Bacterial pneumonia following bone marrow transplantation: HRCT findings*, **

Achados de TCAR nas pneumonias bacterianas após transplante de medula óssea

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Abstract

Objective: To describe HRCT findings in patients with bacterial pneumonia following bone marrow transplantation (BMT). **Methods:** This was a retrospective study involving 30 patients diagnosed with bacterial pneumonia in whom HRCT of the chest was performed within 24 h after the onset of symptoms and the diagnosis was confirmed, based on a positive culture of sputum or bronchial aspirate, together with a positive pleural fluid or blood culture, within one week after symptom onset. There were 20 male patients and 10 female patients. The median age was 21 years (range, 1-41 years). The BMT had been performed for the treatment of the following: chronic myeloid leukemia, in 14 cases; severe aplastic anemia, in 6; acute myeloid leukemia, in 4; Fanconi's anemia, in 3; and acute lymphocytic leukemia, in 3. Two radiologists analyzed the HRCT scans and reached their final decisions by consensus. **Results:** The most common HRCT findings were air-space consolidation (in 60%), small centrilobular nodules (in 50%), ground-glass opacities (in 40%), bronchial wall thickening (in 20%), large nodules (in 20%), pleural lesions (in 16.7%) and tree-in-bud opacities (in 10%). The pulmonary lesions were distributed in the central and peripheral areas in 15 patients, whereas they were exclusively peripheral in 11. Lesions were located in the lower and middle lobes of the lung in 22 and 20 patients, respectively. **Conclusions:** The most common HRCT findings in our patient sample were air-space consolidation, small centrilobular nodules and ground-glass opacities, most often in the central and peripheral regions of the middle and lower lung zones.

Keywords: Bone marrow transplantation; Pneumonia, bacterial; Tomography, X-Ray Computed.

Resumo

Objetivo: Descrever os achados de TCAR em pacientes com pneumonia bacteriana após transplante de medula óssea (TMO). **Métodos:** Estudo retrospectivo com 30 pacientes diagnosticados com pneumonia bacteriana, documentada com TCAR do tórax realizada em até 24 h do início dos sintomas, e com diagnóstico comprovado com base em cultura positiva de escarro ou de aspirado brônquico associada à cultura positiva de líquido pleural ou de sangue dentro de uma semana após o início dos sintomas. Foram avaliados 20 pacientes masculinos e 10 femininos, com mediana de idade de 21 anos (variação, 1-41 anos). O TMO foi realizado para o tratamento de leucemia mieloide crônica (n = 14), anemia aplástica severa (n = 6), leucemia mieloide aguda (n = 4), anemia de Fanconi (n = 3) e leucemia linfoide aguda (n = 3). Dois radiologistas analisaram os exames de TCAR, chegando a decisões finais por consenso. **Resultados:** Os achados de TCAR mais frequentes foram consolidação do espaço aéreo (60%), pequenos nódulos centrolobulares (50%), opacidade em vidro fosco (40%), espessamento de parede brônquica (20%), nódulos grandes (20%), lesões pleurais (16,7%) e opacidades em padrão de árvore em brotamento (10%). As alterações pulmonares estavam distribuídas nas regiões centrais e periféricas dos pulmões em 15 pacientes e somente na periferia em 11 pacientes. As lesões estavam localizadas no terço inferior e no terço médio dos pulmões em 22 e 20 pacientes, respectivamente. **Conclusões:** Os achados de TCAR mais comuns na nossa amostra foram consolidações do espaço aéreo, pequenos nódulos centrolobulares e opacidades em vidro-fosco, distribuídos nas regiões centrais e periféricas dos terços médio e inferior dos pulmões.

Descritores: Transplante de medula óssea; Pneumonia bacteriana; Tomografia computadorizada por raios X.

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Introduction

Pulmonary infections are a common cause of morbidity and mortality following bone marrow transplantation (BMT).[1,2] The most common pathogens are bacteria, fungi and viruses.[3-6] Few previous studies have discussed the HRCT findings in patients presenting bacterial pneumonia after BMT.[4-14] The aim of this study was to describe HRCT findings in such patients.

Methods

This was a retrospective study involving 30 patients with bacterial pneumonia, diagnosed following BMT and confirmed through microbiological studies. All of the patients gave written informed consent, and the institutional review board of our hospital approved the study. The patients had been submitted to HRCT within 24 h after the onset of infectious symptoms, and a definitive diagnosis had been made within the first week after symptom onset. None of the patients presented evidence of another, superimposed, pulmonary complication at that time. The cases were selected from a group of patients who had undergone BMT between 1993 and 2006. Cases in which there had been no bacteriological confirmation of the diagnosis were excluded from the analysis. We then reviewed the medical records of the patients selected.

Of the 30 patients evaluated, 20 (66.7%) were male and 10 (33.3%) were female. The median age was 21 years (range, 1-41 years). Allogenic BMT had been performed as the treatment for one of the following diseases: chronic myeloid leukemia, in 14 cases (46.7%); severe aplastic anemia, in 6 (20%); acute myeloid leukemia, in 4 (13.3%); Fanconi's anemia, in 3 (10%); and acute lymphocytic leukemia, in 3 (10%). The interval between BMT and symptom onset ranged from 10 to 2672 days (mean, 463 days). The diagnosis was made in the neutropenic period (0-30 days after BMT) in 8 cases (26.7%), in the early phase (30-100 days after BMT) in 7 (23.3%) and in the late phase (>100 days after BMT) in 15 (50%). There were 9 patients (30%) who had a histologically proven diagnosis of graft-versus-host disease (GVHD) that did not occur concomitantly with the pneumonia.

The diagnosis of bacterial infection was based on a positive culture of sputum or bronchial aspirate samples, together with a positive blood culture or pleural fluid culture. Bacterial pneumonia was attributed to *Staphylococcus aureus* in 14 cases, *Pseudomonas aeruginosa* in 9, *Streptococcus viridans* in 4, *Klebsiella pneumoniae* in 1, *Stenotrophomonas maltophilia* in 1 and *Enterococcus faecalis* in 1. Among the patients with GVHD, the infectious agent was *S. aureus* in 4, *P. aeruginosa* in 3, *S. viridans* in 1 and *K. pneumoniae* in 1.

The HRCT scans were performed at end-inspiration using 2-mm collimation at 10-mm intervals (Somaton ART; Siemens, Munich, Germany). Images were photographed using a mediastinal window (width, 400 HU; center, 20 HU) and a lung window (width, 1,500 HU; center, −700 HU). Two radiologists analyzed the HRCT scans and reached final decisions by consensus. The following HRCT findings were evaluated: pattern of the abnormalities (nodules, tree-in-bud pattern, air-space consolidations and ground-glass opacities); distribution of the lesions (central or peripheral, unilateral or bilateral and upper/middle/lower zone distribution); bronchial wall thickening; mediastinal lymph node enlargement; and pleural effusion. The nodules were classified as large (≥ 1 cm in diameter) or small (< 1 cm in diameter). Criteria for these findings were those defined in the Fleischner Society Glossary of Terms.[15]

Results

The most common HRCT findings in patients with post-BMT bacterial pneumonia were

Figure 1 - HRCT scan at the basal segment level demonstrating areas of air-space consolidation accompanied by large and small centrilobular nodules in a 25-year-old female patient with *Pseudomonas aeruginosa* pneumonia in the pre-engraftment period after bone marrow transplantation.

as follows (Figures 1 to 5): areas of air-space consolidation, in 18 (60%); small centrilobular nodules, in 15 (50%); ground-glass opacities, in 12 (40%); bronchial wall thickening, in 6 (20%); large nodules, in 6 (20%); pleural lesions, in 5 (16.7%); and tree-in-bud opacities, in 3 (10%).

Of the 14 patients infected with *S. aureus*, 7 (50%) presented air-space consolidation, 6 (42.9%) presented small centrilobular nodules, 4 (28.6%) presented ground-glass opacities, and 2 (14.3%) presented tree-in-bud opacities.

Among the 9 patients infected with *P. aeruginosa*, air-space consolidation was observed in 7 (77.8%), small centrilobular nodules in 5 (55.6%), ground-glass opacities in 3 (33.3%) and a large cavitated nodule in 1 (11.1%).

Of the remaining 7 patients, 5 (71.4%) presented ground-glass opacities, 5 (71.4%) presented bronchial wall thickening, 5 (71.4%) presented large nodules, 4 (57.4%) presented air-space consolidation, 4 (57.4%) presented small centrilobular nodules, and 1 (14.2%) presented tree-in-bud opacities.

The HRCT findings in the patients with GVHD were similar to those obtained in the sample as a whole.

The pulmonary lesions were distributed in central and peripheral areas in 15 patients (50%), whereas they were located exclusively in the peripheral areas in 11 (36.7%). The lesions affected the lower lobes of the lung in 22 cases (73.3%), the middle lobes in 20 (66.7%) and the upper lobes in 5 (16.7%).

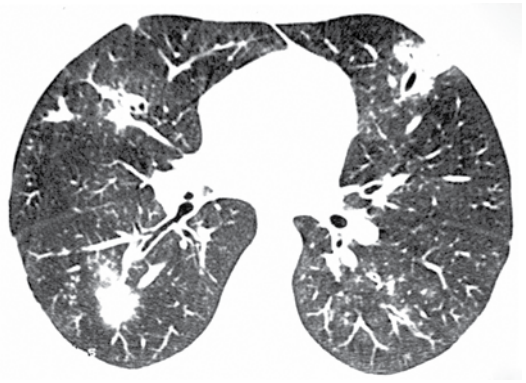

Figure 2 - HRCT scan at the level of the main bronchi showing large nodules with patchy areas of ground-glass opacity in a 22-year-old female patient with *Staphylococcus aureus* pneumonia in the late post-transplantation period after bone marrow transplantation.

Discussion

Pulmonary infection is the most common cause of complications following BMT. Post-BMT pulmonary complications follow a timeline related to the immunological status of the patients. In the pre-engraftment period (post-BMT days 0-30), severe neutropenia and mucous membrane lesions are common. As a result, fungal, bacterial, and respiratory syncytial virus infections can occur during this period.[16,17] In the post-engraftment period (post-BMT days 31-100), there is humoral and cellular immunity impairment, and cytomegalovirus and respiratory syncytial virus are the most common causal agents.[16,18] In the late post-transplantation period (> 100 days after BMT), patients typically present relatively normal immune function, and infections are most often associated with GVHD. In GVHD patients, the immune defects can persist indefinitely, predisposing to bacterial, fungal and viral infections.[1,4,7,16-20] In the present study, most (50%) of the patients presented bacterial pneumonia in the late post-transplantation period, compared with 26.7% in the pre-engraftment period and 23.3% in the post-engraftment period.

The most common organisms causing bacterial pneumonia in the pre-engraftment period after BMT are oral and intestinal mucous Gram-negative bacteria, as well as Gram-positive organisms, especially *Staphylococcus* spp. and *Streptococcus* spp. In the post-engraftment

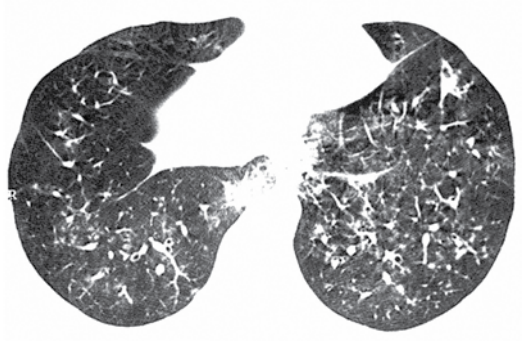

Figure 3 - HRCT scan at the level of the lower lobes demonstrating areas of ground-glass opacity accompanied by small centrilobular nodules in a 40-year-old male patient with *Pseudomonas aeruginosa* pneumonia in the late post-transplantation period after bone marrow transplantation.

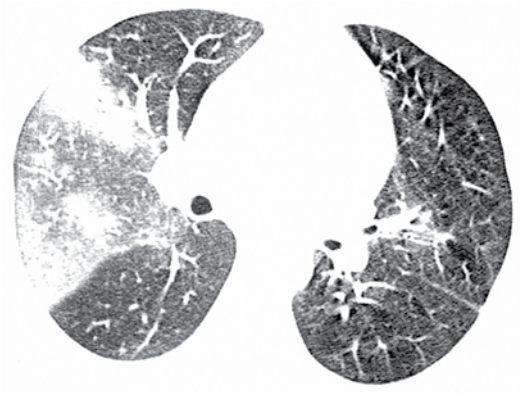

Figure 4 - HRCT scan at the level of the main bronchi demonstrating ground-glass opacities, accompanied by air-space consolidation, in the middle lobes in a 31-year-old female patient with *Staphylococcus aureus* pneumonia in the late post-transplantation period after bone marrow transplantation.

period, Gram-negative bacteria, including *P. aeruginosa* and *Escherichia coli*, are the most common, whereas Gram-positive bacteria, such as *S. pneumoniae* and *S. aureus*, are the most common in the late post-transplantation period.[6,7,10,16] In our patient sample, most of the cases were due to *S. aureus*, *P. aeruginosa* or *S. viridans*.

There have been only a few studies in which imaging findings were evaluated in patients with post-BMT bacterial pneumonia. The chest X-ray findings are similar to those seen in immunocompetent patients, with a predominance of air-space consolidation.[6,10,16] In a study of the chest X-rays related to 52 episodes of post-BMT bacterial pneumonia,[20] segmental infiltrate was observed in 37 (71%), lobar infiltrate in 10 (19%) and patchy infiltrate in 5 (10%). In 12 episodes (23%), the infection involved more than one lobe or segment. Pleural effusion accompanied the parenchymal infiltrate in 7 episodes (13%). One group of authors studied the HRCT findings of 114 patients with bacterial pneumonia, including 35 immunocompromised patients.[14] The authors found the most common alterations to be air-space consolidation (in 85%), ground-glass opacities (in 31%), reticular opacities (in 22%) and small centrilobular nodules (in 17%). These findings are in agreement with those obtained in the present study, in which 60% of the patients presented air-space consolidation and 40% presented ground-glass opacities. However, small centrilobular nodules were more common in our study, being observed in 15 (50%) of the 30 cases. In most of our patients, the alterations identified on the HRCT scans were located in the lower or middle lobes of the lung. Pleural effusion was observed in 10 patients, and none of the patients presented lymph node enlargement. There were no appreciable differences among the various etiologies in terms of HRCT findings.

Figure 5 - HRCT scan at the level of lower lobes showing a well-defined area of ground-glass opacity in the right lower lobe in a 12-year-old male patient with *Staphylococcus aureus* pneumonia in the pre-engraftment period after bone marrow transplantation.

In our study sample, we observed that the most common HRCT findings in patients with post-BMT bacterial pneumonia were air-space consolidation, small centrilobular nodules and ground-glass opacities, typically distributed in the central and peripheral regions of the middle and lower lung zones. Further studies correlating such findings with clinical and laboratory data are needed in order to fully define the diagnosis of bacterial pneumonia after BMT, since the HRCT findings are similar to those seen in other infectious pulmonary complications following the procedure.

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