International Journal of Research and Reports in Hematology

4(2): 21-26, 2021; Article no.IJR2H.68840

A Literature Review and Case Report of Concurrent Myelodysplastic Syndrome and Chronic Lymphocytic Leukemia

Muzeyyen Ak Aslaner[1*] and Birsen Sahip[1]

[1]Department of Hematology, Zonguldak Bulent Ecevit University Faculty of Medicine, Incivez 67100, Zonguldak, Turkey.

Authors' contributions

This study was carried out in collaboration between both authors. Author MAA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the article. Author BS directed the analysis of the study. She directed the literature reviews. Both authors have read and approved the last article.

Article Information

Editor(s):
(1) Dr. Armel Hervé Nwabo Kamdje, University of Ngaoundere, Cameroon.
Reviewers:
(1) Vishal Jindal, Oakland University, USA.
(2) Simona Pagliuca, Cleveland Clinic Foundation, USA.
Complete Peer review History: http://www.sdiarticle4.com/review-history/68840

Case Study

Received 20 March 2021
Accepted 25 May 2021
Published 28 May 2021

ABSTRACT

Coexistence of B-cell Chronic Lymphocytic Leukemia (B-CLL) and Myelodysplastic Syndrome (MDS) is rare condition(1). A 76-year-old female patient presented with pruritic and hyperemic rashes in her whole body, was diagnosed with MDS concurrent with B-CLL as a result of determined leucocytosis(White blood cell count: 52.200/mm^3; 57% lymphocytosis, 33% monocytosis) in the complete blood count. She also had a history of receiving chemoradiotherapy for cervical cancer in her past medical history. A biopsy was performed from her rashes and histopathological findings showed chronic lymphocytic vasculitis. Cases of lymphocytic cutaneous vasculitis associated with hematological malignancies have been reported. Coexistence of B-CLL and MDS is an independent entity from the management of CLL, but receiving chemotherapy for a carcinoma is a risk factor for developing MDS. So, we aimed to present a case, who has a risk factor for developing MDS and skin involvement of B-CLL together, with literature and emphasize that two different hematological malignancies that develop simultaneously or at different times in the same patient may coexist. This rare condition should be considered in lymphocytosis and blast association.

**Corresponding author: E-mail: drmaslaner@hotmail.com;*

Keywords: Myelodysplastic syndrome; lymphocytosis; chronic lymphocytic leukemia; monocytosis.

1. INTRODUCTION

Concurrent occurrence of B cell chronic lymphocytic leukemia (B-CLL) and myelodysplastic syndrome (MDS) is rare [1] Although MDS is associated with previous chemotherapy or radiotherapy in most cases, it may also develop during diagnosis and treatment of B-CLL [2]. Herein, we provide a literature review together with a rare case diagnosed with concurrent MDS and B-CLL.

2. CASE PRESENTATION

A 76-year-old female patient presenting with pruritic rashes in 2019 was found to have a leukocyte count of 52.200/mm3 (57% lymphocytosis, 33% monocytosis), Hgb of 9.2 g/dl, platelet of 39.000/mm3, MCV of 106, AST of 22, ALT of 24, total protein of 7.4 g/dl, albumin of 2.9 g/dl, urea of 56 mg/dl, creatinine of 1.4 mg/dl, LDH of 709 U/L, uric acid of 13.8 mg/dl, and ferritin of 408 ng/ml.

Physical examination showed unremarkable findings, except for reddish raised papules of 1-3 cm in size on both lower extremities. Medical history revealed the presence of diabetes, hypertension, and a diagnosis of cervical cancer dating back to 2011. She had received radiotherapy (RT) together with 6 courses of cisplatin in 2012, followed by another course of chemotherapy in 2013 consisting of paclitaxel and carboplatin. Peripheral blood smear showed polychromasia and macrocytosis in red blood cells, hypogranulation in neutrophils, and mature lymphocytes accompanying 5% blasts. (Fig1). A bone marrow aspiration and biopsy were performed, showing increased number of blasts and dysplastic changes in all three series, with hypo-normo cellular bone marrow and blast percentage of 15% and 30% monoclonal lymphocytes (Fig.2).

Flow cytometric analysis of the bone marrow aspiration showing 15% blasts in the myeloblast area revealed the following: CD33 highly positive; CD7, CD11b, CD13, CD16+CD56+, CD15, CD34 and HLA-DR moderately positive; and CD19, CD19 +, and CD34 + low positive. Although these findings suggested acute myeloid leukemia (AML) blasts, an analysis with lymphocyte gating demonstrated immunophenotypic findings for B-lymphocyte markers that were consistent with B-CLL (i.e. CD19, CD19+CD5+, CD19+CD23+, CD23, CD22 and HLA-DR was moderately positive; CD20 positive) (Fig.3).

The dysplastic changes in bone marrow aspiration affecting all three series and the 15% blast count were thought to be suggestive of MDS with excess blasts-2 (MDS-EB-2). Initial treatment for MDS consisted of 5-Azacytidine 75 mg/m^2 s.c. for 7 days. Since cytogenetic testing was not available in our hospital, genetic testing could not be performed. Also, skin biopsy from the papular lesions showed chronic lymphocytic vasculitis (Fig.4). Lymphocytic cutaneous vasculitis has been reported in association with hematological malignancies [3].

3. DISCUSSION

Chronic lymphocytic leukemia (CLL) is an hematological malignancy characterized by increased percentage of lymphocytes together with an absolute lymphocyte count of greater than $5000/mm^3$. CLL is a well-differentiated CD5 + CD19 + monoclonal B cell malignancy, which exhibits a remarkably wide clinical spectrum and higher incidence in the elderly. Until now, no standard dose of chemotherapy regimen has been shown to be curative. Although allogeneic hematopoietic stem cell transplantation (allo-HSCT) may lead to long term remission and disease control, it is also associated with significant morbidity and mortality [4]. In recent years, targeted agents (eg, Bruton tyrosine kinase [BTK] inhibitors, PI3-kinase inhibitors, BCL2 inhibitors) and other research therapies (eg chimeric antigen receptor T cells) are changing treatment options for recurrent or refractory disease. Complications associated with CLL include infections, autoimmune diseases, transformation into a more aggressive lymphoid malignancy (Richter transformation), secondary solid tumors including melanoma and non-melanoma skin cancers as well as secondary hematological malignancies such as acute leukemia (AL) and MDS [5]. MDS encompasses a heterogeneous group of clonal myeloid stem cell disorder affecting mostly the elderly individuals. In patients with CLL, establishing a diagnosis of MDS may be challenging, particularly in case of marked bone marrow involvement. Anemia, neutropenia and thrombocytopenia are among hematological findings that are commonly observed in both CLL and MDS. If CLL involvement is present in bone

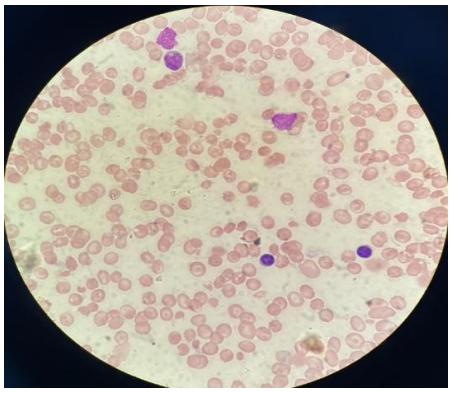

Fig.1. Peripheral blood smear

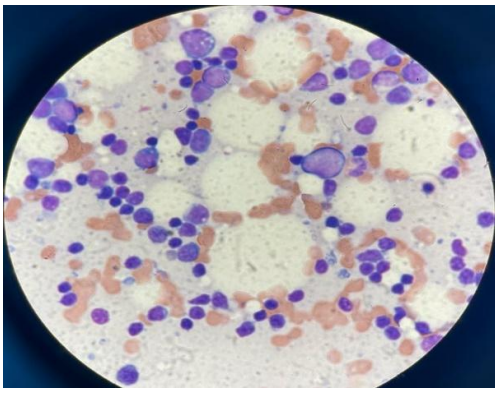

Fig. 2. Bone marrow biopsy

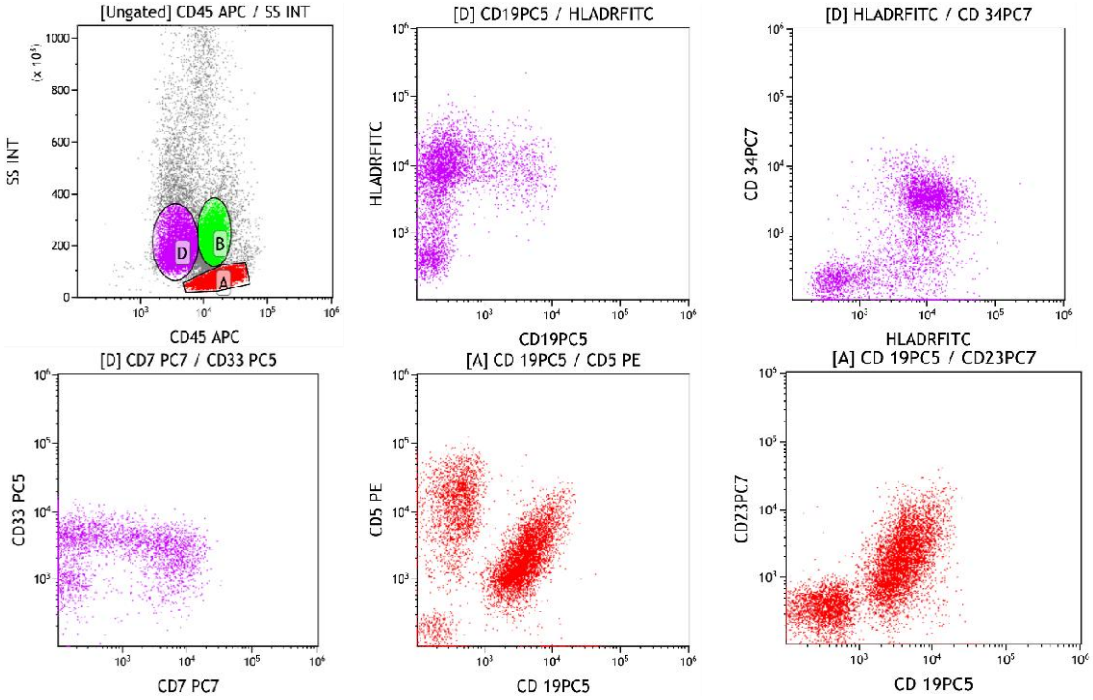

Fig. 3. Bone marrow aspiration flow cytometry analysis (A:CLL lymphocyte zone,B: monocyte zone,D: myeloblast zone)

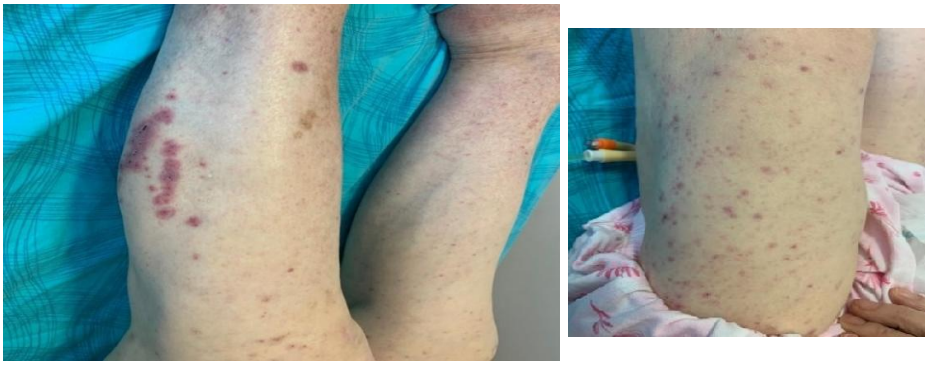

Fig. 4. CLL skin lesions

marrow samples, a detailed examination of the cellular components of the whole bone marrow may be required to confirm the presence of MDS [4] Blast transformation has been reported to occur in less than 2% of the patients with CLL, and most of these cases have acute lymphoblastic leukemia. Co-occurrence of MDS and AML in patients with CLL is rare [6], and most cases are secondary to treatments administered [7]. When we reviewed the literature while evaluating this case, we found that the coexistence of CLL and MDS is rare (Table-1).

In a study by Tambaro FP et al., de novo AL/MDS has been described in CLL patients without a prior chemotherapy history. These patients were older than those developing AL/MDS secondary to CLL treatment [4]. The etiology of concomitant MDS/AML with treatment naïve CLL is unknown.Lima et al. proposed that CLL and myeloid disorder may arise from a common clone, and reported one patient with CLL and de novo AML [2]. Similarly, Ferrera et al. reported a CLL patient with chronic myelomonocytic leukemia, and suggested similar pathogenetic mechanisms [8]. In this case report, advanced age and previous history of chemotherapy due to cervical cancer were consistent with a diagnosis of MDS. Again, peripheral blood smear, bone marrow aspiration, and bone marrow biopsy suggested the same diagnosis. Based on the laboratory findings, she was also diagnosed with CLL, although this was considered a newly occurring hematological disease. We believe that these two hematological malignancies in the same patient may arise from different clones. Biopsy samples from her skin lesions were consistent with chronic lymphocytic vasculitis, which is reported in association with hematological malignancies [3]. Paraneoplastic vasculitis is defined as the vascular inflammation occurring in malignant conditions. Although malignancy represents one of the main causes of vasculitis, other potential culprits include collagen tissue disorders, infections, allergic reactions, and drug reactions [9]. Of all cutaneous vasculitis cases, 1% to 7% have been reported to be associated with solid tumors and hematological malignancies [10], among which leukemias, lymphomas, and myeloproliferative disorders are the most common causative entities. These lesions are characterized by lymphocytic vasculitis, vascular and perivascular lymphocytic infiltration, fibrinoid necrosis, and endothelial hyperplasia [11]. As in our patient, most cases with concomitant lymphocytic vasculitis have been reported in patients with leukemia or MDS [12]. On the other hand, vasculitis in CLL is uncommon, although most patients have leukemic vasculitis characterized by malignant cells and leukemic infiltration within and around the blood vessel walls [13,14]. The frequency of secondary malignancies in CLL patients seems to correlate with immunesuppression and neoplastic clone development [6], and ranges between 9% and 20% [5]. In this patient population, the most commonly encountered secondary malignancies include lung and colon cancer as well as sarcoma. The risk of multiple myeloma in CLL patients is 10-fold higher than in the normal population [5]. Also, impaired B cell functions is associated with infections and cytopenia in many patients with CLL [6].

Table 1. Documented clinicopathological characteristics of patients concurrent CLL and MDS

	Age	Sex	Classification
Bracey AW et al 1989	72 [7]	M	MDS-RAEB to AML
Y Bastion et al 1991	N/A [15]	N/A	
Sylvester LS et al 1997	85 [1]	M	MDS-RA
Lai R et al 1999	67 [6]	M	MDS-RAS
Hana A et al 2004	63 [16]	M	MDS-RCMD
Khalil M Charafeddine et al 2010	69[17]	M	MDS with ring sideroblasts
Luca L et al 2011	83 [18]	M	MDS/MPD
	74	M	MDS/MPD
	64	F	MDS/MPD
Tambaro FP et al 2016	N/A [4]	N/A	MDS
	N/A	N/A	MDS
Kislitsyna M.A et al 2019	N/A	N/A	MDS
	N/A [19]	N/A	MDS
Li, Xiangxin, et al 2021	69 [20]	M	MDS

4. CONCLUSION

The patient described herein underscores possible coexistence of two different hematological malignancies developing simultaneously or at different timepoints. Although the co-occurrence of MDS and B-CLL seem to be independent of the CLL management, previous chemotherapy for cervical carcinoma represents a risk factor for MDS in this patient, who also had skin involvement due to B-CLL. This very rare presentation should be kept in mind in patients with concurrent lymphocytosis and blasts.

CONSENT

Signed Consent was obtained from the patient for the use of patient data for publication.

ETHİCAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Sylvester LS, et al. Concurrent diagnosis of chronic lymphocytic leukemia and myelodysplastic syndrome. 1997;21(7): 619-621.
2. Lima M, et al. Cytogenetic findings in a patient presenting simultaneously with chronic lymphocytic leukemia and acute myeloid leukemia. 1996;87(1):38-40.
3. Çabuk M. et al. Cyclic lymphocytic vasculitis associated with chronic lymphocytic leukemia. 2004;45(4):811-813.
4. Tambaro FP, et al. Outcomes for patients with chronic lymphocytic leukemia and acute leukemia or myelodysplastic syndrome. 2016;30(2): 325-330.
5. Wiernik PHJCtoio. Second neoplasms in patients with chronic lymphocytic leukemia. 2004;5(3):215-223.
6. Lai R, et al. Untreated chronic lymphocytic leukemia concurrent with or followed by acute myelogenous leukemia or myelodysplastic syndrome: A report of five cases and review of the literature. 1999;111(3):373-378.
7. Bracey AW, et al. Coexistence of myelodysplastic syndrome and untreated chronic lymphocytic leukemia with development of acute myeloid leukemia immediately after treatment of chronic lymphocytic leukemia. 1989;30(3):174-180.
8. Ferrara F, et al. Chronic lymphocytic leukemia coexisting with chronic myelomonocytic leukemia. 1992:77(2): 171-173.
9. PaydaŞ S, et al. Vasculitis and leukemia. 2000;40(1-2):105-112.
10. Cohen PR, Kurzrock R. Mucocutaneous paraneoplastic syndromes. in Seminars in oncology;1997.
11. Carlson J, Mihm MC Jr, LeBoit PE. Cutaneous lymphocytic vasculitis: A definition, a review, and a proposed classification. in Seminars in diagnostic pathology;1996.
12. Farrell A, et al. Cutaneous lymphocytic vasculitis in acute myeloid leukaemia. 1996;135(3):471-474.
13. Paydas S, Zorludemir SJBJoD. Leukaemia cutis and leukaemic vasculitis. 2000;143(4):773-779.
14. Longacre TA, Smoller BRJAjocp, Leukemia cutis: analysis of 50 biopsy-proven cases with an emphasis on occurrence in myelodysplastic syndromes. 1993;100(3):276-284.
15. Bastion Y, et al. High risk myelodysplastic syndrome coexistent with chronic lymphocytic leukemia for more than 9 years: inhibition of the myeloid clone by the lymphoid clone? 1991;5(11):1006-1009.
16. Aviv H, et al., Simultaneous appearance of trisomy 8 and trisomy 12 in different cell populations in a patient with untreated B-cell chronic lymphocytic leukemia and myelodysplasia. 2004;45(6):1279-1283.
17. Charafeddine KM, et al. Chronic lymphocytic leukemia associated with myelodysplastic syndrome with ring sideroblasts. 2010;103(8):823-827.
18. Laurenti L, et al. The coexistence of chronic lymphocytic leukemia and myeloproliperative neoplasms: a retrospective multicentric GIMEMA experience. 2011;86(12):1007-1012.

19. Kislitsyna M, et al. Features of cytogenetic diagnosis of synchronous chronic lymphocytic leukemia and myelodysplastic syndrome: description of a clinical case. 2019;14 (3).

20. Li X., et al. Multi Cytogenetic Changes in a Patient as Co-Existing MDS and CLL Progresses. 2021;14:177.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/68840