Anonymous

Review Date: 2021-06-09 14:37

Specific Comments To Authors: The author mentioned donor lymphocyte chimerism many times，but they did not run the analysis. My question: Is DLC really important in the diagnosis of GVHD? please make comments on that.

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Re-Review:

Yes

No

Specific Comments To Authors (File):

Answer: We looked through some of the literature. Taylor investigated the presence of donor lymphocyte chimerism in recipient peripheral blood as a diagnostic aid for GVHD after LT. The donor lymphocyte microchimerism (<1% donor lymphocyte chimerism) is often seen in LT recipients and is deemed crucial for immune tolerance and graft acceptance by the host. However, macrochimerism (1–80%), i.e., donor lymphocyte chimerism in recipient tissues (peripheral blood, skin, GI tract, bone marrow, or buccal mucosa), especially with a high proportion of CD8+ T cells, persists 3-4 weeks after LT and thus is associated with the eventual development of GVHD.

Whereas, there were some data of other repotes different. Zhao reported that they detected peripheral blood donor T-lymphocyte chimerism in 55 peripheral blood samples by STR-PCR in post-LT, and found donor T-lymphocytes chimerism in 11 peripheral blood samples. Among these 11 recipients, eight recipients finally developed aGVHD, and their the percentages of donor T-lymphocytes chimerism were > 10%(21.0%–98%), and the percentage for the other three recipients were < 10% and had no aGVHD. Noguchi et al reported that a GVHD case chimerism analysis of peripheral blood on day 68 revealed that 95% granulocytes were recipient type, but 95% T cells were Donor type. The patient died of multiple organ failure despite treatment with anti-thymocyte globulin. In this case, donor T-lymphocytes chimerism preceded wholeblood donor chimerism and the deterioration of GVHD.

Though chimerism is an important investigation, presence of chimerism in absence of clinical symptoms and histological findings is non-specific, making macrochimerism only a diagnostic tool. Given that whole-blood chimerism analysis can underestimate donortype cell chimerism because of the presence of abundant granulocytes, donor T-lymphocytes chimerism might be useful for the early diagnosis of GVHD. It has been suggested that an increased level of donor CD8+ T/NK cells >10% is indicative of GVHD. Also the severity and duration of chimerism varies with the evolution of patient and monitoring donor T-lymphocytes chimerism in these target organs, even after treatment and resolution of symptoms, could guide the treatment.