CONCISE REPORT

Coincident Chronic Lymphocytic Leukemia and Osteosclerotic Multiple Myeloma

By M. T. Jeha, T. J. Hamblin, and J. L. Smith

We report the first occurrence of chronic lymphatic leukemia (CLL) and osteosclerotic multiple myeloma (MM) in the same patient. The surface Ig of the CLL and the monoclonal serum Ig had different heavy and light chain classes, and CLL lymphocytes failed to secrete the monoclonal Ig in short-term culture. We conclude that they were entirely separate malignancies occurring together by chance.

Both chronic lymphatic leukemia (CLL) and multiple myeloma (MM) are B-cell tumors. On rare occasions, these tumors coexist, and in this circumstance the question should be asked as to whether this represents a progression or maturation of an existing tumor or the occurrence of two separate diseases in the same individual.

The bony lesions of MM are characteristically osteolytic, and the presence of any osteosclerosis calls for the diagnosis to be reconsidered. Osteosclerosis has been described in MM in a small number of cases, particularly around osteolytic lesions or in areas of periosteal new bone formation, but widespread osteosclerosis is extremely rare.1

We describe here the first association between CLL and osteosclerotic MM and demonstrate that they are two entirely separate diseases.

MATERIALS AND METHODS

Clinical Data

A.H., aged 64 yr, complained of tiredness for 2 mo and when examined, had palpable lymph nodes in the left axilla and right submandibular area, and a barely palpable spleen. Full blood count showed Hb 10.3 g/dl, WBC 37.5 x 10^9/liter, with 84% small lymphocytes and a blue background to the film. Erythrocyte Sedimentation Rate (ESR) was 132mm in the first hour. Serum electrophoresis revealed a monoclonal band in the y region, which was identified by immunoelectrophoresis as IgG. Free A light chains were present in the urine at a concentration of 0.13 g/liter. Serum IgG was 83g/liter, IgA 0.4 g/liter, and IgM 0.2g/liter.

Skeletal x-rays showed widespread osteosclerotic lesions in the pelvis and dorsal and lumbar vertebrae, but no evidence of osteolysis, and a radioisotopic bone scan showed a uniformly increased uptake with no "cold" areas.

Bone marrow aspiration yielded peripheral blood only. Trephine biopsy of bone was unsuccessful on two occasions. Clinically, he had a normal prostate, and serum acid phosphatase was normal.

Needle biopsy of the prostate yielded normal prostatic tissue. Eventually, open biopsy of the iliac crest under general anesthesia demonstrated large numbers of plasma cells in the marrow.

He was treated with chlorambucil, 6 mg daily, and prednisolone, 10 mg daily, and on this regime his white count returned to normal but his serum IgG continued to rise. He was then given 4-day courses of Melphalan, 18 mg, and prednisolone, 100 mg, every 6 wk. There was no effect on his monoclonal IgG, and subsequent treatment with cyclophosphamide, vincristine and CCNU was also unsuccessful.

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RESULTS

At the time of study, the peripheral lymphocyte count was \(43.5 \times 10^9\) /liter and contained >99% lymphocytes. Peripheral blood lymphocyte preparations stained for surface IgM (66%) and IgD (5%) heavy chains with \(\kappa\) (68%) light chain, with no evidence for a population of cells with surface \(\lambda\) light chain intracellular Ig. In culture neoplastic cell preparations synthesized 0.1 of their supernatant and 0.4 of their lysate total labeled protein. On gel analysis the cells secreted a light to heavy chain excess of 4.4.

DISCUSSION

Where two different tumors of the same tissue occur in the same individual it is important to determine whether or not they have the same origin, since valuable information on the biology of tumors can be derived from such an event.

A total of 16 patients with coincident CLL and MM has been described in the literature. These cases have been detailed in two reviews, although both omit the case reported by Sany et al. In most of these cases, information on immunoglobulin class is lacking. In our patient, both the heavy and light chain classes of the surface Ig of the CLL and the MM protein differed, and furthermore, CLL lymphocytes held in short-term culture failed to produce immunoglobulin of the class of the MM protein, thus demonstrating that the two tumors had a separate origin. In addition, the CLL responded to chemotherapy, whereas the MM progressed despite several different chemotherapeutic regimes.

Osteosclerotic MM is a rare variant that has recently been reviewed. Sixty-eight patients have been described in the literature of whom 27 had osteosclerotic lesions without osteolyis. Such widespread bony sclerosis as was seen in our patient has only rarely been reported. The syndrome carries a worse prognosis than osteolytic MM and is associated with peripheral neuropathy in approximately 50% of patients. Our patient had no neurologic abnormalities but failed to respond to chemotherapy.

In our patient, the diagnosis of myeloma was difficult to establish because the characteristic radiologic features of MM were absent, and it was not possible to obtain bone marrow samples either by aspiration or trephine.

The osteosclerotic bony lesions were thought to resemble those of metastases from carcinoma of the prostate, but this organ was clinically normal, his serum acid phosphatase was normal, and needle biopsy of the prostate yielded normal prostatic tissue.

In view of the fact that monoclonal immunoglobulins occur in between 1% and 5% of patients with CLL, it was thought necessary to culture the patient’s small lymphocytes to demonstrate that they were not producing the monoclonal IgG, and armed with this information we decided to perform an open biopsy of bone to obtain adequate histology. This demonstrated heavy infiltration with malignant plasma cells.

Several series have demonstrated a high incidence of second malignancies in CLL, and others have suggested that in MM also there is a high incidence of second malignancies.

In our own recently analyzed series of 100 cases of CLL, 27 had second malignancies. It seems likely therefore that in both of these conditions there is an increased incidence of second malignancies, and by chance, they will occasionally occur together quite independently. Both may have a long latent period before they draw attention to themselves and therefore the fact that they are discovered together should not be taken to imply that they arose together.

Table 1.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sig Int. Ig</th>
<th>Total cpm</th>
<th>% Ig/Total</th>
<th>HC LC/HC</th>
<th>Total cpm</th>
<th>% Ig/Total</th>
<th>HC LC/HC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.H.</td>
<td>MDk Negative</td>
<td>87,590</td>
<td>0.1</td>
<td>(\mu) 4.4</td>
<td>788,760</td>
<td>0.4</td>
<td>(\mu) 1.3</td>
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HC, heavy chain; LC, light chain.
REFERENCES

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