(e) ISSN Online: 2321-9599
(p) ISSN Print: 2348-6805

ORIGINAL ARTICLE

ASSESSMENT OF COMPUTED TOMOGRAPHY FINDINGS IN PATIENTS WITH PULMONARY COMPLICATIONS AFTER STEM CELL TRANSPLANTATION: A RETROSPECTIVE ANALYSIS

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ABSTRACT:

Background: Allogeneic haematopoietic stem cell transplantation (allo-HSCT) has been used with increasing frequency in cases of the malignant or non-malignant haematological diseases. Acute graft versus host disease (acute GVHD) and lung injury remain common complications and are significant causes of mortality after allo-HSCT. Aspiration pneumonitis, caused by the acute inhalation of gastric contents, appears on computed tomography (CT) as airway thickening with ground-glass opacities showing a centrilobular and peribronchovascular distribution. Hence; we retrospectively analyzed the findings of CT in patients developing pulmonary complications after allogeneic HSCT. **Materials & methods:** The present study was included in the department of pulmonary medicine of the medical institution and included all those patients who underwent stem cell transplantation and developed pulmonary complications and underwent high-resolution chest CT within 24 h of the onset of symptoms, and were shown to have abnormal findings by high-resolution CT. Clinical characteristics were evaluated in terms of age, sex, the existence of acute and chronic graft-versus-host disease (GVHD),days from HSCT, donor source, disease risk, decrease of cal-cineurin inhibitor (CI) doses, and conditioning regimen. Alemtuzumab-containing regimens were used in HSCT from a two or three antigen-mismatched donor. GVHD prophylax is consisted of a continuous infusion of cyclosporine or tacrolimus combined with short-term methotrexate. The observers evaluated the presence, extent, and distribution of CT findings suggestive of pulmonary complications. CT findings were evaluated as major and minor findings. All the results were analyzed by SPSS software. **Results:** Mean age of the patients was 49.5 years. Acute Myeloid leukaemia (ALL) was the final diagnosis in maximum of 31 percent of the cases while cute lymphoid leukaemia was the final diagnosis in 18 percent of the individuals. Source of donor were related in 30.5 and 32.6 percent of cases in responder and the non-responder group respectively while they were unrelated in 69.5 and 67.4 percent of the individuals respectively. Significant difference was observed while comparing the chronic GVHD parameter in between the two study groups. **Conclusion:** No specific CT findings are predicator of antimicrobial of steroidal response. However, futures studies are advocated.

Key words: CT, Pulmonary

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This article may be cited as: Patil NB, Wadhwani ND. Assessment of computed tomography findings in patients with pulmonary complications after stem cell transplantation: A retrospective analysis. J Adv Med Dent Scie Res 2016;4(5):110-113.

Access this article online	
Quick Response Code	Website: www.jamdsr.com
	DOI: 10.21276/jamdsr.2016.4.6.28

INTRODUCTION

In cases of the malignant or non-malignant haematological diseases, allogeneic haematopoietic stem cell transplantation (allo-HSCT) has been used with increasing frequency. Acute graft versus host disease (acute GVHD) and lung injury remain common complications and are significant causes of mortality after allo-HSCT.[1] Clinicians should be familiar with the different types of aspiration lung disease to enable the correlation of clinical information with main tomographic findings. Diffuse aspiration bronchiolitis is the inflammation of the bronchioles, with symptoms including cough, bronchospasm and dyspnoea.[2] Radiographically, patients with this condition demonstrate unilateral or bilateral tree-in-bud nodularity, centrilobular nodules and areas of increased attenuation. Aspiration pneumonitis, caused by the acute inhalation of gastric contents, appears on computed tomography (CT) as airway thickening with ground-glass opacities showing a centrilobular and peribronchovascular distribution.[3, 4] Hence; we retrospectively analyzed the

findings of CT in patients developing pulmonary complications after allogeneic HSCT.

MATERIALS & METHODS

The present study was included in the department of pulmonary medicine of the medical institution and included all those patients who underwent stem cell transplantation and developed pulmonary complications and underwent high-resolution chest CT within 24 h of the onset of symptoms, and were shown to have abnormal findings by high-resolution CT from 2012 to 2015. Clinical characteristics were evaluated in terms of age, sex, the existence of acute and chronic graft-versus-host disease (GVHD),days from HSCT, donor source, disease risk, decrease of calcineurin inhibitor (CI) doses, and conditioning regimen. With regard to the disease status, we defined acute leukemia and malignant lymphoma in first or second complete remission, low-risk myelodysplastic syndrome, aplastic anemia, myeloproliferative neoplasm, and chronic myeloid leukemia in chronic phase as standard-risk, and other conditions were considered high-risk. Diagnosis criteria of acute GVHD-induced lung injury are as follows:

- patients have manifestations of acute GVHD involving at least one organ, e.g. skin, liver and gut;[5]
- patients have abnormal chest HRCT;
- lung injury induced by infection and heart diseases can be excluded; chest HRCT scans are improved after treatment for acute GVHD.

Air trapping was determined when mosaic appearances were exaggerated on expiratory images. Progression of pulmonary hyperinflation was determined when lung volume enlargement and low-attenuated lung fields were evident as compared to the previous CT scan and chest radiograph. Bronchitis was defined as thickening of the wall of the central bronchi located more than 10 mm away from the pleural surface. Bronchiolitis was defined as centrilobular branching structures or small nodules that corresponded to bronchiolar wall thickening and/or peribronchiolar lesions. Consolidation was defined as areas of increased attenuation with obscuration of pulmonary vessels and bronchial structure. Alemtuzumab-containing regimens were used in HSCT froma two or three antigen-mismatched donor. GVHD prophylaxis consisted of a continuous infusion of cyclosporine or tacrolimus combined with short-term methotrexate. Two radiologists with 13 and 5 years experiences, who were blinded to the clinical information reviewed the images in consensus for evidence of pulmonary complications. The observers evaluated the presence, extent, and distribution of CT findings suggestive of pulmonary complications. CT findings were evaluated as major and minor findings. We classified major findings as lung parenchymal findings and minor findings as associated findings. All the results were analyzed by SPSS software. Chi-square test was used for the assessment of level of significance.

RESULTS

Table 1 shows the clinical parameters of the various patients included in the present study. Mean age of the patients was 49.5 years. Percentage of males and females in the present study was 59.5 percent and 50.5 percent respectively. In cases of patients who survived, median follow-up time was 52.5 years while median follow-up time in patients who died to pulmonary cause was 18. In 29.5 percent of the cases, the death occurred due to non-pulmonary cause. Acute Myeloid leukaemia (ALL) was the final diagnosis in maximum of 31 percent of the cases while cute lymphoid leukaemia was the final diagnosis in 18 percent of the individuals. **Graph 1** shows the clinical responses in the two study groups. Mean age of the patients in the two study groups was 47.6 and 48.2 years respectively. Source of donor were related in 30.5 and 32.6 percent of cases in responder and the non-responder group respectively while they were unrelated in 69.5 and 67.4 percent of the individuals respectively. **Table 2** highlights the p-value for the comparison of various clinical parameters in the two study groups. Significant difference was observed while comparing the chronic GVHD parameter in between the two study groups.

Table 1: Clinical parameter of the patients included in the present study

Parameter		Clinical characteristic
Mean age (years)		49.5
Males (Percentage)		59.5
Females (Percentage)		40.5
Median follow-up time	Survived	52.5
	Death due to pulmonary cause	18
	Death due to non-pulmonary cause	29.5
Final diagnosis (Percentage)	AML	31
	ALL	18
	Aplastic anaemia	7
	Myelodysplastic syndrome	18
	Malignant lymphoma	6
	Multiple myeloma	2
	Any other	18
Acute GVHD	Yes	72.5
	No	27.5
Chronic	Yes	22.5
	No	18.5
	Not evaluated	58

Graph 1: Clinical responses in the two study groups

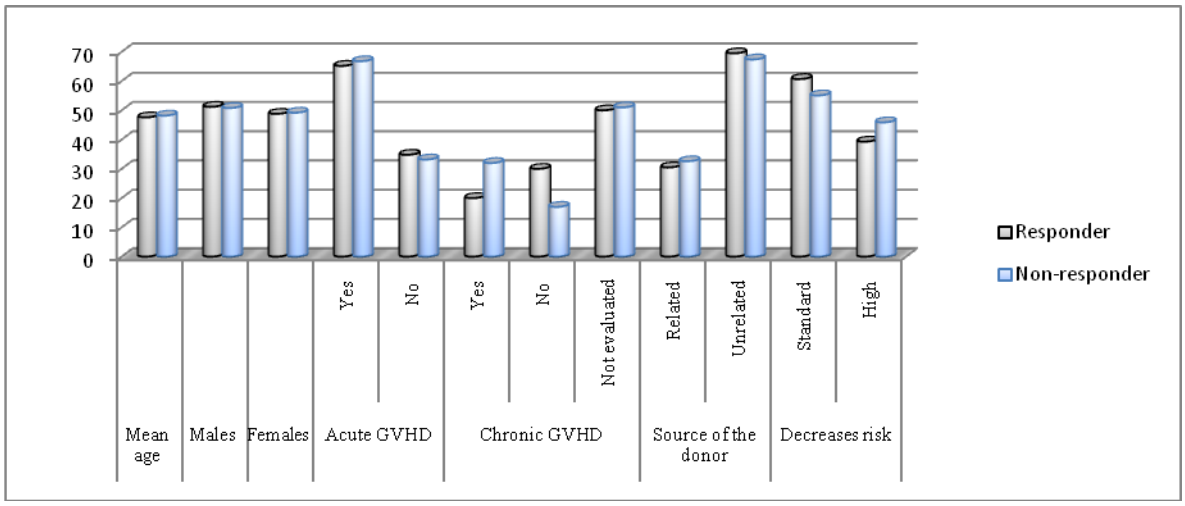

Table 2: P-value for the comparison of various clinical parameters in the two study groups

Parameter		Responder	Non-responder	p-value
Mean age (years)		47.6	48.2	0.52
Males (percentage)		51.2	50.8	0.41
Females (percentage)		48.8	49.2	0.82
Acute GVHD	Yes	65.2	66.8	0.65
	No	34.8	33.2	
Chronic GVHD	Yes	20	32	0.01*
	No	30	17	
	Not evaluated	50	51	
Source of the donor	Related	30.5	32.6	0.09
	Unrelated	69.5	67.4	
Decreases risk	Standard	60.7	55.1	0.12
	High	39.3	45.9	

*: Significant

DISCUSSION

Literature quotes numerous data on the association of lung injuries with chronic graftversus- host disease (cGVHD) as late-onset noninfectious pulmonary complications (LONIPC), chronic pulmonary syndrome, or idiopathic pneumonia syndrome.[6- 9] Although there have been many previous reports on cGVHD, none has described the development pattern of cGVHD in patients with multiple episodes. The prognosis of pulmonary parenchymal injuries varies: Some cases are responsive to treatment, and others are not. As far as we know, there has been no reliable research regarding imaging and the pathological characteristics that are correlated with responsiveness to therapy. Several authors have emphasized the importance of high-resolution computed tomography (CT) in the diagnosis of pulmonary complications after HSCT.[10- 12] High-resolution CT may show pulmonary abnormalities in patients with normal findings on radiographs and is superior to radiography in depicting the pattern and extent of abnormalities.[13] Hence; we retrospectively analyzed the findings of CT in patients developing pulmonary complications after allogeneic HSCT.

In the present study, we observed that no specific CT features were identified as predictors of an antimicrobial response. Since it is difficult to rule out infectious pulmonary complications by CT scan findings, it is often unavoidable to start antibiotics and antifungal therapy in patients with pulmonary complications without evidence of the presence of infectious pathogens. Ugai et al reviewed the high-resolution computed tomography (CT) findings in patients with pulmonary complications after allogeneic hematopoietic stem cell transplantation (HSCT), and to evaluate the relationship between CT findings and clinical outcomes. They collected the clinical data in 96 consecutive patients who underwent CT scan for pulmonary complications after allogeneic HSCT and analyzed the relationships among these clinical characteristics, CT findings and clinical responses. Radiologists who were blinded to clinical information evaluated the CT findings. From the results, they concluded that the presence of cavity formation and pleural effusion might predict a poor prognosis.[14] Liu et al investigated the characteristics of chest high-resolution computed tomography (HRCT) and pathogenesis of acute graft versus host disease (acute GVHD)-induced lung injury after allogeneic haematopoietic stem cell transplantation (allo-HSCT). They assessed 47 patients with acute GVHD of grades II-IV describes the clinical manifestations and characteristics of chest HRCT of acute GVHD-induced lung injury. Detection of serum

interferon gamma (IFNgamma) and tumour necrosis factor alpha (TNFalpha) were performed before the treatment for acute GVHD. From the results, they concluded that the lung might be one of the target organs of acute GVHD and participation of T lymphocyte, macrophage and cytokines such as IFN gamma and TNF alpha might play a role in the pathogenesis of acute GVHD-induced lung injury.[15] Yanagawa et al evaluated the development pattern in patients with multiple episodes of chronic graft-versus-host disease (cGVHD) and to analyze the computed tomography (CT) appearances of the pulmonary parenchymal injury and its relation to treatment response. CT patterns from 41 episodes of cGVHD (25 patients) were evaluated retrospectively and classified into four groups: group 1, airway involvement; group 2, subpleural consolidation or ground glass opacity (GGO); group 3, peribronchovascular/periseptal GGO or consolidations; group 4, others. They analyzed the changing pattern of the CT appearance during multiple episodes and the relation between this CT pattern and response to treatment. None of the patients showed airway involvement (group 1) and pulmonary parenchymal injury patterns (group 2 and 3) simultaneously in one episode. The group 3 CT pattern was more resistant to treatment than that of group 2 ($P < 0.05$). The pathological basis of the group 3 CT pattern varied but was characterized by mural incorporation fibrosis. From the results, they concluded that pulmonary cGVHD affected either the airway or pulmonary parenchyma but did not affect both simultaneously in one episode.[16] Merlini et al illustrated different patterns of LONIPCs on HRCT in allogeneic versus autologous BMT in order to investigate the correlation with chronic GVHD (cGVHD). A total of 67 HRCT scans were performed in 24 patients with noninfectious pulmonary disease at least 3 months after BMT (16 allogeneic, 8 autologous). Abnormality patterns and extension on HRCT images were correlated with the clinical outcome and with the severity of cGVHD. From the results, they concluded that LONIPCs can be a pulmonary manifestation of the disease.[17]

CONCLUSION

From the above results, the authors conclude that no specific CT findings are predicator of antimicrobial of steroidal response. However, futures studies are advocated.

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Source of support: Nil **Conflict of interest:** None declared