OBJECTIVE: Autoantibodies to voltage-gated potassium channel complex (VGKC) are detected in a broad range of neurological disorders, including leucine-rich glioma inactivated 1 (LGI1) and contactin-associated protein-like-2 (Caspr2) encephalitis. To date, there has been no study characterizing patient sera and disease controls. A relatively low prevalence of LGI1 and CASPR2 IgG antibodies in patients with or without VGKC antibodies.

METHODS: To determine the performance characteristics of the LGI1 and CASPR2 antibodies, we analyzed sera from patients with limbic encephalitis (n=25), healthy controls (n=149), and commercial reagents (n=149) that were used as the foundation for specific paraneoplastic syndrome associated antibodies (n=58). The limbic encephalitis patients were either positive for LGI1 (n=10) or CASPR2 (n=10) antibodies. Of the VGKC-screened samples, 20% (31/158) were positive, 44% (69/158) were indeterminate; and, the remaining 37% (57/158) were negative. All sera were evaluated with a 6-Biospot slide (Euroimmun, Lübeck, Germany) consisting of rat hippocampus, rat cerebellum, a transfected eukaryotic cell line (EU90) specifically expressing LGI1 receptors or CASPR2 receptors, non-transfected EU 90 control cells and a human epithelial cell line derived from a larvy cancer; HeP-2. Species were evaluated at a 1:10 dilution and titers to end point if positive fluorescence for either LGI1 or CASPR2 antibodies were observed. This study was conducted in compliance with ARUP policies and Health Insurance Portability and Accountability Act guidelines under University of Utah Institutional Review Board approved protocols.

RESULTS: Sensitivity of 100% was observed for both LGI1 and CASPR2 assays with sera from a limited number of clinically confirmed limbic encephalitis patients. Both assays displayed specificity of 99.4% (148/149) with one self-reported healthy donor serum displaying false-positive fluorescence in both LGI1- and CASPR2-transfected cells. LGI1 antibody was detected in 29% (93/318) of the sera in which the disease was positive for either LGI1 (n=10) or CASPR2 (n=10) antibodies. Of the VGKC-screened samples, 20% (31/158) were positive, 44% (69/158) were indeterminate; and, the remaining 37% (57/158) were negative. All sera were evaluated with a 6-Biospot slide (Euroimmun, Lübeck, Germany) consisting of rat hippocampus, rat cerebellum, a transfected eukaryotic cell line (EU90) specifically expressing LGI1 receptors or CASPR2 receptors, non-transfected EU 90 control cells and a human epithelial cell line derived from a larvy cancer; HeP-2.

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CONCLUSION: These BIOCHIPs demonstrated excellent sensitivity and specificity in the detection of LGI1 and CASPR2 autoantibodies in clinically defined limbic encephalitis patients. We report a relatively low prevalence of LGI1 and CASPR2 antibodies in patients with or without VGKC antibodies. A total of 69 sera were analyzed. These included sera from patients with limbic encephalitis (n=25), healthy controls (n=149), and commercial reagents (n=149) that were used as the foundation for specific paraneoplastic syndrome associated antibodies (n=58).

MATERIALS AND METHODS

STUDY POPULATION: In this study, 318 patient sera were collected from patients with limbic encephalitis, 158 patients were admitted to ARUP for VGKC IgG antibody testing, 57 autoantibody positive patient sera (including amyloidosis, ANA, Ri, Yo, Hu, GAD65, CV2, NMDAR, cycled citrullinated peptide, and rheumatoid factor) and 149 self-reported healthy donor sera were evaluated. The distribution and prevalence of VGKC antibodies in self-reported (1A) and consecutive patient sera (1B) is shown. Reference intervals for the VGKC IgG antibody radioimmunoassay at ARUP were originally established using the receiver operating characteristic (ROC) curve value with optimal sensitivity and specificity of 31 pmol/L (black bars); Negative values can be significantly affected.

DETECTION OF LGI1 or CASPR2 IgG-ANTIBODIES: All sera were evaluated at ARUP Laboratories with a 6-Biospot slide (Euroimmun, Lübeck, Germany) consisting of rat hippocampus, rat cerebellum, a transfected eukaryotic cell line (EU90) specifically expressing LGI1 receptors or CASPR2 receptors, non-transfected EU 90 control cells and a human epithelial cell line derived from a larvy cancer; HeP-2. Species were evaluated at a 1:10 dilution and titers to end point if positive fluorescence for either LGI1 or CASPR2 antibodies were observed.

DETECTION OF VOLTAGE-GATED POTASSIUM CHANNEL IgG-ANTIBODIES: Voltage-gated potassium channel IgG antibody was evaluated with a commercial radioimmunoassay (RIA) as per manufacturer’s instructions (Kronos, St. ID).

REFERENCES


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