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Case Report
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Progression from Chronic Myeloid Leukemia to Chronic Lymphocytic Leukemia: A Rare Case

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Abstract

Background: The occurrence of myeloproliferative and lymphoproliferative diseases in the same individual is rare. However, such cases are described in the literature. CLL and CML co-occurrence in one patient develops in 3 forms - two diseases at the same time, CLL after the diagnosis of CML, or vice versa CML after the diagnosis of CLL.

Case Report: 52 years old male Caucasian patient presented with nose bleeding, fatigue, fever, ascites. CML was considered and was done all necessary tests. CBC, bone marrow aspiration and FISH analysis showed significant results with CML. Ph chromosome was positive in all metaphases. Imatinib 400 mg was prescribed to the patient and after 12 months he achieved MMR. After 11 years CBC showed leukocytosis so imatinib dosage elevated to 600 mg and PCR monitoring for MMR was performed. The patient did not lose MMR but leukocytosis dynamically elevated, so we decided to perform bone marrow trephine-biopsy.

Result: Lymphocytosis. Flow cytometry results: CD19+, CD20+, CD22+, CD5+,CD10-, CD23+, CD43+, CD56-, FMC7-, CD200+, CD11c-, CD103- CLL diagnosis verified and chlorambucil 4 mg was prescribed.

Conclusions: Although it is uncommon, physicians must consider CLL in the spectrum of CML progression along with more common secondary neoplasms such as solid tumors or lymphomas.

Keywords: Coexisting CLL/CML; Chronic lymphocytic leukemia; Chronic myeloid leukemia

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Introduction

The diagnosis of multiple clonal hematologic neoplasms, especially two dissimilar sorts of blood disorders such as myeloproliferative and lymphoproliferative neoplasms in a single patient is rare. And it is not clear whether the neoplasms are pathogenetically related, or they are independently developed disorders. MPNs- clonal hematological disorders that develop as a result of uncontrolled proliferation of one or more myeloid lineages in the bone marrow and cause overproduction of red blood cells, white blood cells and platelets [1]. Lymphoproliferative neoplasms develop as a result of uncontrolled proliferation of lymphocytes that cause lymphocytosis, lymphadenopathy, and can infiltrate bone marrow as well as solid organs [2]. Chronic Lymphocytic Leukemia (CLL) is the commonest leukemia among adults in the western countries and Chronic Myeloid Leukemia (CML) is the commonest myeloproliferative disorder which occurs as a result of a fusion of the BCR gene on chromosome 22 and the ABL gene on chromosome 9. This mutation leads to uncontrolled proliferation of myeloid cells via activating tyrosine kinase pathway. There are several results of studies which have shown that patients with myeloproliferative neoplasms are prone to develop a secondary neoplasm. And as a result, it affects the overall survival of such patients [3,4]. Most of the cases reported in the literature so far are patients with concurrently CLL and CML [5-8] or patients who diagnosed with CML after several years after being treated with chemotherapy or radiotherapy for CLL [9-16]. Based on published data to date, few patients have been reported to develop CLL after diagnosis of CML [17-20]. In this study, we report an additional patient who developed CLL several years after the diagnosis of CML.

Case Presentation

The Caucasian patient is a 52-yr-old man who presented in 13/01/2004 with nose bleeding, fatigue, fever, ascites. ECOG risk stratification was 1. At the time of the diagnosis a CBC test gave the following results: hemoglobin 8.3 g/dl, leukocyte (WBC) count 275 × 10^9/L and platelet count 111 × 10^9/L. The spleen size was 243 mm × 120 mm-massive splenomegaly. Bone marrow aspiration

showed result confident to CML. As all anamnestic and laboratory results suggested CML, so the patient underwent cytogenetic examination for BCR ABL gene analysis. Cytogenetic examination proved CML with 100% positivity in all metaphases. Patient was diagnosed CML chronic phase intermediate risk according to the Sokal scoring system. In physical and ultrasound examination no enlarged lymph nodes were revealed. Due to the high number of WBC and platelet initially patient was prescribed Hydroxyurea 2000 mg daily. After decreasing WBC and PLT count daily 400 mg imatinib orally was administered. Complete cytogenetic response achieved after 7 months, and MMR was obtained after 12 months. Patient visited hospital regularly and continued his treatment with imatinib. Till 2015 he was in remission. Subsequent BCR/ABL analyses from 2005 until now were negative. In March 2014 he had a severe respiratory infection and was hospitalized. CBC test gave following results: hemoglobin 12.7 g/dl, leukocyte (WBC) count 19.8 × 10^9/L, blast 1%, (lymphocytes, 9 × 10^9/L; monocytes, 11 × 10^9/L; eosinophils, 1 × 10^9/L; basophils, 1 × 10^9/L; metamyelocytes, 11 × 109/L; myelocytes, 4 × 10^9/L); and platelet count 459 × 10^9/L. He did not lose MMR. CBC results normalized after patient's recovery from respiratory infection. In 20/04/2015, a CBC showed a 11.77 WBC count and elevated dynamically. 20.04.2015 imatinib dose elevated to 600 mg due to leukocytosis. After 2 monthslymphocytosis-70% was identified. The spleen size was in normal range. Patient continued imatinib treatment. In 2017 an increase in the number of lymphocytes led to a detailed re-examination of the patient. Bone marrow studies were performed to evaluate the patient's CML status and the absolute lymphocytosis 85 % and myelocytes 0.4; metamyelocytes 0.2; rod-core 3.2; segment core 7.6; lymphocytes 85.0 revealed. Immunophenotyping by flow cytometry showed CD19+, CD20+, CD22+, CD5+, CD10-, CD23+, CD43+, CD56-, FMC7, CD200+CD11c-, CD103-, kappa/lambda ratio 53 - B cells. Results of the CT scans showed: Normal upper abdominal CT. In the right iliac bone, near the sacro-iliac joint a nodular lesion of approximately 15 mm × 10 mm in size was observed in a lucent, peripherally sclerotic form. On both sides of the midline in the neck multiple lymph nodes, which's size did not exceed 3 cm, were observed. Inflammatory mucosal thickening was observed in both maxillary sinuses on the left. According to the detailed examination, the patient was diagnosed with CLL. And was prescribed chlorambucil 4 mg. After treatment his condition and lab results improved. Currently the patient continues in morphologic, cytogenetic, and molecular remission of CML. His CLL is in the indolent phase and is being monitored without therapeutic intervention.

Discussion

Chronic Lymphocytic Leukemia (CLL) is the most common leukemia among adults in the western countries and Chronic Myeloid Leukemia (CML) is the most common myeloproliferative disorder. In both disorders there is a higher incidence in males, especially in elder individuals [21]. CLL patients tend to develop secondary malignancies. I can be due to chemotherapy or depressed immune system [22]. Patients with CML are rarely associated with a second neoplasm [23,24]. In contrast to this, the development of secondary neoplasms is common in CLL patients. This is due to the immunosuppression of these patients and the chemotherapy and radiation therapy used in their treatment [22]. But the majority of secondary neoplasms are non hematologic and mostly occur several years after the initial diagnosis of CLL [25]. Unfortunately, associations between these diseases have not widely been reported. CLL\CML coexistence could be affected by interactions between the lymphoid and myeloid lineages. Although it has not been proven, there are currently some assumptions about the mechanism of this condition. In some studies, reported that cells with BCR\ABL fusion gene produce a variety of cytokines. Interleukin- 3 is one of them that influences human CD 34(+) CD 38(−) immature cells and increases the production of B lymphoid cells [26,27]. These effects can cause developing of CLL in CML patents. Results of some trials show that the B-cell receptor inhibitors as well as cytotoxic agents in CLL therapy can cause genetic mutations that lead to progression of myeloid neoplasms [28,29]. There are few studies that have retrospectively analyzed CLL patients who later progressed to CML. The aim of the study was to detect low levels of the BCR-ABL gene with the sensitive method of reverse transcription polymerase chain reaction in the initial CLL diagnosis specimens. But, the BCR-ABL gene was not detected in the initial specimens. These results show that the development of CML may occur later [30,31]. As we mentioned before it is rare for both of these diseases to be diagnosed in a patient concurrently. There are three types of CML\CLL coexistence: CML occurs before CLL, CML occurs after CLL and concurrent occurrence. There were 8 patients with concurrent CLL and CML, according to Laurent et al. [32] Up to the present time, there have been 19 documented cases of patients diagnosed with CLL followed by CML, with durations fluctuating in most cases from 6 to 96 months [33] and 21 years in one case [34]. Up to date, there have been only 4 reported cases who developed CLL after the initial diagnosis of CML [35,36]. In 2 cases CLL developed after 7 years of onset of CML otherwise in other 2 cases it developed after 20 and 36 months. It is reported that in 2 patients CML and CLL arose from distinct clones. Whether these are two different diseases occurring by chance in the same patient or a common defective stem cell that causes leukemia remains to be clarified. In this study we are reporting a patient who developed CLL 11 yr after the diagnosis of chronic phase CML who achieved morphologic, cytogenetic, and molecular remission with imatinib mesylate. The patient developed leukocytosis and absolute lymphocytosis. Bone marrow trephine biopsy and immunophenotypic findings confirmed CLL diagnosis. To our knowledge this is the fifth such case in literature.

Conclusion

It is rare for CML to progress to CLL. Despite its rarity, it is important for clinicians to include CML in the spectrum of CLL progression along with more common secondary neoplasms such as solid tumors or lymphomas. Given the risk of CLL in CML patients, routine screening is recommended to monitor for the occurrence of lymphadenopathy or lymphocytosis in the blood and the faster-than-expected development of organomegaly, which is not characteristic of CML patients treated with a tyrosine kinase inhibitor, in order to make a timely diagnosis. In addition, it should be taken into account that the presence of molecular-cytogenetic mutation indicates genetic instability and an increased risk of developing multiple neoplasms.

References

1. Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, et al. The 5th edition of the World Health Organization Classification of Hematolymphoid Tumors: Myeloid and Histiocytic/Dendritic Neoplasms. Leukemia. 2022;36(7):1703-19.

2. Justiz Vaillant AA, Stang CM. Lymphoproliferative Disorders. StatPearls Publishing: Treasure Island, FL, USA, 2023.

3. Frederiksen H, Farkas DK, Christiansen CF, Hasselbalch HC, Sørensen HT. Chronic myeloproliferative neoplasms and subsequent cancer risk: A

Danish population-based cohort study. Blood. 2011;118(25):6515-20.

4. Landtblom AR, Bower H, Andersson TM. Second malignancies in patients with myeloproliferative neoplasms: A population- based cohort study of 9379 patients. Leukemia. 2018;32(10):2203-10.
5. Maher VE, Gill L, Towners PL, Wallace JE, Savas L, Woda BA, et al. Simultaneous chronic lymphocytic leukemia and chronic myelogenous leukemia: evidence of a separate stem cell origin. Cancer. 1993;71:1993-97.
6. Cresscenzi B, Sacchi S, Marasca R, Temperani P, La Starza R, Matteucci C, et al. Distinct genomic events in the myeloid and lymphoid lineages in simultaneous presentation of chronic myeloid leukemia and B-chronic lymphocytic leukemia. Leukemia. 2002;16:955-6.
7. Vilpo JA, Klemi P, Lassila O, Schroder J, de la Chapelle A. Transformation in chronic granulocytic leukemia. Different blast cell clones in different anatomical sites. Acta Haematol. 1979;62:247-50.
8. Esteve J, Cervantes F, Rives S, Rozman M, Zarco MA, Montesettat E. Simultaneous occurrence of B cell chronic lymphocytic leukemia and chronic myeloid leukemia with further evolution to lymphoid blast crisis. Hematologica. 1997;82:596-9.
9. Faguet GB, Little T, Agee JF, Garver FA. Chronic lymphocytic leukemia evolving into chronic myelocytic leukemia. Cancer. 1983;52:1647-52.
10. Teichmann JV, Sieber G, Ludwing WD, Karow J, Ruehl H. Chronic myelocytic leukemia as a second neoplasia in the course of chronic lymphocytic leukemia. Leuk Res. 1986;10:361-8.
11. Whang-Peng J, Gralnick HR, Johnson RE, Lee EC, Lear A. Chronic granulocytic leukemia (CGL) during the course of chronic lymphocytic leukemia (CLL): correlation of blood, marrow, and spleen morphology and cytogenetics. Blood. 1974;43:333-9.
12. Schreiber ZA, Axelrod MR, Abebe LS. Coexistence of chronic myelogenous leukemia and chronic lymphocytic leukemia. Cancer. 1984;54:697-701.
13. Scholar, Hashimi L, Al-Katib A, Mertelsmann R, Mohamed AN, Koziner B. Cytofluorometric detection of chronic myelocytic leukemia supervening in a patient with chronic lymphocytic leukemia. Am J Med. 1986;80:269-75.
14. Nanjangud DJ, Saikia TK, Chopra H, Kadam PR, Advani SH. Development of Ph positive chronic myeloid leukemia in a patient with chronic lymphocytic leukemia treated with total body irradiation: a rare association. Leuk Lymphoma. 1996;22:355-9.
15. Mossafa H, Fourcade C, Pulic M, Jary L, Cheze S, Szpiro-Tapia S, et al. Chronic lymphocytic leukemia associated with myelodysplastic syndrome and/or chronic myeloid leukemia: evidence of independent clonal chromosomal evolution. Leuk Lymphoma. 2001;41:337-41.
16. Sakditad S, Watsachon P, Yaw A, Nattanicha Ch, Diego OB, Natchaya P, et al. Rare case of an elderly male with progression to chronic myeloid leukaemia secondary to chronic lymphocytic leukaemia. Eur J Case Rep Intern Med. 2024;11(4):004297.
17. Salim R, Wang L, Lin K, Clark RE. Chronic lymphocytic leukemia developing in the course of chronic myeloid leukemia. Leuk Lymphoma. 2002;43:2225-7.
18. Gargallo P, Cacchione R, Chena C, Dupont J, Garay G, Riveros D, et al. Chronic lymphocytic leukemia developing in a patient with chronic myeloid leukemia: evidence of distinct lineage-associated genomic events. Cancer Genet Cytogenet. 2005;161:74-77.
19. Giovanni D'A, Marica G, Luigiana L, Fiorella D'A, Silvia D, Teodora S, et al. Chronic Lymphocytic Leukemia After Chronic Myeloid Leukemia in the Same Patient: Two Different Genomic Events and a Common Treatment? J Clin Oncol. 2012;30(32):e327-30.
20. Sharathkumar B, Vidal B, Harsha D, Domnita C. A Rare Patient with Chronic Myeloid Leukemia and Chronic Lymphocytic Leukemia. Ann Clin Lab Sci Autumn. 2008;38:405-409.
21. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin. 2019;69:7-34.
22. Bartik MM, Welker D, Kay NE. Impairments in immune cell function in B cell chronic lymphocytic leukemia. Semin Oncol. 1998;25:27-33.
23. Jin HH, Won HJ, Myong SC, Lee M, Soon CW. Acute lymphoblastic leukemia without Philadelphia chromosome occurring in chronic myelogenous leukemia with the Philadelphia chromosome. Am J Hematol. 2003;74:218-20.
24. Zhang X, Ji L, Liu S, Wang J. Ph-negative acute lymphocytic leukemia occurring after interferon therapy for Ph-positive chronic myelocytic leukemia. Leuk Res. 2003;27:367-9.
25. Hisada M, Biggar RJ, Greene MH, Fraumeni JF, Travis LB. Solid tumors after chronic lymphocytic leukemia. Blood. 2001;98:1979-81.
26. Peters DG, Klucher KM, Perlingeiro RC, Dessain SK, Koh EY, Daley GQ. Autocrine and paracrine effects of an ES-derived, BCR/ABL transformed hematopoietic cell line that induces leukemia in mice. Oncogene 2001;20:2636-46.
27. Crooks GM, Hao QL, Peterson D, Barsky LW, Bockstoce D. IL-3 increases production of B lymphoid progenitors from human CD34(+) CD38(−) cells. J Immunol. 2000;165:2382-9.
28. Badal S, Thapaliya P, Oh K. Co-existence of chronic lymphocytic leukemia and chronic myeloid leukemia and underlying pathogenetic mechanisms. Eur J Haematol. 2023;110:117-120.
29. Pedersen-Bjergaard J. Insights into leukemogenesis from therapy-related leukemia. N Engl J Med. 2005;352:1591-1954.
30. Jamroziak K, Puła B, Walewski J. Current treatment of chronic lymphocytic leukemia. Curr Treat Options Oncol. 2017;18:5.
31. Hallek M, Al-Sawaf O. Chronic lymphocytic leukemia: 2022 update on diagnostic and therapeutic procedures. Am J Hematol. 2021;96:1679-1705.
32. Laurenti L, Tarnani M, Nichele I, Ciolli S, Cortelezzi A, Forconi F, et al. The coexistence of chronic lymphocytic leukemia and myeloproliperative neoplasms: a retrospective multicentric GIMEMA experience. Am J Hematol. 2011;86:1007-1012.
33. Payandeh M, Sadeghi E, Khodarahmi R, Sadeghi M. Appearance and disappearance of chronic myeloid leukemia (CML) in patient with chronic lymphocytic leukemia (CLL). Int J Hematol Oncol Stem Cell Res. 2014;8:49-53.
34. Sakditad S, Watsachon P, Yaw A, Nattanicha C,Diego OB, Natchaya P, et al. A Rare Case of an Elderly Male with Progression to Chronic Myeloid Leukaemia Secondary to Chronic Lymphocytic Leukaemia. Eur J Case Rep Intern Med. 2024;11(4):004297.
35. Salim R, Wang L, Lin K, Clark RE. Chronic lymphocytic leukemia developing in the course of chronic myeloid leukemia. Leuk Lymphoma. 2002;43:2225-7.
36. Gargallo P, Cacchione R, Chena C, Dupont J, Garay G, Riveros D, et al. Chronic lymphocytic leukemia developing in a patient with chronic myeloid leukemia: evidence of distinct lineage-associated genomic events. Cancer Genet Cytogenet. 2005;161:74-77.