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Pulmonary infections following bone marrow transplantation: High-resolution CT findings in 35 paediatric patients

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Abstract

Purpose: The purpose of this study was to assess the high-resolution CT findings of paediatric patients who had pulmonary infections following bone marrow transplantation (BMT), and to evaluate the differential diagnosis through high-resolution CT of the various pathogens responsible for pulmonary infections after BMT.

Patients and methods: The study included 35 consecutive patients who had documented pulmonary infection, high-resolution CT of the chest performed within 24 h of the beginning of symptoms, and proven diagnosis within 1 week of the onset of symptoms. The pulmonary infections were due to viruses ($n = 16$), bacteria ($n = 9$), fungi ($n = 9$), and protozoa ($n = 1$). Two radiologists analyzed the CT scans and reached final decisions regarding the findings by consensus.

Results: Four patients with confirmed pneumonia had normal high-resolution CT scans. Regarding the viral infections, the most frequent features were areas of ground-glass attenuation (43.7%) and small centrilobular nodules (31.2%). Airspace consolidation (88.9%), small centrilobular nodules (22.2%) and ground-glass attenuation (22.2%) were the most frequent findings in patients with bacterial pneumonia following BMT. Large nodules were seen in 66.7% of the patients with fungal pneumonia, and in only one case of virus infection. The "halo sign" ($n = 5$) was seen only in patients with fungal pneumonia.

Conclusion: In conclusion, the main causes of pulmonary infection in paediatric patients following BMT share similar high-resolution CT findings. Large nodules and "halo sign" are more common in patients with fungal infections.

Keywords: High-resolution computed tomography; Bone marrow transplantation; Pulmonary infections; Paediatric patients

1. Introduction

The bone marrow transplantation (BMT) is a well-established treatment option for haematological paediatric patients. However, the BMT in this group of patients has been associated with increasing number of immunossupressed children and severe complications [1,2]. Pulmonary infections are one of the most common complications following the BMT, representing the main cause of death in these patients. The early diagnosis and specific treatment of the pulmonary infections are essential to long-term success of the BMT [1–6].

The high-resolution computed tomography (CT) is the gold standard imaging technique for early diagnosis or exclusion of pulmonary infections in febrile neutropenic patients following BMT [7–10]. However, the most common high-resolution CT findings are usually non-specific and shared between the different causes of infection after marrow transplant. Correlation of the CT features with the different immunological phases after BMT has been considered helpful in narrowing the differential diagnosis [3,4]. Several studies have described the high-resolution CT manifestations of pulmonary infections occurring after BMT [3,4]. However, these studies were not specific for paediatric patients, including both adults and children who underwent BMT.

The aim of this study was to assess the high-resolution CT findings of 35 paediatric patients who had pulmonary infections following bone marrow transplantation. In addition, we assessed the differential diagnosis throught high-resolution CT

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of the various pathogens responsible for pulmonary infections after BMT.

2. Materials and methods

This retrospective study was based on the review of medical records from a population of 774 patients who underwent BMT at our institution from January 1993 to December 2006. Of these 774 cases, 212 had documented pulmonary complications and 64 of then were at the paediatric age. We reviewed the medical records of all these patients and identified 35 who had proven pulmonary infection during the first week of onset of symptoms and high-resolution CT performed within 24 h of onset of symptoms. Twenty-nine patients were excluded because they had no defined diagnosis, had diagnosis other than infection, or because the high-resolution CT was performed more than 24 h after the onset of symptoms.

There were 18 males and 17 females, with ages ranging from 1 to 15 years (median 8.1 years). All patients underwent allogenic BMT as the treatment for the following diseases: severe aplastic anaemia ($n = 10$), acute lymphocytic leukaemia ($n = 7$), Fanconi anaemia ($n = 6$), chronic myelogenous leukaemia ($n = 6$), acute myelogenous leukaemia ($n = 4$) and myelodisplastic syndrome ($n = 2$).

The infectious complications were due to viruses ($n = 16$), bacteria ($n = 9$), fungi ($n = 9$) and protozoa ($n = 1$). The viral agents included respiratory syncytial virus (RSV) ($n = 10$), cytomegalovirus (CMV) ($n = 4$), herpes simplex virus (HSV) type 2 ($n = 1$) and influenza virus ($n = 1$). The bacterial pneumonias were caused by *Staphylococcus aureus* ($n = 5$), *Pseudomonas aeruginosa* ($n = 3$) and *Enterococcus faecalis* ($n = 1$). All the fungal infections were caused by *Aspergillus* sp., and the protozoa infection was due to *Toxoplasma gondii*. The pulmonary infections were diagnosed during the neutropenic phase in 42.8% of the patients ($n = 15$), in the early phase in 28.6% ($n = 10$) and in the late phase in 28.6% of the cases ($n = 10$).

The pathogens responsible for the infectious episodes were documented by the following methods: bronchoalveolar lavage ($n = 13$), sputum culture ($n = 12$), sputum culture and bronchoalveolar lavage ($n = 7$), and autopsy ($n = 3$). Fungal infection was diagnosed from culture and histological evidence of tissue invasion. Diagnosis of RSV pneumonia was based on positive direct fluorescence antibody testing in specimens obtained at bronchoalveolar lavage. The diagnosis of CMV pneumonia was based on demonstration of the characteristic inclusion bodies in material obtained at bronchoalveolar lavage or autopsy. Diagnosis of bacterial infection was based on a positive culture of sputum or bronchoscopic aspirate combined with positive blood or pleural fluid cultures.

All the high-resolution CT scans of the chest were performed in the same facility (Somaton ART, Siemens, Germany), within 24 h of the beginning of the symptoms. The images were obtained with a low-dose protocol (120 kV and 25–50 mA s) at end-inspiration, using 2 mm collimation at 10 mm intervals, reconstructed with a high spatial frequency algorithm, and photographed using window settings to lung parenchyma (width, 1300 HU/1700 HU; level, −600 HU/−800 HU) and mediastinum (width, 300 HU/500 HU; level, 10 HU/30 HU).

Two radiologists studied the high-resolution CT scans and reached final decisions regarding the findings by consensus. The following high-resolution CT findings were evaluated: large nodules (1 cm or more in diameter), small centrilobular nodules (<1 cm), tree-in-bud pattern, air-space consolidation, ground-glass attenuation, bronchial wall thickening (bronchial wall greater than 1/6 of the bronchial diameter), interlobular or intralobular septal thickening, mediastinal lymph node enlargement (greater than 10 mm in short axis diameter, and pleural effusions. Criteria for these findings were those defined in the Fleischner Society's Glossary of Terms [11].

3. Results

Parenchymal abnormalities were seen on the high-resolution CT scans of 31 patients (88.6%). Four patients (11.4%) with normal CT scans had infections caused by RSV ($n = 3$) and bacteria ($n = 1$).

The most common high-resolution CT findings seen in the patients with abnormal CT scans are shown in Table 1. Regarding the viral infections, the most frequent features in patients with RSV infection were areas of ground-glass attenuation ($n = 4$) and small centrilobular nodules ($n = 3$) (Fig. 1); the patients with CMV pneumonia showed more commonly areas of ground-glass attenuation ($n = 3$) (Fig. 2). The patients with fungal infection demonstrated large nodules ($n = 6$) with halo sign ($n = 5$) and air-space consolidation ($n = 5$) as the most common abnormalities (Fig. 3). Finally, airspace consolidation ($n = 8$), small centrilobular nodules ($n = 2$) and ground-glass attenuation ($n = 2$) were the most frequent findings in patients with bacterial pneumonia following BMT (Fig. 4). Lymph node enlargement was not seen in this series.

Comparing the high-resolution CT findings between the patients with viral, bacterial and fungal pneumonia, all the features but large nodules and halo sign were similar among the groups. Large nodules were seen in six patients with fungal pneumonia and in only one case of RSV infection. In addition, the halo sign was demonstrated only in patients with fungal pneumonia.

4. Discussion

Pulmonary complications are common in paediatric patients who underwent BMT, and are usually related to severe immunosupression following the procedure [1,5,12,13]. The causes of the pulmonary complications after BMT follow a time-line related to the immunological status of the patients. There are three main immunological stages following the BMT: neutropenic (days 0–30), early (days 31–100), and late (days >101) phases. The neutropenic phase is characterized by a severe neutropenia and injury to the mucosal membranes, predisposing to aggressive infections, such as fungal and bacterial pathogens. In the early phase, the complications are related to the cellular and humoral impairment, and viruses, mainly CMV and RSV, are the main cause. In the late phase, the pulmonary complications