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Community-acquired respiratory paramyxovirus infection after allogeneic haematopoietic stem cell transplantation: a single-centre experience

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Background: Respiratory tract infections (RTIs) caused by paramyxoviruses such as respiratory syncytial virus (RSV), parainfluenza virus (PIV) and human metapneumovirus (hMPV) are associated with significant morbidity and mortality after allogeneic hematopoietic cell transplantation (alloHCT). While these viruses are closely related there are no comparisons regarding epidemiology, management and outcome of RTIs in patients after alloHCT.

Material/methods: We retrospectively identified symptomatic RSV, PIV or hMPV RTIs in alloHCT recipients diagnosed by multiplex PCR from nasopharyngeal swabs or bronchoalveolar lavage fluid collected between June 2010 and December 2014. Data on baseline characteristics, clinical presentation and course, treatment with systemic ribavirin (RBV) (oral or intravenous) and/or intravenous immunoglobulin (IVIG), and outcome of RTI episodes were analysed. Severe

immunodeficiency (SID) was defined as transplantation in the previous 6 months, T or B cell depletion in the previous 3 months, graft-versus-host disease [grade≥2], leukopenia, lymphopenia, or hypogammaglobulinemia < 4.5 g/L.

Results: A total of 103 RTI episodes (48 (46.6%) PIV, 33 (32%) RSV and 22 (21.4%) hMPV infections) in 66 alloHCT recipients were identified, which occurred in 84.5% at >100 days post-HCT (median 518; IQR, 212-1014). Lower RTIs accounted for 43.7% of PIV infections, for 36.4% of RSV infection and for 50% of hMPV episodes. 63 (61.2%) episodes occurred in patients with SID and 19 (30.2%) fulfilled ≥2 SID criteria without differences between the paramyxoviruses.

A total of 39/103 (37.9%) episodes were treated with RBV±IVIG and 24/103 (23.3%) with IVIG only. PIV RTIs were less frequently treated with RBV±IVIG than those with RSV or hMPV ($p \leq 0.001$). There were 40 (38.8%) episodes, which did not receive any antiviral therapy. SID patients were more frequently treated with antiviral drugs ($p = 0.001$).

The median duration of viral shedding did not differ between the different viruses ($p=0.280$). Six episodes (5.8%) progressed from upper to lower RTI. 40/103 (38.8%) of RTI episodes required hospitalization. Patients with lower RTI were more frequently hospitalized than with upper RTI ($p<0.001$). The overall mortality was 5.8% (6/103 RTI episodes), and did not differ between the 3 viruses. Patients fulfilling ≥2 SID criteria tended to have a higher progression rate ($p=0.075$), were more frequently hospitalised and transferred to the ICU ($p < 0.001$), and showed a higher mortality ($p < 0.001$). Haemolysis occurred in 25/39 (64.1%) RBV-treated episodes, requiring discontinuation in <10%.

Conclusions: Paramyxovirus RTI are frequent >100 days after alloHCT and clinically more severe in SID patients despite preferential antiviral treatment. Although no definite conclusions about efficacy can be made, current mortality was reduced compared to our earlier studies. The data suggest that timely diagnosis and early treatment with effective pan-paramyxovirus antivirals will have a major impact on morbidity and mortality of SID alloHCT patients.