IMMUNE RESPONSE TO TBE INFECTION OR TBE VACCINATION? DIFFERENTIAL SEROLOGICAL ANALYSIS

Background

The protection rate of TBE vaccination has been estimated at more than 95% according to field studies. However, vaccine failures occur – often despite IgG antibodies being present in patients. Mostly, viral RNA cannot be detected at the onset of symptoms, and therefore, serological discrimination between vaccine-induced antibodies and those elicited by acute infection and measuring the immune response following vaccination is important. Non-structural protein 1 (NS1) is synthezised in TBE virus infected cells, but is not incorporated into TBE virus particles. Thus, NS1 is not present in (inactivated whole virus) TBE vaccines. Therefore, vaccinees should not develop NS1 antibodies and as a result serological response to NS1 should be a useful tool to distinguish between an immune response caused by an infection vs. antibodies induced from vaccination.

Results

A suspension multiflex immunoassay (SMIA) has been developed by which an immune reponse can be analysed to TBE whole virus (WV) or NS1. Sera from 50 patients with high IgM and low IgG concentrations (according to commercial assays) were analysed by SMIA and for comparison, serum samples from 50 healthy individuals were analyzed – drawn i) on day 0 of vaccination, ii) 30 days after the second dose, and iii) 30 days after the third injection. All 50 acute-phase TBE samples showed WV-specific IgM measured by SMIA, and 46 patients also had NS1-specific IgM. In contrast, only seven of the serum samples from vaccinees had a (weak) IgM response to WV, and only one sample was slightly positive for NS1 IgM. All 50 samples from TBE patients had WV-specific IgG and 43 had developed NS1-IgG. In contrast, only three of the 150 samples (after one, two and three immunizations) had NS1-specific IgG.

The neutralisation IgG avidity index (AI) was low in acute phase patients and also in vaccinees after the first and second injection, while a pronounced increase of AI could be determined in vaccinees after three injections indicating that at least three doses of TBE vaccine are needed to achieve a high neutralising antibody avidity as measured by SMIA.

Discussion

The presence or absence of NS1-specific IgM/IgG antibodies and the determination of IgG AI may help to discriminate between a serological response after an infection or vaccination and to analyse sera in detail (e.g. of immuno-compromized individuals and for seroprevalence studies). In addition, the use of SMIA may offer an alternative to neutralization tests for which a biosafety 3 level is required.

Literature

Albinsson et al.

Distinction between serological responses following tick-borne encephalitis (TBEV) infection vs vaccination. Sweden 2017

Euro Surveill. 2018; 23(3):pii=17-00838. https://doi.org/10.2807/1560-7917.ES.2018. 23.3.17-00838

Author: Dr. Michael Bröker

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