once the oral route becomes impossible to use. With our titration regimen, all five evaluated patients in the study had a reduced pain score on Day 5.

According to our unit guidelines, doses of up to 2 mg of clonazepam were used in this case series. These guidelines follow the results of studies of clonazepam in neuropathic pain syndromes in which doses of up to 8 mg of clonazepam were used, but a number of patients developed marked drowsiness. Despite these lower doses of clonazepam, some patients in the series experienced drowsiness suggesting this to be a limiting side effect when clonazepam is used for cancer-related neuropathic pain.

The results of this small preliminary study suggest that a randomized, controlled trial about the use of clonazepam as an adjuvant analgesic in neuropathic pain should be performed.

Heino Hugel, MD, MRCP
John E. Ellershaw, FRCP
Andrew Dickman, BsC (Hons), MSc, MRPharmS
Marie Curie Center Liverpool
Liverpool, United Kingdom

References

Chronic Lymphocytic Leukemia Resembling Metastatic Bone Disease—An Unusual Manifestation

To the Editor:

Chronic lymphocytic leukemia (CLL) with features resembling metastatic bone disease is very rare. We report such a case with a literature review.

Case Report

Mrs. A. first presented with left breast cancer in 1997 at the age of 66. Pathology of the lumpectomy specimen showed a 2 cm intracystic papillary carcinoma with atypical ductal hyperplasia. Because of positive margins, she subsequently had a modified radical mastectomy that showed no residual disease. Axillary lymph nodes and metastatic work up were all clear. Hormone receptors were positive and she was started on tamoxifen for 5 years.

In January 2002, she presented with posterior cervical triangle lymphadenopathy and mild leucocytosis. Clinical examination also revealed mild splenomegaly. The hemoglobin was 149 g/L, white blood cell count 16.2 × 10^9/L, neutrophil count 0.3 × 10^9/L, lymphocyte count 0.6 × 10^9/L, and platelet count 177 × 10^9/L with smudge cells. Serum calcium was normal. Peripheral lymphocyte immunotyping studies showed changes of a clonal B-cell proliferation consistent with chronic lymphocytic leukemia (CLL). She had Stage 0 disease and no therapy was offered.

In the summer of 2002, she presented with back pain. Bone scintigram scan and computerized tomography (CT) of the spine revealed mixed lytic and sclerotic lesions at T8/T9. CT of the sacrum revealed a 2.4 × 1.3 cm lobulated
soft tissue mass at mid-coccyx level. A biopsy of that lesion was consistent only with CLL for the underlying marrow.

There was no other evidence of breast cancer relapse but it was uncommon for CLL to present with fractures similar to thoracic spinal bone metastases. A CT-guided biopsy of the lytic lesion in T8 was performed. Pathology with immunoperoxidase profile supported a diagnosis of metastatic CLL. There was no evidence of metastatic breast cancer. The patient was started on fludarabine. Palliative radiotherapy was administered to her lytic bone lesions at T8/T9.

She developed thrombocytopenia after the first cycle of fludarabine. A bone marrow biopsy was performed. The marrow was mildly hypercellular with several ill-defined lymphoid aggregates, most within intertrabecular locations. They were composed of small, mature lymphocytes with indistinct chromatin and absent nucleoli. By immunohistochemistry, these were weakly CD 20 positive and positive for BcL-2 and CD23: a profile characteristic for CLL. Erythroid and myeloid elements were readily identified with no features of myelodysplasia. Megakaryocytes were increased in number in keeping with a peripheral destructive mechanism for the marked thrombocytopenia. There was no evidence of metastatic carcinoma. The final conclusion was CLL with megakaryocytic hyperplasia consistent with immune thrombocytopenia. The cytogenetics by FISH showed absence of abnormalities for 11q, 13q, and 17p deletion. However, it revealed the presence of an abnormal clone containing an additional chromosome 12 in the bone marrow of this patient.

She was treated with a steroid without significant recovery of her platelet counts. A newer generation bisphosphonate, risendronate, was commenced in view of her bony involvement. Despite that, her pain was poorly controlled and her disease continued to progress with a new compression fracture of L2. There was, however, marked improvement of the previous abnormalities at T8/T9 following the palliative radiotherapy. She was treated with a trial of palliative CVP chemotherapy.

**Comment**

CLL presenting with features resembling lytic bone metastases is very rare. Six cases have been reported in English (Table 1)1–5 and two cases in other languages.6,7 Most of the cases have hypercalcemia as the presenting symptom. It is postulated that hypercalcemia is a result of localized bone resorption by activated osteoclasts in the vicinity of tumor cells metastatic to bone.1–3,5 Other cytokines and local regulatory factors such as interleukin-1, tumor necrosis factor, IL-6, and prostaglandins have been postulated to account for hypercalcemia as well.5

Hypercalcemia is a poor prognostic feature in a number of hematologic malignancies.2 The prognosis for patients with advanced CLL presenting with bone metastases and hypercalcemia was generally measured in weeks despite treatment directed at both the CLL and the hypercalcemia.4

### Table 1: Features of Metastatic Bone Disease in Chronic Lymphocytic Leukemia

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Age/Sex</th>
<th>Pathological Fractures</th>
<th>Bone Lesions</th>
<th>Hypercalcemia</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. BMJ/1970</td>
<td>62/M</td>
<td>multiple</td>
<td>lytic</td>
<td>yes</td>
<td>chlorambucil cyclophosphamide</td>
<td>succumbed to illness</td>
</tr>
<tr>
<td>2. McMillian/1980</td>
<td>73/F</td>
<td>right humerus left hip</td>
<td>lytic</td>
<td>yes</td>
<td>chlorambucil</td>
<td>alive and normal lifestyle</td>
</tr>
<tr>
<td>3. Redmond/1983</td>
<td>65/M</td>
<td>nil</td>
<td>lytic</td>
<td>yes</td>
<td>chlorambucil prednisone</td>
<td>not mentioned</td>
</tr>
<tr>
<td>4. Littlewood/1990</td>
<td>72/M</td>
<td>femur pelvis</td>
<td>lytic</td>
<td>yes</td>
<td>chlorambucil prednisone</td>
<td>died from pneumonia</td>
</tr>
<tr>
<td>5. Littlewood/1990</td>
<td>70/F</td>
<td>left humerus vertebrae</td>
<td>lytic</td>
<td>no</td>
<td>chlorambucil</td>
<td>died from pneumonia</td>
</tr>
<tr>
<td>6. Van de Castelee/1994</td>
<td>40/M</td>
<td>nil</td>
<td>lytic</td>
<td>yes</td>
<td>chlorambucil prednisone</td>
<td>died from hypercalcemia and sepsis</td>
</tr>
</tbody>
</table>
Although our patient did not have hypercalcemia, her clinical course was complicated by immune thrombocytopenia. She carried Trisomy 12 which appears to be associated with a relatively poor prognosis. She continued to have further disease progression despite fludarabine and bisphosphonates. Our reporting this case hopes to add further information in the literature about this rare manifestation of CLL.

Vivian Yau  
University of Toronto  
Toronto, Ontario, Canada

Monique Christakis, MD  
Nadia Ismiil, MD  
Edward Chow, MB BS  
Bone Metastases Site Group at Sunnybrook & Women’s College Health Sciences Center  
Toronto, Ontario, Canada

Sandeep Sedhiev, MD  
Anthony Cuthbert, MD  
William Oder Health Center  
Brampton Memorial and Etobicoke General Campuses  
Toronto, Ontario, Canada


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References


