OMCR

OMCR 2014 12 (3 pages)
doi:10.1093/omcr/omu060

Case Report

Plasma cell leukaemia: a management conundrum

Sriram Ravichandran[1,*], Monali Gupta[2], Mayur Parihar[3], Anupam Chakrapani[1], Reena Nair[1] and Mammen Chandy[1]

[1]Department of Clinical Haematology, Tata Medical Center, Kolkata, India, [2]Department of Laboratory Haematology, Tata Medical Center, Kolkata, India and [3]Department of Cytogenetics, Tata Medical Center, Kolkata, India

*Correspondence address. Department of Clinical Haematology, Tata Medical Center, Kolkata 700156, India. Tel: +91-9903940382; E-mail: sriramravic@gmail.com

Received 13 October 2014; revised 25 November 2014; accepted 7 December 2014

Primary plasma cell leukaemia in a young transplant eligible patient brings forth a number of perplexing questions and many remain unanswered. There are good data to suggest the superiority of novel agents over conventional chemotherapy regimens, however choosing between autologous and allogeneic haematopoietic stem cell transplant in first remission remains a therapeutic conundrum. We report a case of primary plasma cell leukaemia in a young patient and the dilemmas in its management.

INTRODUCTION

Primary plasma cell leukaemia (pPCL) is a rare disorder with dismal prognosis. It is defined by the presence of $>2 \times 10^9$/l peripheral blood plasma cells or if plasma cells comprise >20% of the differential count. Primary PCL differs from secondary plasma cell leukaemia in a number of ways (Table 1). The biology of pPCL is unique. The tumour cells have an increased ability to recirculate in blood and hence extramedullary disease is frequent. Several molecular aberrations contribute to bone marrow-independent tumour growth, evasion of immune surveillance and inhibition of apoptosis [1]. The natural history of pPCL is characterized by a short period of remission and poor response to standard chemotherapy.

Here, we present a case of pPCL in a young adult and discuss the dilemmas in its management.

CASE REPORT

A 24-year-old female presented with history of backache, nausea, vomiting and abdominal pain of 2 weeks duration. Clinical examination was noteworthy for pallor and tachycardia. Laboratory evaluation was remarkable for anaemia (7.2 g/dl), leucocytosis (97 000/μl) with 70% plasma cells (Fig. 1), elevated serum creatinine (9.9 mg/dl), total protein, and proteinuria (2.72 g/day). IgG kappa monoclonal paraprotein was identified and kappa light chain was elevated (Table 2). Bone marrow showed diffuse infiltration with plasma cells (CD 138+, kappa restriction). Cytogenetic analysis showed a complex karyotype. Skeletal survey revealed two tiny lytic lesions in the skull. Based on the above presentation, a diagnosis of pPCL was made.

The patient received therapy with bortezomib, thalidomide and dexamethasone (VTD). She achieved complete remission (CR) after six cycles. She then underwent autologous haematopoietic stem cell transplant (HSCT) with high-dose melphalan (200 mg/m^2) as the conditioning regimen. Six months after the autologous transplant (Table 2) atypical plasma cells were noted in the peripheral blood (CD138+, CD56+, CD38+, kappa restriction).

Based on one case report [2] the patient was treated with hyper-CVAD. After two cycles of chemotherapy, she achieved VGPR. As there was no matched sibling/unrelated donor, she underwent an allogeneic HSCT from a haplo-identical donor [3]. She received myeloablative conditioning with Fludarabine-Busulfan and post-transplant Cyclophosphamide along with

Table 1: pPCL Vs. sPCL

Primary plasma cell leukaemia	Secondary plasma cell leukaemia
Occurs *de novo*	Leukaemic transformation of multiple myeloma
Younger age at presentation	Older at presentation
Bone disease uncommon	Bone disease common
Extra-medullary involvement common	Extra-medullary involvement uncommon
Renal failure pPCL > sPCL > MM	

Tacrolimus and Mycophenolate as GVHD prophylaxis. She engrafted on D +14 and was discharged on D+21.

Five months after allogeneic HSCT, she developed a nodular subcutaneous lesion in the left lumbar region. Fine needle aspiration from this lesion showed many atypical plasmacytoid cells (strongly positive for CD 138). Further testing revealed systemic relapse (Table 2). She was treated with palliative radiotherapy to the affected area along with donor lymphocyte infusion. She could not receive any further therapy as she developed severe graft vs. host disease (grade III skin + gut). Despite the above measures, she died of progressive disease 24 months after diagnosis.

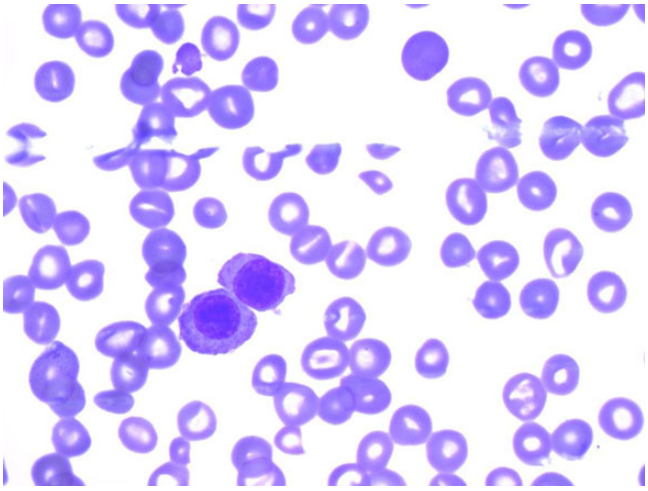

Figure 1: Plasma cells in peripheral blood.

DISCUSSION

There is paucity of prospective data to guide treatment of pPCL. Therapy with conventional chemotherapy is ineffective with median survival of 7 months only [4]. Novel agents have improved the outlook for pPCL. In a retrospective analysis of 31 patients treated within the IFM [5], treatment with bortezomib ($n = 24$, 15 upfront, 9 at relapse, 13 received single agent bortezomib) in combination with other drugs (doxorubicin, thalidomide, dexamethasone) resulted in the best response rates (ORR 70%, CR+ VGPR 45%). It is therefore recommended to use these agents upfront in induction.

The optimal approach to consolidation is not clear. Two large retrospective analyses by the CIBMTR [6] and the EBMT [7] have shown encouraging results after autologous HSCT. In the CIBMTR cohort 97 patients received autologous HSCT (68 single autologous + 25 tandem autologous + 4 tandem auto + allo). At 3 years, PFS and OS were 34 and 64%, respectively. However, there was a high incidence of relapse (61%). Additionally a trend towards superior survival was noted in the tandem auto-auto cohort (56 vs. 84%).

Table 2: Laboratory data at diagnosis and its evolution

Parameter	At diagnosis	Post VTD	6 months post Auto HSCT	Post Allo HSCT (D + 28)	Post allo 6 month
Haemogloin(13–17 g/dl)	7.2	10.3	10.6	11.5	9.9
TLC(4000–12 000/cumm)	97 000	6200	4700	7700	5400
Plasma cells (PB)	74.00%	Nil	11.00%	Nil	Nil
Creatinine (0.7–1.3 mg/dl)	9.9	0.7	0.7	0.7	0.5
Calcium (8.4–10.2 mg/dl)	6.8	9.4	9.1	8.8	9.4
M band (g/dl)	2.63	Neg	1.58	Neg	0.24
LDH	1538	NA	NA	NA	NA
Immunofixation	IgG Kappa	Faint	Prominent	Neg	IgG Kappa
sFLC					
Kappa	731.5	6.87	524	54.57	40.15
Lambda	5.32	10.25	5.17	10.85	10.01
Bone marrow aspirate	Hemodilute, 22% plasma cells	<5%	46% plasma cells	NA	NA
Bone marrow biopsy	Diffuse infiltration with plasma cells, CD138+, kappa restriction	Cellular marrow with no plasma cell infiltrates	Diffuse infiltration with plasma cells, CD138+, CD79a+, CD56+, kappa restriction	NA	NA

Karyotype (at diagnosis)
44,XX,−1,i(1)(q10),del(3)(q21),rob(14;14)(q10;q10),add(22)(q13),+mar[1]/46, −X,−X,−1, i(1)(q10),−3,del(4)(q27),+9,+12,−14,−14,−17,add(22)(q13),+5mar[1]/43,XX,−1,i(1)(q10), del(3)(q21),−5,−8,+9,+12,−14,−16,−17,add(22)(q13),+2mar[1]/46,XX[17]

Karyotype (after 6 cycles of VTD)
46,XX

In the European cohort ($n = 272$), the median PFS was 14.3 months and the median OS was 25.7 months (95% confidence interval 19.5–31.9 months). The 5-year OS was only 27.2%.

The role of allogeneic HSCT is uncertain in pPCL. An analysis by the CIBMTR ($n = 147$, allogeneic 50, autologous 97) failed to show any survival benefit in recipients of allogeneic transplant when compared with autologous HSCT [6]. The cumulative incidence of relapse at 3 years was significantly lower in the allogeneic group (61 vs. 38%) but this was balanced by high TRM (41 vs. 5%) and the OS was better in the autologous group (64 vs. 39%).

CONCLUSION

This case illustrates the pugnacious nature of pPCL. Cytotoxic chemotherapy is ineffective and combination therapy with novel agents is recommended upfront. Good responses have been seen with the use of bortezomib and hence it is recommended as front-line treatment. Autologous HSCT by itself is insufficient treatment for pPCL as most patients will relapse, on the other hand, allogeneic HSCT is associated high TRM. Therefore, innovative approaches incorporating novel agents and newer conditioning regimens are required. In this context use of novel agents in the conditioning regimens, tandem auto-allo HSCT and maintenance treatment with novel agents holds promise. This strategy needs to be evaluated prospectively.

REFERENCES

1. Usmani SZ, Nair B, Qu P, Hansen E, Zhang Q, Petty N, *et al.* Primary plasma cell leukemia: clinical and laboratory presentation, gene-expression profiling, and clinical outcome with total therapy protocols. *Leukemia* 2012;**26**:2398–2405.
2. Hosono N, Yamauchi T, Nakamura T, Yamashita T, Ueda T. Plasma cell leukemia induced to complete remission with negative minimal residual disease by qualitative PCR analysis after hyper-CVAD and high-dose melphalan followed by autologous peripheral blood stem cell transplantation. *Gan To Kagaku Ryoho* 2008;**35**:533–537.
3. Nonami A, Miyamoto T, Kuroiwa M, Kunisaki Y, Kamezaki K, Takenaka K, *et al.* Successful treatment of primary plasma cell leukaemia by allogeneic stem cell transplantation from haploidentical sibling. *Jpn J Clin Oncol* 2007;**37**:969–972.
4. Garcia-Sanz R, Orfao A, Gonzalez M, Taberneo MD, Blade J, Moro MJ, *et al.* Primary plasma cell leukemia: clinical, immunophenotypic, DNA ploidy, and cytogenetic characteristics. *Blood* 1999;**93**:1032–1037.
5. Chaoui D, Leleu X, Roussel M, Royer B, Rubio M, Ducastelle S, *et al.* Has the prognostic of primary plasma cell leukemia improved with new drugs? [ASH Annual Meeting Abstracts]. *Blood* 2009;**114**:3869.
6. Mahindra A, Kalaycio ME, Vela-Ojeda J, Vesole DH, Zhang M-J, Li P, *et al.* Hematopoietic cell transplantation for primary plasma cell leukemia: results from the Center for International Blood and Marrow Transplant Research. *Leukemia* 2012;**26**:1091–1097.
7. Drake MB, Iacobelli S, van Biezen A, Morris C, Apperley JF, Niederwieser D, *et al.* Primary plasma cell leukemia and autologous stem cell transplantation. *Haematologica* 2010;**95**:804–809.