Research Article

Engraftment Syndrome: A Retrospective Analysis of the Experience at a Tertiary Care Institute

Raja Pramanik[1], Harish Kancharla[1], Sameer Bakhshi[1], Atul Sharma[1], Ajay Gogia[1], Prabhat Malik[1], Ranjit Kumar Sahoo[1], Atul Batra[1], Sanjay Thulkar[2], Lalit Kumar[1,*]

[1]*Department of Medical Oncology, All India Institute of Medical Sciences, New Delhi, India*
[2]*Department of Radiodiagnosis, All India Institute of Medical Sciences, New Delhi, India*

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ABSTRACT

Engraftment syndrome (ES) is a clinical syndrome that occurs in the early neutrophil recovery phase following hematopoietic stem cell transplant (HSCT). Although also described for allogenic HSCT, it is basically diagnosed in the context of autologous HSCT. We retrospectively reviewed 171 consecutive HSCTs performed between January 2013 and January 2015 in our Bone Marrow Transplant (BMT) unit and analyzed all cases of noninfectious fever and strong clinical features suggestive of ES in the peri-engraftment period for up to 7 days. We observed the incidence of ES to be 12.3% (16/130) in the autologous and 4.8% (2/41) in the allogeneic cohort. Among plasma cell disorders, which constitute 50% of our study population, the incidence of ES was 19.7%. Among the ES cases of autologous transplants, 81.2% (13/16) patients satisfied the Maiolino criteria (MC) and 87.5% (14/16) patients the Spitzer diagnostic criteria (SC). A total of 68.7% (11/16) patients satisfied both MC and SC, and two patients (12.5%) did not satisfy either (MC- SC-). There was no significant difference in days of hospitalization and usage of supportive care between ES and non-ES patients, and there was no mortality due to ES. On univariate analysis, female patients (p < 0.013) and those with diagnosis of a plasma cell disorder (p < 0.03) had higher risk of ES. In conclusion, the incidence of ES in our study population is consistent with that of many others, but severity evaluation needs exploration in larger cohorts with pragmatically modified diagnostic criteria.

1. INTRODUCTION

Engraftment Syndrome is a febrile syndrome that occurs in the early neutrophil recovery phase following hematopoietic stem cell transplant (HSCT), and is characterized by noninfectious fever and clinical findings, such as skin rash, pulmonary infiltrates, weight gain, hypoxia, and diarrhea. It is a poorly understood but increasingly recognized complication of HSCT, mediated by proinflammatory cytokines, endothelial damage, and degranulation products of neutrophils [1–2]. Although occasionally described for allogenic HSCT, ES is mainly diagnosed in the context of autologous HSCT.

The two most commonly used diagnostic criteria are the Spitzer criteria (SC) [1] and the Maiolino criteria (MC)[3]. SC include three major or two major plus one minor criteria within 96 hours of engraftment Major criteria include noninfectious fever, rash, hypoxemia; minor criteria includes weight gain, renal or hepatic dysfunction, and transient encephalopathy. The MC criteria system is simpler, and requires noninfectious fever with either rash, pulmonary infiltrate, or diarrhea from 24 hours before engraftment to any time after it. Cappizzi *et al.* [4] limited the diagnosis to fever and

pulmonary injury occurring within 5 days of neutrophil engraftment. Dispenzieri *et al.* [5] had suggested uncoupling of the time limit in SC and MC, and Carreras *et al.* [6] found MC to be better but suggested adding C-reactive protein (CRP). Thus, diagnostic criteria are still evolving. Given its pleiotropic manifestations and varying working definitions, the transplant field is still struggling to define ES clearly [7]. Since there is no uniform definition, reports of the incidence for the ES have varied widely among different publications depending on the criteria used to define ES. In studies using stringent criteria, the incidence ranges between 7% and 10%, while in studies using wider criteria incidences up to 72% have been reported [3,6,8–11]. Identification of ES and differentiating it from other peri-engraftment complications is especially relevant and potentially life-saving, given the dramatic response that occurs to steroids in ES. In this study, we have analyzed our institutional experience of ES with a special focus on incidence and clinical features.

2. MATERIALS AND METHODS

2.1. Patients and Method

We retrospectively analyzed the clinical information of all consecutive HSCTs performed in our transplant unit between January

2013 and January 2015. After approval from the institute ethical committee, the flow-sheets, daily-notes, and summaries in the hospital files were screened to extract the data. To detect all cases with a possible ES, we analyzed all patients with noninfectious fever developing within 7 days of engraftment (first day of absolute neutrophil count (ANC) ≥ 500 on two consecutive days). We also included those patients who did not have fever but had other strong clinical features suggestive of ES such as skin rash, respiratory distress, unexplained diarrhea, and vomiting in the peri-engraftment period up to at least 7 days.

We applied SC and MC (Table 1) to all patients as defined above to comprehensively evaluate the presence or absence of the remaining clinical manifestations and laboratory abnormalities. Further, we analyzed all these patients for disease and transplant-related variables that could have an effect on development of ES (age, gender, underlying disease, previous treatments, disease status at transplant, number of CD34 positive cells infused, and days to engraftment). Treatment given for ES and responses were also noted.

2.2. Statistical Analysis

We used descriptive statistical analysis for various clinical parameters. Clinical characteristics were compared between groups using appropriate statistical tests. To compare dichotomous variables, Fisher (two tailed) and Chi-square tests were used. To compare the continuous variables t-test and Wilcoxon rank-sum tests were used. Logistic regression analysis was used to find factors significantly related to ES. For all statistical analysis $p < 0.05$ was considered significant and STATA version 13 was used for analysis of the data.

3. RESULTS

Complete records were available for 171 consecutive patients who received HSCT between January 2013 and January 2015. The baseline patient, disease, and transplantation parameters are listed in Table 2. The patient population comprised 127 (74 %) males and 44 (26%) females. Their median age was 43 years (3.5 months–65 years). Autologous HSCT was done for 74 % of the patients

and allogeneic HSCT for 24 %. The most common indication was multiple myeloma (54%) followed by acute myeloid leukemia (AML) (17.5%). In 91 cases (53.2%), the underlying disease was in complete response, in 61 (35.6%) it was in partial response and 19 (11.1%) patients had active disease. Granulocyte colony

Table 2 | Clinical characteristics of patients with and without engraftment syndrome.

	All Patients (n = 171)	ES (n = 18)
Age [median (range)] years	43 (0.29–65)	44 (16–62)
Gender (M:F)	127:44	9:9
Diagnosis		
MM	92 (53.8)	16 (88.9)
POEMS	4 (2.3)	0
pPCL	1 (0.6%))	0
AL amyloidosis	1 (0.6%)	
AML	30 (17.5)	0
ALL	7 (4.09)	0
HD	10 (5.8)	1 (5.6)
NHL	11 (6.4)	0
PNET	4 (2.3)	1 (5.6)
NB	4 (2.3)	0
NONMALIGNANT	3 (1.7)	0
Type of transplant		
Autologous	130 (76)	16 (88.9)
Allogenic	41 (24)	2 (11.1)
Source of stem cells		
PBSC	164 (95.3)	18 (100)
BM	1 (0.6)	0
CORD	6 (3.5)	0
Status of Disease at transplant [(n (%)]		
CR	91 (53.2)	7 (38.8)
PR	46 (26.9)	6 (33.3)
VGPR	15 (8.7)	3 (16.6)
ACTIVE	19 (11.1)	2 (11.1)
CD34 + cells (× 10^6/KG)	3.27 ± 1.82	3.29 ± 1.35
Days to engraftment [median (range)]	11 (8–120)	10 (8–14)
Prior Radiotherapy n (%)	39 (22.8)	3 (16.7)
Serum Albumin[g/dl] (mean ± SD)	3.88 (0.413)	4.01 (0.413)
Baseline weight [kg] (mean ± SD)	55.9 (18.43)	58.7 (13.27)
Conditioning regimen n (%)		
CYBU	22 (12.9)	0
BUCY	5 (2.9)	0
FLUMEL	17 (9.9)	2 (11.1)
FLUBU	3 (1.8)	0
MEL	97 (56.7)	16 (88.9)
BUMEL	8 (4.7)	0
BEAM	3 (1.8)	0
BEAC	4 (2.3)	0
CEC	1 (0.6)	0
CBV	11 (6.4)	0
Previous lines of chemotherapy [n (%)]		
0	3 (1.8)	0
1	84 (49.1)	0
2	65 (38)	8 (44.4)
3	10 (5.8)	7 (38.9)
4	7 (4.1)	3 (16.7)

MM: Multiple myeloma; pPCL: Primary plasma cell leukemia; AML: Acute myeloid leukemia; ALL: Acute lymphoblastic leukemia; HD: Hodgkins disease; NHL: Non-Hodgkin lymphoma; PNET: Primitive neuroectodermal tumor; NB: Neuroblastoma; PBSC: Peripheral blood stem cells; BM: Bone marrow; CORD: Cord blood; CR: Complete response; PR: Partial response; VGPR: Very good partial response; CYBU: Cyclophosphamide followed by busulfan; BUCY: Busulphan followed by cyclophosphamide; FLUMEL: Fludarabine + melphalan; FLUBU: Fludarabine + buslphan; MEL: Melphalan; BUMEL: Busulfan + melphalan; BEAM: BCNU + etoposide + araC + Melphalan; BEAC: BCNU + Etoposide + araC + Carboplatin; CBV: Cyclophosphamide + etoposide + BCNU; CEC: Cyclophosphamide + Etoposide + Carboplatin.

Table 1 | Criteria for diagnosis of engraftment syndrome.

Spitzers Criteria	Maiolino Criteria
Three major, or two major and one minor, within 96 h of engraftment	Noninfectious fever plus:
Major: noninfectious fever,[a] skin rash,[b] pulmonary edema[c] and hypoxemia	• skin rash, or • pulmonary infiltrates, or • diarrhea,[d]
Minor: weight gain,[e] hepatic or renal dysfunction,[f] and transient encephalopathy[g]	commencing 24 h before or at any time after the first appearance of neutrophils

(a) New fever (38°C) without clinical or microbiological documentation or response to antimicrobial treatment. (b) Maculo-papular exanthema involving > 25% of body surface area. (c) Documented by X-ray or CT if there were no signs of infection, cardiac failure, or pulmonary embolism. (d) At least two episodes of liquid depositions/day without microbiological documentation of infection. (e) Higher than 2.5% of basal. (f) Bilirubin ≥2 mg per 100 mL or Aspartate amino-transferase (ASAT)/Alanine amino-transferase (ALAT) ≥2 times or creatinine ≥2 times normal. (g) If unexplained by other causes.

stimulating factor (G-CSF) mobilized peripheral blood stem cells was the commonest source utilized. The working diagnosis of ES was made in 18 (10.5%) patients whose clinical characteristics are listed in Table 2. The median age was 44 years (16–62 years). The male to female ratio was a 1:1. The incidence of ES in the autologous HSCT cohort was 12.3 % (16/130) and for allogenic HSCT 4.8 % (2/41). Plasma cell disorders had a high incidence of ES (16.3%). Among individual malignancies, the highest incidence of ES at 17 % (16/92) was found in multiple myeloma. As ES is predominantly described among autologous transplant patients, we performed a detailed analysis of this cohort. Only two patients had ES in the allogenic cohort and, therefore, we present a descriptive analysis for them in a later section.

3.1. Engraftment Syndrome in Autologous Transplants (n = 130)

Baseline characteristics of the patients with (n = 16) and without ES (n = 114) are shown in Table 3. There was no significant difference between the two groups except for the predominance of females (p = 0.02), earlier engraftment (p = 0.04), and a higher serum albumin among ES patients (p = 0.02). Culture-negative fever and skin rash were documented in 81.2% (13/16), while respiratory distress, pulmonary infiltrates, and hypoxemia were observed in 56.2% (9/16), with 12.5% (2/16 patients) requiring mechanical ventilation. Weight gain (>2.5% of baseline) was observed in 14 patients (87.5%), and unexplained new onset renal dysfunction in two, transient encephalopathy in two. No patient developed hepatic dysfunction. (Table 4). The median time to onset of ES was 10 days (Range 7–15 days).

3.1.1. Comparison of SC and MC (Table S3)

MC was satisfied in 12 (75%) patients and the SC in 10 (62.5%) A total of 10 (62.5%) patients fulfilled both MC and SC, and four (25%) did not satisfy either criteria. Among the latter, three patients had "weight gain and rash" and another one had only "noninfectious fever and weight gain." The sensitivity of MC and SC in detecting ES in this study population was 75% (12/16) and 62.5% (10/16), respectively.

3.1.2. Treatment

Diuretics alone were used in four patients, steroids in five, both steroids and diuretics in six, while one patient improved during observation alone. The median duration of steroid administration was 1.5 days (range 0–10 days) and the median time to resolution of symptoms was 24 hours. ES did not lead to death in any patient. Treatment details and captured responses are consolidated in Table S1.

3.1.3. Supportive care

There was no significant difference in supportive care between ES and non-ES patients in terms of anti-fungal use, days on antibiotics, hospital stay, and packed red blood cells transfusion. However, the single donor platelets requirement was significantly lower among patients with ES (p = 0.001) (Table S2)

Table 3 | Comparison of the clinical characteristics of patients who developed engraftment syndrome *versus* those who did not (n = 130).

	No ES (n = 114)	ES (n = 16)	p-Value
Age [median (range)] years	48 (2–65)	44.5 (16–62)	0.79
Gender (M :F)	89:25	8:8	0.02
Diagnosis			0.63
MM	77 (64.9)	15 (93.7)	
POEMS	4	0	
pPCL	1	0	
AL amyloidosis	1	0	
AML	6	0	
HD	10	1 (6.3)	
NHL	11	0	
Others	10	0	
Source of stem cells			
PBSC	114 (100)	16 (100)	
Status of Disease at transplant [(n (%)]			0.69
CR	59 (51.7)	7 (43.7)	
PR	40 (35.1)	6 (37.5)	
VGPR	12 (10.5)	3 (18.7)	
ACTIVE	3 (2.6)	0	
CD34 + cells ($\times 10^6$/KG)	3.07 ± 1.78	3.14 ± 1.15	0.88
Days to engraftment [median (range)]	11 (8–120)	10 (8–14)	0.04
Prior Radiotherapy n (%)	34 (29.8)	3 (18.7)	0.55
Serum Albumin[g/dl](mean ± SD)	3.79 ± 0.41	4.04 ± 0.43	0.02
Baseline weight [kg] (mean ± SD)	58.86 ± 16.73	58.31 ± 13.84	0.89
Previous lines of chemotherapy [n (%)]			0.45
1	70 (61.4)	8 (50.0)	
2	33 (28.9)	6 (37.5)	
3	5 (4.4)	2 (12.5)	
>3	6 (5.2)	0	

MM: Multiple myeloma; pPCL: Primary plasma cell leukemia; AML: Acute myeloid leukemia; ALL: Acute lymphoblastic leukemia; HD: Hodgkins disease; NHL: Non Hodgkin lymphoma; PNET: Primitive neuroectodermal tumor; NB: Neuroblastoma; PBSC: Peripheral blood stem cells; BM: Bone marrow; CORD: Cord blood; CR: Complete response; PR: Partial response; VGPR: Very good partial response.

Table 4 | Clinical characteristics of patients with ES (n = 16) diagnosed in the autologous transplant cohort.

Clinical Features	N	%
Noninfectious fever	13	81.2
Skin rash	12	75.0
Diarrhea	1	6.2
Respiratory distress	9	56.2
Pulmonary infiltrates	9	56.2
Hypoxemia	9	56.2
Ventilator required	2	12.5
New renal dysfunction	2	12.5
New hepatic dysfunction	0	
Weight gain	14	87.5
Transient encephalopathy	2	12.5

3.1.4. Determining risk factors

Table 5 shows the incidence of ES among the different subgroups of patients. On univariate analysis, female gender (p = 0.016) and a diagnosis of plasma-cell disorder (p = 0.031) were significantly associated with the risk of developing ES. However, on multivariate analysis only female gender was found to be significant, (OR = 3.43, 95%CI = 1.14–10.32, p = 0.028) (Table 5).

Table 5 | (a) Univariate and (b) multivariate analysis of risk-factors for engraftment syndrome in patients undergoing autologous transplantation (N = 130).

Parameter	Engraftment Syndrome (n = 16)	No Engraftment Syndrome (n = 114)	p-Value
(a) Univariate			
Gender			0.016
Male	8	89	
Female	8	25	
Age			0.90
≤40 years	6	41	
>40 years	10	73	
Serum albumin			0.17
≤3.5 g/dL	0	13	
>3.5 g/dL	16	101	
RT received	3	34	0.27
CD 34 ($\times 10^6$/Kg)			0.82
<2.5	6	46	
≥2.5	10	68	
Previous lines			0.38
≤1	8	70	
>1	8	44	
Disease status at transplant			0.54
CR	7	59	
CR	9	55	
Diagnosis			0.031
Plasma cell disorder	15	77	
Others	1	37	

Variable	Odds Ratio	95% CI	p-Value
(b) Multivariate			
Female gender	3.43	1.14–10.32	0.028
Plasma cell disorder	6.94	0.87–55.38	0.067

RT: Radiotherapy; CR: Complete Remission.

3.2. ES in Plasma Cell Disorders

Plasma cell disorders (PCD) constituted 57.3% (98/171) of our study population. Allogenic HSCT was done for one patient while the remaining 97 underwent autologous HSCT. The majority of PCDs were multiple myeloma (93.8%, 92/98), followed by POEMS syndrome in four patients, systemic AL amyloidosis in one, and primary plasma cell leukemia in one. ES was diagnosed in 15 patients. Their median age was 44 (range 28–62 year). The M:F ratio was 9:8. The incidence of ES was 15.3 % (15/98) for all PCD and 19.4% (15/77) for multiple myeloma. Culture-negative fever was found in 82% patients, skin rash in 70.5%, respiratory distress, pulmonary infiltrates, and hypoxemia in 52.9% each, with 11.7% (two patients) requiring mechanical ventilation. Renal dysfunction and transient encephalopathy were found in two patients each while none had hepatic dysfunction. Diuretics alone were used in five patients, steroids alone in four, both steroids and diuretics in six while two patients improved on observation alone. None of the ES patients had died.

3.3. ES in Allogenic HSCT

Allogenic HSCT was performed in 41 patients during this study period. The incidence of ES in this population was found to be 4.8% (2/41). The median age was 20.9 years (Range 0.3–49 years) and the M:F ratio was 1.9:1. The most common indication was AML (24/41,58.5%) followed by ALL (5/41,12 %). Myeloablative conditioning (cyclophosphamide and busulfan) was used in 21

patients and the remaining 20 received a fludarabine-based non myeloablative regimen. The median stem cell dose was 3.2×10^6 cells/mm^3 and the median time to engraftment was 12 days (range 8–120 days). Patient 1 (26 y/M) underwent myeloablative allogeneic HSCT for CML blast crisis. He developed noninfectious fever with rash, weight gain, pulmonary infiltrates, and renal dysfunction on day + 10, which responded to steroids within 24 hours. Patient 2 (37 y/F) had undergone myeloablative allogenic HSCT for relapsed AML. She developed rash, weight gain, respiratory distress with pulmonary infiltrates on chest x-ray on day + 10 without any fever. Her respiratory distress, rash, and weight gain were resolved within 1, 2 and 4 days, respectively, after diuretics alone. Neither patient developed acute or chronic GVHD on follow up. Patient 2 died on day + 30 due to severe sepsis, while patient 2 was alive by day + 100. Although, patient 1 satisfied both SC and MC, patient 2 fulfilled only SC.

4. DISCUSSION

In the present retrospective analysis of 171 transplants, we observed a 4.8% (2/41) in an allogeneic cohort and a 12.3% (16/130) incidence of ES in an autologous cohort. The latter is quite low compared to a recent publication from India by Sheth *et al.* [12] where they reported an incidence of 25.8% (46/178) in autologous transplant recipients over an 8-year observation period (2008–2014). Although we used similar criteria, our observed incidence is almost half of theirs. However, it compares well with the 13% from a Spanish study by Carreras *et al.* [6] and the 7% Portuguese study by Lopes *et al.* [13]. It has already been highlighted that these figures vary according to the stringency or laxity of the criteria used.

If we compare the diagnostic performance of MC [3] and SC [1] in our study population, 12 (75%) patients satisfied the MC and 10 (62.5%) patients the SC separately. In our study, MC performed better than SC, an observation which is consistent with Carreras *et al.* [6] and Sheth *et al.* [12]. In all these studies, MC has been found to be the more sensitive one. Two patients fulfilled the MC but could not satisfy the SC and four patients (25%) did not satisfy either (MC- SC). It is noteworthy that the SC do not include patients with only fever and skin rash or with diarrhea which would otherwise be sufficient for the diagnosis of ES by the MC. But a patient without fever, with typical skin rash, pulmonary infiltrates, and weight gain will satisfy two major + one minor criteria of SC, but not MC. Because the dynamics of engraftment is widely variable from patient to patient, and given the pleiotropic manifestations of ES, we feel that rather than specifying fixed criteria, the concept of grade (as applied to acute GVHD) should be better used. We therefore propose a scoring system, where each feature mentioned either in SC or MC is given a weighted score based on its severity, and then a final combined score would define the severity of ES. We also agree with the approach of a unifying definition of ES and autologous GVHD as suggested by Cornell *et al.* in their recent review [7]. This can ease the diagnosis and simultaneously grade it appropriately making therapeutic decisions more accurate. Carreras *et al.* [6] have demonstrated that raised CRP is a useful diagnostic biomarker for this syndrome. A cut-off level of 6 mg/dL has approximately 90% sensitivity. Although we did not do this test routinely and this information is thus lacking in our series, we agree that it can be an important aid and should be incorporated into the diagnostic/ severity scoring of ES. In our practice, serum procalcitonin has also been a valuable adjunct in many cases to confidently

rule out a gram-negative sepsis in a timely manner. The role of this biomarker in the diagnosis of ES merits investigations.

Unlike Sheth *et al*'s findings [12], we could not demonstrate a significant difference in days of hospitalization and median duration of antibiotic usage between ES and non-ES patients. Eleven out of 18 patients required steroids and the median duration was 1.5 days, while the remaining seven improved with diuretics and observation alone. Clinical decision for the administration of steroids was taken based on the severity of symptoms in all cases. Two patient required mechanical ventilation and both improved with steroids. There was no mortality attributable to ES in our cohort. On multi variate analysis, only female gender was significantly predictive of ES (p = 0.013) while none of the other parameters (age, albumin level, prior lines of treatment, prior RT, CD34 cell count) was significantly associated. This is consistent with several previous reports [11,12,14–16].

Among plasma cell disorders, which constituted 50% of our study population, the incidence of ES was 19.7%. The Majority of these were multiple myelomas, while only 4 had POEMS. Interestingly, none of those with POEMS developed ES, which is not consistent with the published evidence stating a high incidence of ES in POEMS [5]. The reason for this may be the fact that our patients underwent ASCT as a consolidation after induction therapy, while at many Western centers (with high incidence of ES in POEMS) most patients are transplanted upfront. Moreover, it is possible that beside chemotherapy-associated toxicities, neutrophils and/or soluble factors released during the neutrophil recovery phase may play a role, facilitating the development of ES [8]. Future studies are required to better characterize the risk factors and underlying mechanisms in ES. The development of a grading system, such as that for NIH criteria for acute and chronic GVHD [17], would be a useful guide for determination of management decisions for ES. There is an unmet need for investigations on the utility of various biomarkers such as CRP, pro calcitonin, elafin as possible diagnostic tools or predictors of ES. If their value is confirmed, they could be included in the criteria for diagnosis of ES to improve its sensitivity.

CONFLICT OF INTEREST

Authors declare no conflict of interests for this article.

AUTHORS' CONTRIBUTIONS

RP, HK, LK: concept, design, data collection, analysis and drafting the manuscript; AS, SB, AG, RKS, AB, PSM, ST: acquisition and interpretation of data for the work; all authors approved the final version of the manuscript.

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Table S1 Therapy given and response to therapy in ES patients (n = 16).

	N	%
Treatment given		
Diuretics alone	4	25.0
Steroids alone	5	31.2
Diuretics + steroids	6	37.5
Observation only	1	6.2
Steroids used		
Dexamethasone	1	6.2
Prednisolone	10	62.5
Median number of days to start steroids after onset of symptoms	1 day	
Median duration of steroids	1.5 days (0–10)	
Time to response (days)		
Fever	1	
Weight gain	2	
Rash	1	
Hypoxia	1	
Resolution of chest infiltrates	1	
Resolution of diarrhea	1	
Death in 100 days	0	

Table S2 Comparison of patients undergoing autologous transplantation who experienced Engraftment Syndrome *versus* those who did not (N = 130).

Parameter	Engraftment Syndrome (n = 16)	No Engraftment Syndrome (n = 114)	*p*-Value
Use of amphotericin B	4	18	0.27
Median number of days on antibiotics (range)	9.5 (8–12)	11 (5–17)	0.09
Median number of days requiring hospitalisation (range)	20 (17–26)	20 (14–28)	0.26
Median PRBC requirement (range)	0 (0–2)	0 (0–3)	0.72
Median SDP requirement (range)	2 (0–3)	3 (1–4)	0.001
100-day mortality	0	1	0.59

PRBC: Packed red blood cells; SDP: Single donor platelets.

Table S3 Comparison of Spitzer's criteria (SC) and Maiolino criteria (MC) among patients with engraftment syndrome among the autologous transplant cohort. (16/130).

CLINICAL CRITERIA OF Engraftment Syndrome (N = 16)	N	%
MC+	12	75.0%
SC+	10	62.5%
MC+ SC+	10	62.5
MC+ SC-	2	12.5
MC- SC+	0	0
MC- SC-[a]	4	25.0

[a]Three patients had characteristic rash + weight gain (>2.5% of baseline), one patient had noninfectious fever + weight gain.