Chronic myeloid leukemia after chemotherapy for adenocarcinoma of the rectum: A case report

Likhasit Sanglutong*
Somchai Insiripong*


Chronic myeloid leukemia (CML) after chemotherapy for any primary malignancy has been occasionally reported. Herein we reported one definite case of CML who was diagnosed after the treatment of adenocarcinoma of the rectum. A 79-year-old Thai man was diagnosed with moderately differentiated adenocarcinoma of the rectum invading the urinary bladder. And he was treated with rectal resection and lymph nodes excision, followed by 5-fluoro-uracil and leucovorin therapy. He remained in complete remission for 1.5 years until he suddenly passed the hematochezia for one day and very high white blood cell and platelet counts without weight loss. The physical examination revealed no hepatosplenomegaly, no abdominal mass. The blood tests revealed: hemoglobin 10.6 g%, white blood cell 57,100/mm², platelet 2,898,000/mm², neutrophil 68 %, lymphocyte 6 %, basophil 20 %, band 1 %. The chromosome study from the blood was positive for 46,XY,t(9;22)(q34;q11.2)[20] but negative for JAK-2 V617F mutation. Serum Carcinoembryonic antigen (CEA) level was continually normal both before the surgery and through out the follow-up. His definite diagnosis was established as CML, the accelerated phase with the history of 5-FU chemotherapy for the adenocarcinoma of the rectum. He did not accept further investigations for detecting the local recurrence of the rectal adenocarcinoma and refused tyrosine kinase inhibitor therapy. He could survive one year after the diagnosis of CML without serious symptom while this study was being reported. So far it could not be concluded that the occurrence of CML after the chemotherapy of the rectum adenocarcinoma is just co-incidental or has any relationship.

Keywords: Chronic myeloid leukemia, adenocarcinoma of rectum.

Correspondence to: Insiripong S. Department of Medicine, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima, 30000.
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*Department of Medicine, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima, 30000
มะเร็งเม็ดเลือดขาวเรื้อรัง (chronic myeloid leukemia หรือ CML) ที่เป็นตามหลังการได้รับยาเคมีบำบัดเพื่อรักษามะเร็งชนิดต่าง ๆ นั้น ยังพบได้ไม่น้อยมาก ในรายงานนี้เป็นของผู้ป่วยมะเร็งเม็ดเลือดขาวเรื้อรัง ที่เป็นหลังจากผู้ป่วยได้รับยาเคมีบำบัดเพื่อรักษา adenocarcinoma ของลำไส้ตรง ผู้ป่วยเป็นชายไทย อายุ 79 ปี เคยรับการรักษาวินิจฉัยว่าเป็น moderately differentiated adenocarcinoma ของลำไส้ตรง ที่เริ่มแพร่กระจายเข้ากระเพาะปัสสาวะ และได้รับการรักษาด้วยการผ่าตัด rectal resection and lymph node excision และ ต่อมาได้รับยาเคมีบำบัดด้วย 5-fluoro-uracil และ leucovorin ผู้ป่วยมีอาการในระยะย่อยสลายในระหว่างการรักษา เหลือเวลาน้อยในระยะสุดท้าย แต่ผู้ป่วยมีการตอบสนองต่อการรักษาดังกล่าว ผู้ป่วยมีการหายคลาสการแพร่กระจายของมะเร็งเม็ดเลือดขาว แต่ไม่สามารถจัดการด้วยการรักษาด้วยยาเคมีบำบัด ผู้ป่วยมีการตอบสนองต่อการรักษาด้วยยาเคมีบำบัด แต่ไม่สามารถจัดการด้วยการรักษาด้วยยาเคมีบำบัดได้ดีกว่า ผู้ป่วยมีอาการดีขึ้น แต่ไม่สามารถจัดการด้วยการรักษาด้วยยาเคมีบำบัดได้ดีกว่า

การตรวจในเรื่องการแพร่กระจายของมะเร็งเม็ดเลือดขาว ได้รับการตรวจอย่างละเอียดและมีการสังเกตการณ์อย่างต่อเนื่อง การตรวจพบว่าผู้ป่วยมีการแพร่กระจายของมะเร็งเม็ดเลือดขาวในระยะเร่งเร้าตามหลังการได้รับยาเคมีบำบัดสำหรับการรักษา adenocarcinoma ของลำไส้ตรง ผู้ป่วยไม่ได้รับการตรวจเพิ่มเติมเพื่อหาการกลับเป็นซ้ำที่ตำแหน่งเดิมของโรคเรื้อรัง adenocarcinoma ของลำไส้ตรง

คำสำคัญ: มะเร็งเม็ดเลือดขาวเรื้อรัง, มะเร็งเม็ดเลือดขาวเรื้อรัง, มะเร็งเม็ดเลือดขาวเรื้อรัง, มะเร็งเม็ดเลือดขาวเรื้อรัง, มะเร็งเม็ดเลือดขาวเรื้อรัง.
Chronic myeloid leukemia (CML) is one of the clonal myeloproliferative neoplasms (MPN) especially the white blood cell precursors. Therefore it is mainly characterized by the high peripheral white blood cell count with the young forms of all stages of the differentiation and the existence of the BCR-ABL translocation in most patients. (1) Almost all cases of CML occur spontaneously as de novo CML whereas the secondary CML following any solid tumor from various organs with or without chemotherapy is considered rare. It has been found as a case report in the patients with the esophageal carcinoma, lymphoma, breast carcinoma or thyroid carcinoma with radioactive iodine therapy. (2,3) Likewise, only 4 cases of CML were occasionally reported after the diagnosis and treatment of adenocarcinoma of the colo-rectum. All of them were males and three of four cases were more than 60 years old, whereas the rest was only 25. (4) And all were presumed to be due to the various regimens of chemotherapy resulting in treatment-related CML. The time interval between the diagnosis of the primary cancer and the treatment-related CML was 1 - 16 years. (9) Likewise, the occurrence of adenocarcinoma of colon is either hardly found in cases with CML, viz., only two of 150 patients with CML, chronic phase who were treated with imatinib. (5) Herein, we report a Thai man who emerged a definite CML after he was diagnosed as having pathologically proven adenocarcinoma of the rectum and the treatment with chemotherapy.

Case Report

A 79-year-old Thai man was referred to a hematologist because of a sudden passing of hematochezia for one day and high white blood cell and platelet counts in the periphery, without fever, or weight loss.

One and a half years ago, he had passed the hematochezia for 1 month, and he was found to have a mass at the finger tip from the per rectum examination. The colonoscopy and the cystoscopy found a mass at the upper rectosigmoid colon invading into the wall of the urinary bladder. The microscopic pathology revealed moderately differentiated adenocarcinoma of the rectum. The rectal resection and lymph nodes excision with sigmoid colostomy were performed and one of three lymph nodes excised was found positive for cancer. He was treated with 6 courses of 5-fluoro-uracil 425 mg/m² + leucovorin 20 mg/m² as the adjuvant chemotherapy, no radiation. Nine months after chemotherapy, the ultrasonography of the abdomen was unremarkable while complete blood counts (CBC) was tested and found unremarkable every 3 months until the last one showed marked leukocytosis as above.

The follow-up physical examination revealed no hepatosplenomegaly, no abdominal mass.

The blood tests: hemoglobin (Hb) 10.6 g%, hematocrit (Hct) 33.9 %, White blood cell (WBC) 57,100/mm³, platelet 2,898,000/mm³, MCV 81.3 fl, RDW 19.0 %, neutrophil 68 %, lymphocyte 6 %, monocyte 1 %, eosinophil 4 %, basophil 20 %, band 1 %

The chromosome study from the blood showed positive for 46,XY,t(9;22)(q34;q11.2)[20] but negative for JAK-2 V617F mutation, carcinoembryonic antigen (CEA) 8.5 ng/mL (0 -15), normal liver and kidney function tests.
The ultrasonography of the abdomen showed no hepatosplenomegaly, no abdominal mass.

His definite diagnosed as established as CML, accelerated phase after the chemotherapy of adenocarcinoma of the rectum. However, the patient refused further investigations for detecting the local recurrence of rectal cancer and likewise the tyrosine kinase inhibitor therapy. He didnot attend the clinic again while this study was being reported, he was known still alive without any serious symptom one year after the diagnosis of CML by phone.

Discussion

The CML was definitely diagnosed based on the high WBC and the presence of BCR-ABL translocation and it was in the acceleration phase because of the high basophil count (20 %)(13) while adenocarcinoma of the rectum was diagnosed based on tissue pathology, although CEA did not increase. Actually, the very high level of CEA is found in only 41.2 % of colorectal carcinoma. (14)

CML after chemotherapy or treatment-related CML is rare. Some authors propose that 5-FU may stimulate the dormant hematopoietic stem cells, especially CML(15), which may be carcinogenic(9) or chemotherapy may induce the translocation of the genes of the bone marrow stem cells. (16)

In the analysis of the incidence of second cancers among CML patients before the era of tyrosine kinase inhibitors, there are increased risks for many cancers such as the stomach (standardized incidence ratios or SIR = 2.8, 95% CI: 1.3, 5.1), skin (or SIR = 5.4, 95% CI: 3.2, 8.5), the urogenital tract (SIR = 1.6, 95% CI: 1.2, 2.2), and lymphoid leukemia (SIR = 5.5, 95% CI: 1.8, 12.9) in comparison with the general population, no risks for the colorectal cancer or non-Hodgkin lymphoma. (17)

Both CML and the colorectal carcinoma have chromosomal aberrations. While BCR-ABL mutation is found in most cases of the former(18), the genomic changes in some cases of the latter include the activation of proto-oncogenes (K-Ras) and the inactivation of at least 3 tumor suppression genes, namely, loss of APC (region 5q21), loss of p53 (region 17p13), and loss of heterozygosity for the long arm of chromosome 18 (18q LOH), others including the TGFB and PIK3CA. (19) However, the relationship between these two sets of the chromosomal aberrations from both groups has not been mentioned.

BCR-ABL translocation was found in our case.

So far it cannot be simply concluded that the emergence of CML after colon carcinoma and vice versa suggesting their truly causal relationship or just a co-incidence. (20)

Conclusion

A 79-year-old Thai man was definitely diagnosed as CML, 1.5 years after 5-FU therapy for rectal cancer. However, the relationship between CML and the rectal cancer with or without chemotherapy could not be simply concluded.

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