Reviewer #1:
Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors: The authors attempted treatment of a patient a 43-year-old male patient with severe AA-carrying BRIP1, TINF2, and TCIRG1 mutations. Screening of the family pedigree revealed the same TINF2 mutation in his mother and older brother, and his older brother also carried the BRIP1 variant but with normal telomere length and hematopoietic function. Whilst the manuscript had some innovative and useful ideas, this manuscript is not suitable for publication in its current status. This case report had some limitations that should be highlighted.
1. Several recent studies showed heterozygous TINF2 mutation in 1–5% of patients with acquired aplastic anemia (Walne et al, 2008; Du et al, 2009). The subjects of these studies were Caucasian, Black, and Hispanic. Analysis of the TINF2 gene among adult Asian populations of AA and myelodysplastic syndrome (MDS), to the best of our knowledge, had never been done.

We thank the reviewer for this comment. As you mentioned, several studies showed heterozygous TINF2 mutation in non-Asian DC and acquired AA patients, but TINF2 mutation has also been reported in Chinses DC patients (Hematology. 2022 Dec;27(1):1041-1045. PMID: 36073719; Int J Hematol. 2019 Mar;109(3):328-335. PMID: 30604317), as well as in Japanese acquired AA patients (Ref. 13: Br J Haematol. 2010;150(6):725-7. PMID: 20560964). The study demonstrated that 2/142 Japanese acquired BMFS patients carried TINF2 mutations, with an incidence rate of 1.4%, which is similar to that of other ethnic groups. Our current study may serve as a reference, attracting more researchers to focus on TINF2 mutations carried by Asian AA patients.

2. Mutations in the TINF2 gene have been associated with certain conditions related to telomere dysfunction, such as dyskeratosis congenita (DC) and other disorders that fall under the spectrum of telomere biology disorders. Whether a TINF2 mutation should be considered clinically important depends on the specific variant and its impact on the protein's function. Some TINF2 mutations may cause significant disruption to telomere maintenance, leading to severe clinical phenotypes like DC. Other variants might have milder effects and may be associated with less severe or asymptomatic presentations.

We appreciate the professional comments and agree with the reviewer. Actually, we first considered choosing unrelated donor or cord blood for transplantation, but no matched donor was found. Based on the condition of the patient's brother, we carefully selected him as a donor after clinical evaluation showed no abnormality in blood, bone marrow aspiration, bone marrow biopsy, bone marrow CD34 count, and telomere length measurement. This provides the hope and evaluation strategy of transplantation for patients lacking high-quality donor clinically. However, we understand and recognized that whether a TINF2 mutation should be considered clinically important depends on the specific variant and its impact on the protein's function. Some TINF2 mutations may

cause significant disruption to telomere maintenance, leading to severe clinical phenotypes like DC. Other variants might have milder effects and may be associated with less severe or asymptomatic presentations. If further basic experiments can be conducted in the future to confirm the differences in the effects of TINF2 mutations at different sites on protein expression and function, as well as clinical characteristics of patients, it will be helpful to more effectively define the pathogenesis and guide treatment. These have been added in the revised manuscript on page 4 in the **In conclusion** section.