Transfusion-associated graft-versus-host disease: A brief comment on blood safety

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Dear Editor,

A recent paper from Dr Elliot published in *Transfusion,* entitled 'Missed irradiation of cellular blood components from vulnerable patients: Insight from 10 years of SHOT data' updates on Transfusion-associated graft-versus-host disease and blood safety.

Transfusion-associated graft-versus-host disease (TA-GVHD) represents a rare and fatal event observed in immunocompromised and immunocompetent individuals. The main features of TA-GVHD are pancytopenia, erythema, diarrhea, hepatitis due to T lymphocytes engraftment and host tissue attack. This complication is commonly observed 1 or 2 weeks after transfusion of cellular blood components (eg red blood cells, platelets, granulocytes units and non-frozen plasma). A definitive diagnosis is based on clinical suspect and a confirmatory biopsy or molecular assays (chimerism testing).[1,2] At present, the gold standard procedure to prevent this transfusion reaction is X or Gamma irradiation of blood components.[1,2]

The United Kingdom (UK) hemovigilance scheme, Serious Hazard of Transfusion (SHOT), collects data on adverse events related to transfusion since 1996. Pre-storage leucodepletion of blood cellular components is standard in UK since 1999.[3] No confirmed cases of this complication were documented by SHOT reports from 2010 to 2019. In this period, 784 incidents of missed cellular blood components irradiation were recognized and 172 cases were excluded from the analysis because of missing diagnosis or data regarding stem cell transplant or indication for irradiation.[3]

The indications for irradiation most often missed were observed in patients treated with purine analoges (46.6%) or alemtuzumab (8.8%) and Hodgkin lymphoma (24.5%). Few cases, among these incidents, occurred in severe T cell-deficient patients (3,1%), in neonates after intrauterin transfusion (1,9%) and recipients of autologous and allogenic haematopoietic stem cell transplantation (5,6%). The majority of these events were recognized in hematology (55.7%) and clinical setting (88.7%), more generally due to poor communication between single organization and different hospitals.[3]

A total of 12 of this complication were recognized in retrospective SHOT analysis prior the introduction of pre-storage leucodepletion (November 1999) and 2 cases after this period.[4] Similarly, 2 cases of TA-GVHD were documented by the United States Food and Drug Administration, from 2010 to 2018.[5]

A systematic review of the last 5 decades and 26 countries, published by Kopolovic reported 348 cases of this transfusion complication.[6] A total of 282 cases of TA-GVHD were recognized between 1966 and 1999, 66 cases were noted between 2000 and 2013. Leukoreduction status was detailed in 135 cases (38.8%). Among these cases, only 2 blood components were pre-storage leucoreduced and 2 other were irradiated at a dose of 25 Gray (Gy).[6] Therefore, it is possible that technical modern standards reduces the risk for TA-GVHD.[2]

Interestingly, analysis of SHOT data summarized key points of blood safety on TA-GVHD (Figure 1).[3,8] This hemovigilance scheme underlines the importance of staff education regarding blood administration, the utility of electronic blood management systems, the need of haematological studies (eg long-term immune function in Hodkgin lymphoma and severe T–cell deficiency) and further improvement of questionnaries.[3]

Recently, guidelines on the use of irradiated blood components were updated on behalf of the British Society for Haematology Guidelines Transfusion Task Force.[4] In summary, patients undergoing chimeric antigen receptor T-cell (CAR-T) therapy should receive irradiated blood components, 7 days prior the harvest and continue until 3 months following CAR-T

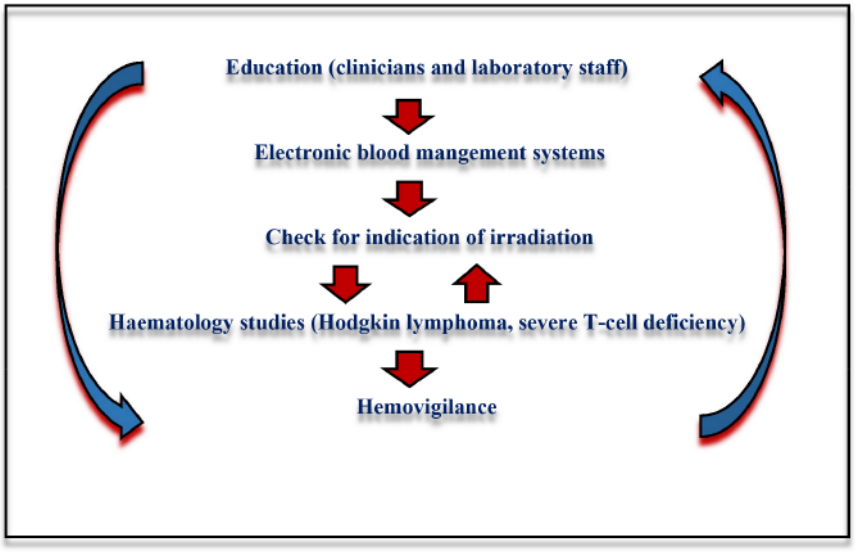

Figure 1. Key points of blood safety, focus on Transfusion-associated graftversus-host disease.

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cell infusion. Infants with congenital familial haemophagocytic lymphohistiocytosis represent another subset of severe T-cell deficiency in which irradiation of cellular blood components should be considered.[4]

In conclusion, guidelines for irradiation of cellular blood components varies in different countries.[7] Transfusion of fresh red cells and a high degree of homozigosity of Human Leucocyte Antigen (HLA) are well known risk factors for TA-GVHD.[2] In addition, high-risk groups for this complication are recipient of haematopoietic stem cell transplantation (HSCT), severe T-cell deficient patients, neonates and immunocompetent individuals who receive cellular blood components from their relatives.[2] The standard for preventing TA-GVHD is irradiation of cellular blood components.[2]

A retrospective analysis of 10 years of SHOT hemovigilance scheme suggest the utility of pre-storage leucodepletion to possibly reduce the risk for this complication, the need of haematological studies (eg Hodgkin lymphoma and T-cell deficiency), the importance of collaboration between clinicians and laboratory staff.[3,9,10]

References

1. Gehrie EA, Snyder EL, Ryder AB. Transfusion-associated graft-versus-host-disease. In: Rossi's Principles of Transfusion Medicine. Wiley Blackwell; 2016. p 680-684.
2. Hod EA, Francis R. Non infectious Complications of Blood Transfusion. In: 20th Technical Manual. AABB; 2020. p 627-657.
3. Elliot J, Narayan S, Poles D, et al. Missed irradiation of cellular blood components for vulnerable patients: Insights from 10 years of SHOT data. Transfusion 2020; 1-8.
4. Foukaneli T, Kerr P, Bolton-Maggs PHB et al. Guidelines on the use of irradiated blood components. BJH 2020;191:704-24.
5. US Food and Drug Administration (FDA) and Center for Biologics Evaluation and Research. Fatalities reported to FDA following blood collection and transfusion. Rockville, MD: FDA and Center for Biologics Evaluation and Research, 2018.
6. Kopolovic I, Ostro J, Tsubota H, et al. A systematic review of transfusion- associated graft-versus-host disease. Blood 2015;126:406-14.
7. Pritchard AE, Shaz BH. Survey of Irradiation Practice for the Prevention of Transfusion-Associated Graft-versus-Host Disease. Arch Pathol Lab Med 2016;140:1092-7.
8. Nascimento F. Steps for a safety clinical transfusion. ISBT Science Series 2011;6:72-5.
9. Howard PR. Adverse Complications of Transfusions. In: Basic and Applied Concepts of Blood Banking and Transfusion Practices. Elservier; 2017. p 265-266.
10. Robinson S, Harris A, Atkinson S et al. The administration of blood components: a British Society for Haematology Guideline. Transfus Med 2018; 28:3-21.