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Pulmonary hypertension after hematopoietic stem cell transplantation in children

Bonnet D. (1), Moshous D. (2), Szezepanski I. (1), Neven B. (2), Blanche S. (2), Fischer A. (2), Levy M. (1)

1-M3C-Necker Enfants malades, Université Paris Descartes, Paris, France

2-Unité d'Immuno-hématologie, Hôpital Necker Enfants malades, Paris, France

Background and objectives

Pulmonary hypertension (PH) is a rare but important cause of mortality after hematopoietic stem cell transplantation (HSCT) in children. We report here a series of children who developed PH after HSCT.

Population and methods

Over a period of 7 years, 367 children underwent HSCT (age range 0.5-252 months - median 20.3 months). After HSCT, cardiac echo scans, motivated by respiratory and/or hemodynamic symptoms, identified 31 patients with elevated tricuspid regurgitation velocity (> 2.8 m/s). Indications for HSCT were: 10 lymphohistocytosis, 11 SCID, 3 osteopetrosis, 1 Griscelli syndrome, 1 CD40 Ligand deficiency, 1 chronic granulomatose disease, 3 neuroblastoma, and 1 medulloblastoma.

Results

Seventeen patients had PH confirmed at right heart catheterization (RHC) (mean PAP= 40.1 ± 10 mmHg (range 28-62mmHg), PVRi= 17.3 ± 11.1 WU.m² (range 8-42)). Vasoreactivity testing identified 13 responders according to Sitbon criteria. Five patients who were in too poor condition did not have RHC but were treated for PH according to echo signs. Nine patients did not have PH at RHC. Initial therapy was: calcium channel blockers in 6, oral monotherapy with PDE5i or ERA in 7, oral combo with ERA+PDE5i in 4, and up-front triple therapy with ERA+PDE5i+treprostinil in 5. Sequential add-on therapy was done in all 7 patients receiving mono- or oral combo. All patients receiving CCB needed add-on or switch for ERA and/or PDE5i. Seven/22 (32%) patients died: 6 of severe and progressive PH despite aggressive PH treatment, and one of infection after normalization of pulmonary pressure. Fifteen/22 PH patients are alive after a mean follow-up of 6.5 ± 2.3 years. All survivors could be weaned of PH treatment after a mean follow-up of 6.2 ± 3.1 months. The delay between clinical symptoms and initiation of PH therapy was significantly longer in patients who subsequently died (33.5 ± 23 days-median 30) than in survivors (7 ± 3 days) ($p < 0.001$).

Conclusion

PH after HSCT is often misdiagnosed in the context of multiple co-morbidities. Interpretation of vasoreactivity testing is questionable and CCB non efficacious. Aggressive up-front combination therapy allowed frequent normalization of pulmonary pressure and improved survival. Systematic screening for PH after pediatric HSCT can be suggested to allow early detection and treatment.