Abstract n° 6188

Persistence of yellow fever vaccine-induced antibodies after allogeneic haematopoietic stem-cell transplantation

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BACKGROUND

Immunization using live attenuated vaccines, such as the yellow fever vaccine (YFV), is contraindicated in allogeneic haematopoietic stem cell transplantation (allo-HSCT) recipients within 2 years after transplantation. In patients who underwent solid-organ transplantation and were vaccinated prior to transplantation, long-term persistence of YF antibodies has been reported. However, persistence of YFV-induced antibodies has not been investigated yet in adult allo-HSCT recipients. Our study aimed to determine the persistence of YF neutralizing antibodies in a cohort of bone marrow recipients who had been vaccinated prior to allo-HSCT.

PATIENTS AND METHODS

We retrospectively retrieved allo-HSCT recipients who were immunized with the YFV prior to transplantation in our institution. We measured protective levels of YF neutralizing antibodies using the plaque-reduction neutralization test, which is the standard technique for assessing the humoral response to YF immunization.

RESULTS

We identified 21 allo-HSCT recipients who where immunized with YFV before HCST. To date, serological analyses are available for 16 patients **(Table 1)**. Median age was 47 years (range: 28-67). All patients underwent HSCT as treatment of a haematological malignancy **(Figure 1)**. Conditioning regimen consisted of a myeloablative conditioning in 5 cases. Patients received transplant from matched related donors (N=10), matched unrelated donors (N=5) and haploidentical donor (N=1).

For 13 (81%) patients, **YF-neutralizing antibodies titres were above the protective level** (≥ 10 U/L) after a median duration of 12 months post-HCST (**Figure 1**). Three patients had received a graft for < 6 months. The median YF-antibody level was 20 U/L (interquartile: 20–40).

For 3 (19%) patients, **YF-neutralizing antibodies titres were under the protective level** (≤ 5 U/L). In 1 case, YF antibody level was at 20 UI/L at 2 months post-HCST but, 4 months later, had decreased to ≤ 5 UI/L, suggesting that pre-graft YF immunity level has waned. In 2 cases, YF-antibody level measurement was ≤ 5 UI/L at 32 and 150 months post-HCST. YF-negative patients did not statistically differ from YF-positive patients for any available characteristic.

We retrieved the YF-vaccination status of 9 (69%) donors of the 13 YF-positive patients: 5 had a positive YF-serology, 3 declared a previous vaccination (no serology) and 1 never been vaccinated (a boy who have never travelled to YF-endemic country, no serology). Except for this latter case, we were not able to determine if detectable YF-antibodies were produced by donor or persisting recipient lymphocytes.

CONCLUSION

Protective YF-antibody titres were observed in a large majority of patients who were immunized against yellow fever prior to HSCT. Allogeneic stem-cell recipients who intend to travel to YF-endemic countries should be tested for YF-antibody before travelling. Further studies are needed to determine if YF-antibodies are produced by donor or recipient lymphocytes.

Table 1: clinical characteristics of the 16 patients with available YF-serology

Patients (N)	**16**
Women/Men, N	6/10
Age at transplant in years, N (range)	47 (28-67)
Country of birth, N (%)	France: 11 (69%) YF-endemic country: 5 (31%)
Hematopoietic stem cell transplantation (HSCT)	
Matched unrelated donor	5 (31)
Related donor (10 genoidentical and 1 haploidentical)	11 (69)
Graft source peripheral blood stem cells, (%)	100%
Conditioning intensity: myeloablative/reduced intensity, N	5/11
Follow-up	
Full donor chimerism at day 180	15 (94%)
Acute graft-versus-host disease (GVHD) with systemic corticosteroids	7 (44%)
Chronic GVHD with immunosuppression ≥ 2 years	5 (31%)

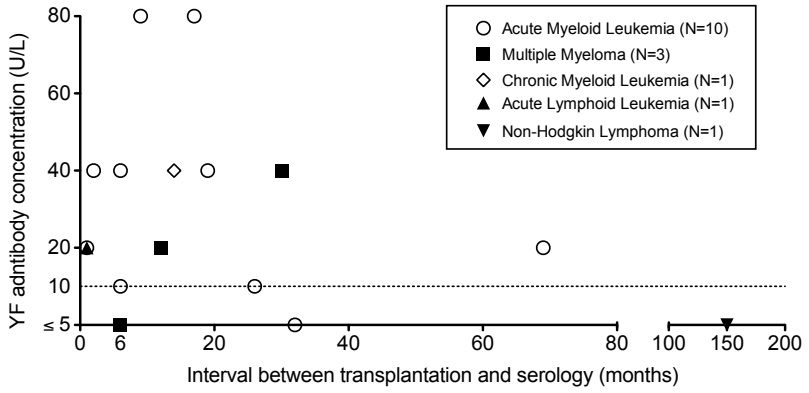

Figure 1: Levels of yellow fever antibodies in 16 stem-cell transplant recipients.
Serum yellow fever (YF) antibody levels (U/L) in relation to the interval between HCST and serology (months). The horizontal dotted line shows the lowest YF antibody level corresponding to a protective immunity (10 U/L). There were no significant differences in antibody levels related to the type of previous haematological disease, conditioning intensity, the presence of GVHD, a full donor chimerism or immunosuppressive drugs.