)-globulins, whereas cells in the red pulp of the adult spleen contain one or the other but not both types.
Fig. 2.—Immunoelectrophoresis of fractions in peak A and peak B. Both react with antiserum to human serum.

Fig. 3.—Immunoelectrophoresis of fractions in peak A and peak B. Peak A reacts with antiserum to Bence Jones protein, type L; and peak B reacts with antiserum to Bence Jones protein, type K.

On the other hand, Potter\(^7\) has shown in mouse myeloma induced by intraperitoneal injection of adjuvant-staphylococci mixtures or of mineral oil that several different protein producing cell lines may develop in a single host.

In the patient reported here, if we hypothesize that the two Bence Jones proteins and the serum myeloma protein are all produced in the same cell and that the light chains and heavy chains are formed independently, we would expect to see two myeloma proteins in the serum, one of type K and the other of type L, due to competition by the separate type K and type L light chains for the available heavy chains.\(^8\) The fact that this does not occur suggests that, as in the mice, the two Bence Jones proteins are being produced in at least two cell lines.
Summary

In summary, two Bence Jones proteins, one of type K and the other of type L immunologic specificity, and a serum myeloma protein of type L were demonstrated in the same patient with multiple myeloma. It is probable that, in this instance, dissemination from at least two clones of plasma cells has occurred.

Summario in Interlingua

Duo proteinas Bence Jones—con specificitates immunologic le un del typo K e le altere del typo L—e un seral proteina de myeloma del typo L eseva demonstrate in le mesme patiente con myeloma multiple. Es probable que in iste caso dissemination habeva occurrite ab al minus duo clones de plasmo-cytos.

References

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