

Letter to the Editor

Is There an Entity of Radiation-Induced Chronic Myeloid Leukemia? Report of a Case and Brief Review of the Literature

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TO THE EDITOR

Radiotherapy along with chemotherapy has been routinely used for the treatment of cancer. Therapy-related acute leukemia or myelodysplastic syndrome are well-recognized entities, whereas less is known about the incidence of secondary chronic myeloid leukemia (CML) after cytotoxic treatments, particularly radiotherapy, for a primary malignancy. We present a case of CML diagnosed 12 years after radiotherapy for prostate cancer.

In 2017, a 77-year-old man, although asymptomatic, was found to have leukocytosis. Laboratory findings included a hemoglobin level of 12.7 g/dL, a platelet count of $390 \times 10^9/L$, and a white blood cell count of $43.3 \times 10^9/L$, with 1% promyelocytes, 9.5% myelocytes, 3% metamyelocytes, 6.5% band neutrophils, 55.5% segmented neutrophils, 10% lymphocytes, 3% monocytes, 5.5% eosinophils, and 6% basophils. Hepatic and renal function tests were normal. The lactic dehydrogenase level was increased to 305 U/L (normal range: 124–222 U/L). Bone marrow examination revealed the Philadelphia chromosome t(9;22)(q34;q11) without additive cytogenetic abnormalities. No hepatosplenomegaly or lymphadenopathy was found on computed tomography. A diagnosis of CML was made and the patient was started on daily dasatinib at 70 mg. After one month, however, the drug was discontinued because he developed right pleural effusion. The pleural effusion resolved in one week and the drug was restarted with good control of leukocytosis. After three months of dasatinib treatment, complete cytogenetic response was achieved, with disappearance of the Philadelphia chromosome in the bone marrow. Deep major response has been maintained as of November, 2019.

The past history was notable in that the patient was diagnosed with prostate cancer (stage T1cN0M0) at the age of 65. The prostate-specific antigen (PSA) value was increased to 6.02 ng/mL (normal range: < 4 ng/mL). Needle biopsy of the prostate demonstrated well-differentiated adenocarcinoma. He was treated using ^{192}Ir high-dose-rate brachytherapy (18 Gy in 3 fractions) to be followed by three-dimensional conformal external beam radiotherapy (40 Gy in 20 fractions). No chemotherapy was administered. Since then, the PSA values remained in the normal range and he did well until 2017, when his annual blood test revealed leukocytosis.

The present case suggests a link between CML and

preceding radiotherapy for prostate cancer. Bauduer *et al.*¹ reported that CML developed as a secondary neoplasm in a patient 10 years after radiotherapy for breast cancer and in a patient 25 years after radiotherapy for uterine cervix cancer. Secondary CML was also reported in two patients four and 10 years after radioiodine treatment for thyroid cancer.² Recently, the Japanese CML Cooperative Study Group compiled a list of 11 cases of CML subsequent to chemotherapy and/or radiotherapy for different solid cancers.³ This list includes two patients who developed CML two and five years after radiotherapy, which was the sole treatment for prostate cancer and pharyngeal cancer, respectively. Similarly, a survey on three cohorts (thyroid, prostate, and uterine corpus cancer survivors) initially treated by radiotherapy demonstrated that they had an increased risk of myeloid neoplasms, including CML.⁴ Considering the previous radiotherapy for prostate cancer, our patient likely developed radiotherapy-related CML.

Although a significant number of secondary CML cases have been reported to be associated with preceding chemotherapy,^{3,5} radiotherapy-related CML may be rare. In addition to therapeutic radiation, diagnostic radiation may increase the risk of CML when used repeatedly in the same individual. Ju *et al.*⁶ reported a patient who developed CML following repeated exposure to radiography and computed tomography over a year for recurrent pneumothorax. Au *et al.*⁷ also presented a possible case of diagnostic radiation-induced CML, and they hypothesized that the cumulative radiation exposure at a young age is an important pathogenic factor for the development of CML.

Recent studies reported that patients with therapy-related CML exhibited a good therapeutic response to tyrosine kinase inhibitors and favorable outcomes similar to *de novo* CML.^{3,5,8} However, these studies comprised patients who were treated by chemotherapy alone, chemotherapy with radiotherapy, or immunosuppressive therapy for previous diseases. Thus, further case accumulation of radiation-related CML and long-term prospective epidemiologic studies are needed to define this peculiar condition as a distinct clinical entity. Molecular analysis using modern techniques, such as deep sequencing, may reveal differential gene mutations between radiation-related CML and *de novo* CML.

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CONFLICT OF INTEREST

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