

Pulmonary complications of bone marrow transplantations

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Over the last decades, allogeneic hematopoietic stem cell transplantation (HSCT) has emerged as an important treatment option for several malignant and non-malignant diseases in childhood and adolescence, by using either bone marrow or peripheral stem cells after high-dose chemo(radio-)therapy. However, myeloablative high-dose regimens are limited by severe side effects contributing to significant morbidity and mortality rates. Transplant-related mortality is reported to occur in 10-30% of patients, often due to septicemia but also due to severe pulmonary complications. In 40% to 60% of the recipients pulmonary complications develop. These complications may be due to infectious or noninfectious conditions and are classified as early or late depending on whether they occur before or after day 100 post transplantation.

Early complications include pulmonary edema, infectious pneumonia, obstructive lung disease, and idiopathic interstitial pneumonitis. Late-onset non-infectious pulmonary complications (LONIPCs) encompass different entities occurring later than 3 months after HSCT, such as idiopathic pneumonia, bronchiolitis obliterans (BO), and lung fibrosis. Other classifications include bronchiolitis obliterans with organizing pneumonia (BOOP), diffuse alveolar damage (DAD), lymphocytic interstitial pneumonia (LIP), and non classifiable interstitial pneumonia (NCIP). The pathogenesis of these diseases mostly remains unclear, however a strong association between LONIPCs and chronic GVHD has recently been assumed. Historically, about 50% of all pneumonias observed after HSCT have been due to bacterial, viral, or fungal infections, but the strict use of broad-spectrum antibiotics in case of febrile neutropenia or as pneumocystis carinii prophylaxis, preemptive anti-viral therapies and modern infection-monitoring techniques in recent years has shifted the prevalences from infectious to non-infectious etiologies. However, non-infectious lung pathology responds poorly to standard therapeutic approaches, hence identification of predisposing factors is crucial for the development of preventive strategies.

Data from previous studies suggest that immunologically, the alveolar microenvironment differs significantly from other tissues or even blood. Therefore, respiratory tissue seems to react with a unique pattern of inflammatory processes, leading to specific injury and pathology after HSCT. These changes have been discussed to be due to genetic polymorphisms in alveolar cells, leading to altered secretion of cytokines, chemokines and growth factors.

The talk will give an overview of the most important pulmonary pathologies due to immunosuppression after HSCT in childhood, discussing underlying genetic changes and inflammatory mechanisms leading to acute and chronic respiratory tissue damage.