H1N1 in allogeneic stem cell recipients: courses of infection and influence of vaccination on graft-versus-host-disease (GVHD)
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Abstract: Seasonal influenza causes substantial morbidity and mortality in immunocompromised allogeneic blood stem cell recipients. In view of 2009 pandemic influenza A (H1N1) and against the background of the preventive nationwide availability of the vaccine PandemrixTM (GlaxoSmithKline) in Germany since October 2009, the question was raised if patients after allogeneic hematopoietic stem cell transplantation (HSCT) should be vaccinated or not. A major concern against the use of an adjuvant containing vaccine was the apprehension of chronic graft-versus-host-disease (GVHD) exacerbation or deterioration.

Response to Reviewers: All suggestions by the reviewers were considered in the revised version and the addressed points were changed.
H1N1 in allogeneic stem cell recipients: courses of infection and influence of vaccination on graft-versus-host-disease (GVHD)

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It is well known that seasonal influenza causes substantial morbidity and mortality in immunocompromised allogeneic blood stem cell recipients. In view of 2009 pandemic influenza A (H1N1) and against the background of the preventive nationwide availability of the vaccine Pandemrix™ (GlaxoSmithKline) in Germany since October 2009, the question was raised if patients after allogeneic hematopoietic stem cell transplantation (HSCT) should be vaccinated or not. A major concern against the use of an adjuvant containing vaccine was the apprehension of chronic graft-versus-host-disease (GVHD) exacerbation or deterioration.

Out of 370 HSCT-recipients with ambulatory clinic visits between October 2009 and February 2010 10 (2.7 %) presented with mild to moderate flu-like symptoms and positive throat swab. Median post-transplant follow up was 10 months and all patients were under moderate systemic immunosuppressive medication for GVHD management (n=5) or primary GVHD prophylaxis (n=5). Immediate initiation of oseltamivir at a dose of 75 mg twice a day resulted in remission of clinical symptoms in 5 patients without sequel but 2 required non-invasive and 3 invasive mechanical ventilation emerging disastrous and finally lethal in two cases. Seven patients needed to be hospitalized.

On the other hand 55 patients (14.9 %) with a median post-transplant follow up of 20 (3-192) months underwent single dose 3.75 µg antigen (A/California/7/2009 (H1N1)v-like strain (X-179A)) vaccination formulated with the adjuvant system AS03 (Pandemrix™). Local and systemic events were generally mild and adjuvant vaccination was not associated with acute worsening of GVHD symptoms in 31 HSCT recipients suffering from limited (n=19) or extensive (n=12) chronic GVHD. Patients without chronic GVHD (n=24) did not develop de novo vaccine-related allo-immune phenomena within 3 months of post interventional surveillance. Except one patient who got infected with H1N1 4 days after vaccination none of the vaccinated subjects presented with signs of influenza manifestations in the sequel.

These single centre experiences during the peak of 2009 H1N1 pandemic in Germany confirm the anticipated potentially serious outcome of H1N1 infection in immunodeficient high risk population groups. The experiences demonstrate that by taking all available measures it might be possible to
prevent even patients highly susceptible to any kind of infection from epidemic fatalities. Apart from the fact that the effectiveness of vaccination needs to be evaluated by verifying immune responses on the laboratory scale the application of vaccines with adjuvant formulation primarily does not seem to have any adverse immune stimulating effects. Therefore, besides common reasonable precautions active vaccination of allogeneic HSCT recipients may provide a safe strategy to conquer new healthcare challenges.

References:


*Conflict of interest
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