NÖRO PSİKİYATRİ ARŞİVİ

Editorial

Arch Neuropsychiatry 2017; 54: 1-2 • DOI: 10.5152/npa.2017.01201701

Neuronal Autoantibodies Call for Attention in Epilepsy

Ebru VANLI YAVUZ[1], Esme EKİZOĞLU[2,3]

[1]Department of Neurology, Koç University School of Medicine, İstanbul, Turkey
[2]Department of Neurology, İstanbul University İstanbul School of Medicine, İstanbul, Turkey
[3]Department of Neuroscience, İstanbul University, Institute of Experimental Medicine, İstanbul, Turkey

The concept of autoimmune epilepsy has gained considerable interest over the last few years. After the detection of a plethora of antibodies in patients with acute and established epilepsy, prospective cohorts started investigating factors of inflammation. In a recent report, Dubey et al. reported neurological autoantibodies (NAAs) among patients with epilepsy of unknown etiology. They investigated 112 patients for various NAAs including anti-GAD and found NAAs in 34.8% of the cases (1). It is most notable that our recent studies showed very similar antibody prevalence and clinical associations as those of Dubey et al. We investigated identical patient groups, namely, focal epilepsy of unknown cause and mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) 3 years ago, and published our results of 81 patients (2). We found antibodies to the glycine receptor (GLY-R) in 6.2% of our patients, CASPR2 in 4.9%, NMDAR in 2.5%, and VGKC-complex in 2.5% (2).

Furthermore, we recently investigated 111 consecutive patients with MTLE-HS; in this prospective series, we found antibodies to CASPR2 in 11 patients, GLY-R in 5, VGKC-complex in 4, NMDAR in 4, and $GABA_A$ receptor antibodies in 1. This systematic screening study of various NAAs showed 22.5% seropositivity mostly belonging to VGKC-complex antibodies in the largest series of patients with MTLE-HS, emphasizing a VGKC-complex autoimmunity-related subgroup (3).

It is also worth emphasizing that "autonomic dysfunction" is a clinical feature strongly correlated to seropositivity (1). This high prevalence of seropositivity was previously reported by our group in 17 of 58 (29.3%) patients with documented peri-ictal autonomic findings in a retrospective study design (4). We are also happy to see that the authors have replicated our previous finding that patients with NAA positivity are more likely to have good seizure outcomes (3).

As the antibody presence in, prevalence of, and risk factors for autoimmune epilepsy have been established by multiple groups, the remaining important question is how seropositive patients (particularly anti-epileptic drug-resistant patients) should be treated. Current diagnosis and treatment algorithms for autoimmune disorders do not address chronic autoimmune disorders in patients presenting with seizures. In this context, epilepsy surgery and its aftermath constitute an important field of investigation. Surgical treatment is widely performed for patients with anti-epileptic drug-resistant MTLE, which is frequently associated with hippocampal sclerosis (HS) as the underlying etiology. Memory failure is an important negative factor, which should be considered, even though seizure control is achieved after surgery. For this reason, cognitive evaluation is systematically done before and after epilepsy surgery. In many centers, attempts have been made to standardize memory tests; in addition, attempts are being made to predict the severity and type of memory decline that may occur after surgery.

In general, many previous studies have shown that the resection of non-dominant mesial temporal structures mostly causes visual memory decline, whereas the resection of dominant mesial temporal structures causes verbal memory decline. However, in recent years, it has been emphasized that HS is associated with a diffuse memory decline rather than a material-specific memory malfunction.

In our study that compared cognitive findings in patients having bilateral HS with those having unilateral HS, we found a significant difference in terms of verbal memory involvement among the patients. Besides, we showed that there is no difference in terms of visual memory decline (5). We also determined that mental retardation was frequent in patients with voltage-gated potassium channel antibodies in our large HS cohort screened for various neuronal autoantibodies. Our results showed that seizure outcome after surgery is beneficial in these patients (3). Nevertheless, whether resection of seizure foci (putative brain region expressing target antigens for anti-neuronal autoimmunity) and/or immunotherapy ameliorate seizure frequency in NAA-positive patients with epilepsy should be tested in larger cohorts.

Correspondence Address: Esme Ekizoğlu, İstanbul Üniversitesi İstanbul Tıp Fakültesi, Nöroloji Anabilim Dalı, İstanbul, Türkiye
E-mail: esmeekizoglu@yahoo.com
Received: 10.02.2017 • **Accepted:** 20.02.2017

In conclusion, studies have consistently shown that autoimmune epilepsy is not uncommon but is rather under-recognized. These autoantibodies can be markers of unknown immunopathological processes rather than having a central role in pathogenesis. They should be screened for ascertaining early immune treatment possibilities.

REFERENCES

1. Dubey D, Alqallaf A, Hays R, Freeman M, Chen K, Ding K, Agostini M, Vernino S. Neurological Autoantibody Prevalence in Epilepsy of Unknown Etiology. JAMA Neurol. doi: 10.1001/jamaneurol.2016.5429. [Epub ahead of print].
2. Ekizoglu E, Tuzun E, Woodhall M, Lang B, Jacobson L, Icoz S, Bebek N, Gurses C, Gokyigit A, Waters P, Vincent A, Baykan B. Investigation of neuronal autoantibodies in two different focal epilepsy syndromes. Epilepsia 2014; 55:414-422.
3. Vanli-Yavuz EN, Erdag E, Tuzun E, et al. Neuronal autoantibodies in mesial temporal lobe epilepsy with hippocampal sclerosis. J Neurol Neurosurg Psychiatry 2016; 87:684-692.
4. Vanli-Yavuz EN, Erdag E, Tuzun E, Ekizoglu E, Baysal-Kirac L, Ulusoy C, Peach S, Gundogdu G, Sencer S, Sencer A, Kucukali CI, Bebek N, Gurses C, Gokyigit A, Baykan B. Neuronal autoantibodies in epilepsy patients with peri-ictal autonomic findings. J Neurol 2016; 263:455-466.
5. Vanli- Yavuz EN, Bilgiç B, Matur Z, Bebek N, Gürses C, Gökyiğit A, Oktem O, Baykan B. Comparison of cognitive parameters between bilateral and unilateral hippocampal sclerosis. Arch Neuropsychiatry 2016; 53:199-204.