

trombopag in aplastic anemia following autologous stem cell transplant: case report and review of the literature. *Pharmaceuticals (Basel)* 2022;15:419.

6. Young NS. Aplastic anemia. *N Engl J Med* 2018;379:1643-56.
7. Jang JH, Tomiyama Y, Miyazaki K, et al. Efficacy and safety of romiplostim in refractory aplastic anaemia: a phase II/III, multi-centre, open-label study. *Br J Haematol* 2021;192:190-9.
8. Song GY, Jung SH, Kim JS, et al. Busulfan and thiotepea as a conditioning regimen for autologous stem cell transplantation in patients with multiple myeloma: a study of the Korean Multiple Myeloma Working Party (KMMWP-1801 study). *Front Oncol* 2022;12:959949.
9. Park YH, Kim DY, Kim S, et al. Management of immune thrombocytopenia: 2022 update of Korean experts recommendations. *Blood Res* 2022;57:20-8.
10. Lutfi F, Skelton WP, Rosenau E, et al. Poor graft function following autologous stem cell transplant (ASCT): a retrospective analysis over two decades at a transplant center. *Blood* 2017;130 Suppl 1:4529.
11. Prabahan A, Koldej R, Chee L, Ritchie D. Clinical features, pathophysiology, and therapy of poor graft function post-allogeneic stem cell transplantation. *Blood Adv* 2022;6:1947-59.
12. González-Porras JR, Mingot-Castellano ME, Andrade MM, et al. Use of eltrombopag after romiplostim in primary immune thrombocytopenia. *Br J Haematol* 2015;169:111-6.
13. Ise M, Iizuka H, Kamoda Y, Hirao M, Kida M, Usuki K. Romiplostim is effective for eltrombopag-refractory aplastic anemia: results of a retrospective study. *Int J Hematol* 2020;112:787-94.
14. Ahn HJ, Byun JM, Kim I, et al. Eltrombopag for post-transplant poor graft function in East Asian patients. *J Korean Med Sci* 2022;37:e48.

Clinico-pathological features and treatment outcomes of high-grade B cell lymphoma—a tertiary cancer center experience

TO THE EDITOR: High-grade B-cell lymphoma (HG-BCL), an uncommon condition, displays a blastoid morphology and an aggressive disease course, but lacks the features of Burkitt's lymphoma or diffuse large B-cell lymphoma [1, 2]. Previously termed "B cell lymphoma having features intermediate between DLBCL and Burkitt's lymphoma" [3], its rarity has primarily resulted in descriptions of isolated case series.

We conducted a retrospective study on 14 patients diagnosed with HG-BCL who were registered in our department between January 1, 2020 and April 30, 2022. Their clinicopathological variables and outcomes at the end of the follow-up period are outlined in the Results.

RESULTS

Epidemiology

The median age was 55.5 (range, 29–7) yr. Most patients were men (N=10, 71.4%). The common comorbidities were diabetes (N=3, 21.4%) and hypertension (N=2, 14.3%). The median symptom duration before diagnosis was eight (range, 1–20) wk. Seven (50%) patients did not have any B symptoms, whereas weight loss (N=3, 21.4%) and fatigue (N=4, 28.6%) were observed in the remaining seven (50%).

Disease workup

Bone marrow biopsy showed disease involvement in six (42.9%) patients. Central nervous system (CNS) involvement was confirmed in 1 out of 14 (7.1%) by a positive cerebrospinal fluid cytology. Four patients (28.6%) showed involvement of the spleen. Extra nodal site involvement was categorized as 1 site (N=7, 50%), ≥2 sites (N=4, 28.6%), and none (N=3, 21.4%). The median IPI and CNS IPI score was 3. High IPI (score of 4–5) and High CNS IPI (score of 4–6) were observed in three (21.4%) patients each.

The common stages observed were stages IV (N=8, 57.1%) and II (N=3, 21.4%). On IHC, five (35.6%) patients were found to be double-expressors of the markers C-MYC, BCL-2, and BCL-6. On analysis by FISH, C-MYC rearrangement was found in two (15.4%) patients with none having concurrent rearrangement of BCL-2 or BCL-6, as shown in Table 1.

Therapy

Nine (64.2%) patients received R-CHOP and five (35.7%) received R-DA-EPOCH as first-line therapy. CNS prophylaxis with intrathecal-methotrexate (IT-MTx) was administered concurrently with the R-DA-EPOCH regimen in all five patients, whereas five out of nine patients treated with R-CHOP received the same. High-dose MTx was administered to the remaining four patients on R-CHOP. Three (21.4%) patients relapsed and received salvage chemotherapy with R-GDP (N=2) and R-DHAP (N=1) regimens.

Treatment outcome

The median follow-up duration was 10.5 (1.13–19.3) mo. Response rates after first-line therapy were: complete response (CR), 71.4% (N=10); partial response (PR), 14.2% (N=2); stable disease (SD), none, and progressive disease (PD), 14.2% (N=2), with overall response rates (ORR) of 85.7%. One patient progressed rapidly on first line and died soon after starting therapy. Of the three (21.4%) patients who relapsed, two (14.2%) died from disease progression. The third death was due to COVID-19 pneumonia (Table 2).

Survival

The mean progression-free survival (PFS) and overall survival (OS) were 14.86 (median, not reached) and 15.58 (median, not reached) mo, respectively. One-year PFS and OS were both 76.2%.

Table 1. Molecular marker profiles of patient cohort.

Patient	MIB-1, %	IHC-Bcl2	IHC-Bcl6	FISH-C-myc	FISH-Bcl2	FISH-Bcl6
1	85	-	+	-		
2	90	+	+	-		
3	90	+	-	+	-	-
4	90	+	+	+	-	-
5	90			-		
6	85	+		-		
7	90	+	+	-	-	-
8	80	-		-	-	-
9	90	+	+			
10	95	-		-		
11	90	+	+	-		
12	85	+	-	-		
13	95	-	+	-	-	-
14	95	-	+	-	-	-

Table 2. Clinical outcomes of patient cohort.

Patient	1L [CHOP] no. of cycles	1L [EPOCH] no. of cycles	Outcomes of 1L therapy	Deaths	Cause of death	Disease status at last FU
1	0	6	CR	No	NA	CR
2	6	0	PD	Yes	PD	NA
3	1	0	PD	Yes	PD	NA
4	6	0	PR	Yes	PD	NA
5	0	6	CR	No	NA	CR
6	6	0	PR	Yes	COVID-19 (unrelated)	NA
7	6	0	CR	No	NA	CR
8	6	0	CR	No	NA	CR
9	2	0	CR	No	NA	CR
10	6	0	CR	No	NA	CR
11	7	0	CR	No	NA	CR
12	4	2	CR	No	NA	PR
13	4	2	CR	No	NA	CR
14	4	2	CR	No	NA	PR

Abbreviations: 1L, first line; CR, complete response; FU, follow-up; NA, not applicable; PD, progressive disease; PR, partial response; SD, stable disease.

Adverse effects

Acute cytopenia (during and within 6 wk of treatment completion) observed in eight (57.1%) patients was the most common adverse effect. Maximum grade of toxicity was CTCAE 5 (N=3, 21.4%), whereas most common grade was CTCAE 2 (N=11, 78.5%).

To conclude, reports on HG-BCL data in India are scarce [4, 5]. Our study showed promising overall response and survival rates in patients with HG-BCL, despite most patients being in advanced disease stages. However, due to the small cohort size and short follow-up period, variables affecting the outcomes could not be studied. Multicenter pooling can provide greater insight into HG-BCL in the Indian context.

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Received on Sep. 1, 2023; Revised on Nov. 18, 2023; Accepted on Nov. 27, 2023

<https://doi.org/10.5045/br.2023.2023169>

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

REFERENCES

1. Chen BJ, Fend F, Campo E, Quintanilla-Martinez L. Aggressive B-cell lymphomas—from morphology to molecular pathogenesis. *Ann Lymphoma* 2019;3:1-22.
2. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood* 2016;127:2375-90.
3. Perry AM, Crockett D, Dave BJ, et al. B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and burkitt lymphoma: study of 39 cases. *Br J Haematol* 2013;162:40-9.
4. Moharana L, Dasappa L, Babu S, et al. Comparison between CHOP and DA-EPOCH with or without rituximab in adult high grade B cell lymphoma, not otherwise specified; a retrospective study from a tertiary cancer hospital in South India. *Indian J Hematol Blood Transfus* 2022;38:15-23.
5. Karunakaran P, Selvarajan G, Kalaiyarasi JP, et al. Therapeutic outcomes in high-grade B-cell lymphoma, NOS: retrospective analysis. *South Asian J Cancer* 2022;11:68-72.

Lenalidomide as a treatment for patients with AL amyloidosis and cardiac involvement

TO THE EDITOR: Immunoglobulin-light-chain (AL) amyloidosis is a disease in which clonal plasma cells create excess monoclonal immunoglobulin light chains that aggregate into amyloid fibrils and accumulate in organs, ultimately leading to organ dysfunction. Current treatments for amyloidosis target clonal plasma cells to prevent the production of excess light chains and promote amyloid clearance through immunologic functions [1]. As such, anti-myeloma agents have been used to treat AL amyloidosis. The current standard treatment regimen comprises a combined regimen of daratumumab into bortezomib, cyclophosphamide, and dexamethasone [2]. Interestingly, daratumumab exerts immunomodulatory activity on immune cells, driving a depletion of regulatory T and B cells, as well as myeloid-derived suppressor cells, to facilitate amyloid clearance [3]. Likewise, lenalidomide, an immunomodulatory drug, is anticipated to have a therapeutic effect in amyloidosis. With this in mind, we planned a prospective single-arm study using lenalidomide and dexamethasone for relapsed/refractory AL amyloidosis patients with cardiac involvement.

Positron emission tomography (PET) has high sensitivity and specificity for amyloids, making it a useful tool to assess the myocardial amyloid burden [4]. In this study, we utilized 18F-florbetaben PET to quantify myocardial amyloid deposits and evaluate chemotherapy response in treated patients.

Due to competing studies, this study was terminated prematurely. However, we believe that it is nevertheless worthwhile to share the results obtained in the limited cases treated with lenalidomide and evaluated using amyloid PET.

METHODS

This study was registered under the study protocol number NCT04298372. This trial investigated the efficacy of a combination therapy of oral lenalidomide (15–25 mg/day, days 1–21) and dexamethasone (40 mg/day, IV or PO, days 1–4) every 28 days. The starting dose of lenalidomide was 15 mg/day; when tolerated, the dose was increased to 20 mg/day for the next cycle, up to a maximum dose of 25 mg/day. If chemotherapy was well tolerated, treatment continued for up to 12 cycles. At the end of each cycle, hematological and organ responses were assessed. PET was performed before treatment and every 6 months after treatment initiation. The maximal uptake in the myocardium divided by the average liver uptake (myocardium-to-liver ratio, MLR) at a delayed time point (90 min after injection of 18F-florbetaben 300 MBq) was used to assess changes in amyloid deposits.

CASE 1

A 61-year-old Korean man presented with general weakness. Echocardiography revealed concentric left ventricular hypertrophy with mild pericardial effusion. Cardiac magnetic resonance imaging revealed diffuse fuzzy sub-endocardial enhancement of the global left ventricle. Endomyocardial biopsy was performed to confirm AL amyloidosis. Serum protein electrophoresis (PEP) and immunofixation electrophoresis (IFE) were normal; however, urine PEP/IFE revealed lambda-type Bence-Jones proteinuria with M-spike. The difference between the involved and uninvolved FLC (dFLC) was 109.7 mg/L. Bone marrow exam revealed hypercellular marrow (cellularity 51–60%) with Lambda-restricted plasma cells (4.4%), with no evidence of amyloid deposit in the bone marrow.

The patient was initially treated with oral melphalan (10 mg per square meter of body surface area, days 1–4) and high-dose dexamethasone (40 mg/day, days 1–4) (MelDex). After four cycles of MelDex, hematologic complete response (CR) and renal response were achieved (decrease in 24 h urinary protein from 1.8 g/day to 0.26 g/day). MelDex was discontinued at the request of the patient. After four years, he experienced relapse; urine PEP/IFE revealed lambda-type Bence-Jones proteinuria with M-spike. At this time, his dFLC level was 68.3 mg/L.

The patient was enrolled in the lenalidomide trial. After six cycles of lenalidomide plus dexamethasone, serum FLC levels normalized, the dFLC level reduced to 2 mg/L, and serum and urine immunofixation showed negative results. His 24 h urinary protein decreased more than 50% from 3.4 g/day to 0.29 g/day, while NT-proBNP levels decreased from 77,160 ng/L to 51,290 ng/L. PET showed a significant