LETTER TO THE EDITOR

Neurofascin as target of autoantibodies in Guillain–Barré syndrome

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Sir, We have read with great interest the McGonigal et al. (2010) article, which addresses the pathogenic role of GD1a antibodies and complement activation for node of Ranvier dysfunction. Nodal injury might explain several electrophysiological features and clinical symptoms in patients with Guillain–Barré syndrome including the sometimes rapid recovery from paralysis. In our opinion, the reported mechanisms by which loss of axonal conduction can occur, may account not only for GD1a, but also for further nodal proteins once patients with Guillain–Barré syndrome develop antibodies against them. We therefore analysed sera from patients with Guillain–Barré syndrome for the presence of autoantibodies against two important nodal targets, neurofascin and contactin, and identified autoimmunity against the axonal and glial cell adhesion molecule neurofascin.

Sera were obtained from 52 patients with Guillain–Barré syndrome [43% female, mean (SD) age 53.4 (17.7) years] and 44 healthy volunteers [54% female, mean age 42.7 (19.1) years] with informed consent as published (Görtzen et al., 1999). Patients and controls did not significantly differ in serum albumin [3995 (951) versus 4238 (254) mg/dl, P = 0.42] or serum IgG concentrations [1111 (244) versus 982 (204) mg/dl, P = 0.08]. Antibody titres were determined using enzyme linked immunosorbent assay with recombinant rat neurofascin or human contactin-2 protein (R&D Systems) and specificity was confirmed by western blots (Fig. 1A). Serum neurofascin-IgG levels were significantly elevated compared with controls (P = 0.0019, Mann–Whitney test, Figure 1). Patients with Guillain–Barré syndrome had significantly higher neurofascin (but not contactin) antibody titres than controls. GBS = Guillain–Barré syndrome.

Figure 1 Detection of specific autoantibodies using competitive enzyme linked immunosorbent assay with recombinant neurofascin or contactin-2. (A, left) Absorbance of representative Guillain–Barré syndrome sera could be blocked using preincubation with recombinant neurofascin (0.001–10 µg/ml). (A, right) Confirmation of antibody specificity in western blots (0.5 µg neurofascin per lane). Guillain–Barré syndrome sera (1:100) with high neurofascin antibody titres (Lane 2) and the positive control antibody (Lane 4; 1:200, kindly provided by Mat Rasband), but not sera after preabsorption (Lane 3) or with low titres (Lane 1) detected the specific band. (B) Patients with Guillain–Barré syndrome had significantly higher neurofascin (but not contactin) antibody titres than controls. GBS = Guillain–Barré syndrome.
two-tailed), while IgG levels against contactin-2 were not different ($P = 0.27$, Fig. 1B).

Increased humoral responses against neurofascin in patients with Guillain–Barré syndrome have not been observed so far and might be relevant for development or augmentation of the autoimmune process in a subgroup of patients with Guillain–Barré syndrome. Interestingly, in McGonigal et al.’s (2010) paper, the staining pattern for neurofascin was lost or disrupted at injured nodes of Ranvier. Neurofascin antibodies might be candidates to disrupt sodium channel function and axon conduction at nodes, trigger axonal injury and inhibit remyelination. Indeed, in a rat model of Guillain–Barré syndrome, neurofascin autoantibodies emerged prior to demyelination (Lonigro et al., 2009). Moreover, the complement-dependent pathophysiology of neurofascin autoantibodies for axonal injury was demonstrated in a multiple sclerosis model (Mathey et al., 2007). McGonigal et al. (2010) give good evidence for the role of anti-GD1a antibodies for nodal injury in mice. Based on our human findings, however, we propose that further proteins must be considered as potential immunological targets in peripheral nerve pathology, including neurofascin, gliomedin or caspr.

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References


