A Rare Case of Chronic Myelogenous Leukemia and Plasma Cell Myeloma in the Same Patient

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Dear Editor

CML and plasma cell myeloma (PCM) arise from pluripotent stem cells and lymphoid cells, respectively [1]. Since different cell lines give rise to CML and PCM, development of both malignancies in one patient is uncommon; only 17 such cases have been reported worldwide [2-5]. Here, we attempt to address questions about the mechanisms of co-existence of these two diseases.

A 76-yr-old Korean male was referred to our hospital in April 2010 with thrombocytosis and leukocytosis with basophilia. Radiographic examination revealed splenomegaly. Using bone marrow (BM) analysis and quantitative reverse-transcription PCR, the patient was diagnosed as having chronic phase BCR-ABL1-positive CML. After three weeks of imatinib mesylate (IM) therapy, the patient’s leukocyte and platelet counts normalized.

Three years later, examination of the patient’s BM revealed normal cellularity, but with plasma cells accounting for 17.5% of all nucleated cells (Table 1). Hypercalcemia, uremia, anemia, and lytic bone lesions were not observed. Serum electrophoresis and immunofixation electrophoresis revealed immunoglobulin (Ig)A lambda type monoclonal protein. The patient was diagnosed as having asymptomatic PCM. No chemotherapy was administered for PCM, but IM therapy achieved maintenance of the CML major molecular response status. Clinical and laboratory findings are summarized in Table 1.

No symptoms or blood tests indicated the presence of PCM at the time of CML diagnosis. However, since it is possible that a PCM clone was present at the time of CML diagnosis, we retrospectively performed immunohistochemical staining of a BM specimen. This staining was positive for CD138 and IgA lambda. We also analyzed Ig heavy chain gene rearrangements (InVivoScribe Technologies, San Diego, CA, USA) in initial and follow-up BM samples. DNA samples from both time points showed gene rearrangement at the same diversity region, indicating that the same PCM clone was present at CML diagnosis.

When we reviewed the previously reported cases of CML and PCM in the same patient (Table 2), we first asked whether the malignancies occurred spontaneously, or whether treatment of the first neoplasm induced the second malignancy. Among the 17 cases, six patients were diagnosed first as having CML, and then PCM. Five of those six patients received IM, while one received busulfan. The mean interval before discovery of the second malignancy was 37.7 months (range, 3 to 88 months). IM has been reported to have both stimulatory and inhibitory effects on PCM cell proliferation [6]. Studies have found no evidence that IM treatment increases the occurrence of any secondary malignancies compared with the lifetime risk of cancer in the general population [7, 8]. There is no clear evidence that IM used for CML treatment caused PCM; however, because IM becomes widely used as an effective target therapy in other...
cancers as well as CML, close investigation of this issue is necessary.

Another five of the 17 patients were diagnosed as having PCM first, and then CML. Two of them were not treated for PCM until their CML diagnosis. The remaining three patients received melphalan, dexamethasone, and other drugs, which have not been reported to cause CML. Two patients with PCM underwent radiation therapy (RT) before their CML diagnosis. In general, irradiation is known to cause leukemia. One study calculated the theoretical probability of an individual exposed to radiation acquiring the t(9;22) translocation to be 0.007/Gy, with a minimum lapse of 5.1 yr [9]. Since the intervals between irradiation and CML development in these cases were less than two years, it seems unlikely that RT induced CML.

Concurrent development of CML and PCM was identified in six of 17 patients, and two patients developed CML before being treated for PCM. Therefore, 8 patients (47%) had a secondary malignancy without having received therapy, so it is difficult to conclude that treatment of the first neoplasm caused a secondary malignancy.

Another important question is whether the two cancers have the same origin. Since CML arises from pluripotent hematopoietic stem cells, it may be possible that CML cells can transform into malignant plasma cells. No Philadelphia chromosomes or BCR-ABL1 transcripts were found when our patient was diagnosed as having PCM, suggesting that the myeloma cells did not evolve from pre-existing CML cells.

We have described a patient with both CML and PCM. The mechanism of co-existence is unclear. To identify more cases, it is important for clinicians and pathologists to be aware that co-existence of CML and PCM is rare, but possible.

Authors’ Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.
Table 2. Reported cases of CML and PCM occurring in the same patient

| Concurrent | Age (yr)/gender | Interval between two diseases (month) | CML | PCM | Reference |
|------------|----------------|--------------------------------------|-----|-----|-----------|
|            |                |                                      | WBC (×10^9/L) | CT  |           |            |
| 1          | 58/M           | 0                                    | 140 | HU, BU, TG | IgG κ | MP | 3,300 cGy | [2] |
| 2          | 72/F           | 0                                    | 162.4 | HU, IFN, BU | IgG κ | IFN, VD, PD | None | [2] |
| 3          | 81/M           | 0                                    | 28.7 | None      | IgA κ | MP | None | [3] |
| 4          | 66/M           | 0                                    | 171 | HU, IFN, BU | IgG κ | MP | None | [2] |
| 5          | 85/F           | 0                                    | 8.1  | UK        | IgG λ | UK | UK   | [2] |
| 6          | NS             | 0                                    | NS  | IM        | NS   | BD | None | [4] |
|            |                |                                      |     |           |       |    |      |     |
| PCM→CML    |                |                                      |     |           |       |    |      |     |
| 7          | 77/M           | 33                                   | 145 | 6-MP      | BJP | BD, Cy, Len | None | [2] |
| 8          | 71/M           | 24                                   | 40.8 | HU        | IgG κ | MP | Yes  | [2] |
| 9          | 70/M           | 33                                   | 25.2 | UK        | IgG κ | MP | None | [2] |
| 10         | 47/M           | 33                                   | 23.9 | UK        | BJP κ | None | UK   | [2] |
| 11         | 64/F           | 17                                   | 14  | DA        | IgG κ | None | 3,000 cGy | [2] |
| CML→PCM    |                |                                      |     |           |       |    |      |     |
| 12         | 65/F           | 88                                   | 43  | BU        | IgG κ | BU, PM | 2,000 cGy | [2] |
| 13         | 68/M           | 20                                   | NS  | IFN, IM   | IgG λ | MP | None | [2] |
| 14         | 71/M           | 38                                   | NS  | IM        | BJP λ | UK | UK   | [2] |
| 15         | 76/M           | 14                                   | NS  | IFN, IM   | IgA κ | MP | None | [2] |
| 16         | 72/F           | 3                                    | 31.3 | IM        | IgG κ | None | None | [2] |
| 17         | 57/F           | 65                                   | 52.38 | IM     | IgA κ | Thal, Dox, BD | None | [5] |
| 18         | 79/M           | 36                                   | 18.8 | IM        | IgA λ | None | None | The present case |

Abbreviations: PCM, plasma cell myeloma; BD, bortezomib and dexamethasone; BJP, Bence-Jones protein; BU, busulfan; CT, chemotherapy; Cy, cyclophosphamide; DA, dasatinib; Dox, doxorubicin; F, female; HU, hydroxyurea; IFN, interferon; IM, imatinib mesylate; Len, lenalidomide; M, male; MP, mercaptopurine; NS, not stated; PD, prednisolone; PM, phenylalanine and mustard; RT, radiation therapy; TG, thioguanine; Thal, thalidomide; UK, unknown; VD, vindesine; WBC, white blood cell.

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