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LETTER TO THE EDITORS

Anti-HLA sensitization: should we abandon skin allografts for extensively burned patients?

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Dear Sirs,

We read with great interest the article by Duhamel *et al.* entitled *Anti-HLA sensitization in extensively burned patients: extent, associated factors, and reduction in potential access to vascularized composite allotransplantation* [1]. We would like to discuss three points raised by this retrospective study:

- Origin of anti-HLA antibodies

All 29 patients were transfused, and 14 of those who did not receive skin allografts developed HLA sensitization. The remaining 15 patients were both transfused and grafted: seven received glycerol-preserved allografts (GPSA), three received cryopreserved skin allografts (CPSA), and five received both types of allograft. They all developed HLA sensitization, except for one patient grafted with GPSA.

A recent study of primary kidney transplant candidates showed a substantial risk of HLA sensitization among transfused patients (transfused with leukoreduced blood), compared to nontransfused patients [2].

The 100% rate of HLA sensitization observed by Duhamel *et al.* among nonallografted patients might be explained by massive and repeated transfusions (36 ± 13 units of packed red blood cells per patient). As mentioned by the authors themselves, they did not determine whether HLA sensitization was due to skin allografting (15/29) or blood transfusion (29/29).

- Contribution of allografts to HLA sensitization and quality of coverage

Duhamel *et al.* found that GPSA seemed less likely than CPSA to induce HLA sensitization. They cited Cinamon *et al.* [3] and Richters *et al.* [4], but neither team provided information on the respective contributions of CPSA and GPSA to HLA sensitization.

The quality of coverage is still debated [5]. Duhamel *et al.* referred to three studies: Dhenin *et al.* [6] reported their clinical experience with GPSA; Wachtel *et al.* [7] compared fresh allografts and two types of thawed CPCA in a clinical study; and Cinamon *et al.* [3] found that CPSA gave better coverage than GPSA in mice. None of these studies compared CPSA vs. GPSA in humans.

A recent study by Kua *et al.* [8] showed a trend towards lower mortality and shorter hospital stays with CPSA vs. GPSA in severely burned patients. Nevertheless, human studies comparing the immune responses to CPSA and GPSA remain to be carried out.

- Vascularized composite allotransplantation

We fully agree that HLA sensitization must be avoided, when possible, to keep open the option for vascularized composite allotransplantation (VCA). But, in the acute phase of extensive burn injury, priority must be given to immediate survival and effective coverage.

Predictive criteria could help to optimize the later use of VCA. A multiparameter scale needs to be established, including the percentage of total burn surface area, the affected body areas, and blood transfusion. A threshold value would be useful to judge whether the risk of sensitization is justified by the need for coverage: for example, concerning the recommended use of CPSA for wound-bed preparation before the application of cultured autologous keratinocytes [9].

The study by Duhamel *et al.* should further encourage the development of skin substitutes able to provide effective coverage during the acute phase of burn injury without causing HLA sensitization.

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Conflict of interest

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References

1. Duhamel P, Suberbielle C, Grimbert P, *et al.* Anti-HLA sensitization in extensively burned patients: extent, associated factors, and reduction in potential access to vascularized composite allotranspantation. *Transpl Int* 2015; **28**: 582.
2. Leffell MS, Kim D, Vega RM, *et al.* Red blood cell transfusions and the risk of allosensitization in patients awaiting primary kidney transplantation. *Transplantation* 2014; **97**: 525.
3. Cinamon U, Eldad A, Chaouat M, *et al.* A simplified testing system to evaluate performance after transplantation of human skin preserved in glycerol or in liquid nitrogen. *J Burn Care Rehabil* 1993; **14**: 435.
4. Richters CD, Hoekstra MJ, van Baare J, *et al.* Immunogenicity of glycerol-preserved human cadaver skin *in vitro*. *J Burn Care Rehabil* 1997; **18**: 228.
5. Vloemans AF, Middelkoop E, Kreis RW. A historical appraisal of the use of cryopreserved and glycerol-preserved allograft skin in the treatment of partial thickness burns. *Burns* 2002; **28**(Suppl 1): S16.
6. Dhenin Ch, Desbois I, Yassine A, Benissad H, Lignée J. Utilisation of glycerolized skin allografts in severe burns. *Burns* 2002; **28**(Suppl 1): S21.
7. Wachtel TL, Ninnemann J, Fisher JC, Frank HA, Inancsi W. Viability of frozen allografts. *Am J Surg* 1979; **138**: 783.
8. Kua EH, Goh CQ, Ting Y, Chua A, Song C. Comparing the use of glycerol preserved and cryopreserved allogenic skin for the treatment of severe burns: differences in clinical outcomes and *in vitro* tissue viability. *Cell Tissue Bank* 2012; **13**: 269.
9. Cuono CB, Langdon R, Birchall N, Barttelbort S, McGuire J. Composite autologous-allogeneic skin replacement: development and clinical application. *Plast Reconstr Surg* 1987; **80**: 626.

