



Recent Treatment Therapies for Autoimmune Encephalitis

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Abstract

Autoimmune encephalitis is a rare condition but its contribution to total acute encephalitis syndrome cases has been observed to increase in recent years. The cause of auto immune encephalitis is due to the presence of antibodies against intracellular or extracellular receptors of neurons. Out of these receptors extracellular receptors are very important for which different options of medication and therapies are adopted. In this article a brief overview regarding treatment options available to clinicians have been discussed.

Keywords: Autoimmune Encephalitis; Treatment; Therapies

Abbreviations: NSABs: Neuronal Cell Surfaces; LGI1: Leucine-rich Glioma Inactivated-1 Antibodies; IVIg: Intravenous Immunoglobulins; PLEX: Plasma Exchange; IL-6: Interleukin-6; MMF: Mycophenolate Mofetil.

Introduction

Autoimmune encephalitis (AE) is an illness caused by the immune system that generally manifests as cognitive deterioration, seizures, mental symptoms, and motor abnormalities. Despite the growing number of antibodies implicated, identifying autoimmune encephalitis remains difficult due to clinical overlap with a wide variety of other neurological disorders [1]. Along with the identification of novel antibodies linked with the condition, clinical experience and outcomes with a variety of immunotherapeutic drugs in the treatment of autoimmune encephalitis are growing. AE is classified based on the site of the antigen, either intracellular or on the cell surface, because each categorization is associated with distinct clinical characteristics, most notably cancer association and immune treatment responsiveness [1]. Antibodies directed towards neuronal cell surfaces (NSABs) are another type of antibody found in AE. NSABs

specifically target an extracellular epitope, and the antigens they recognize are frequently synaptic receptors or constituents of synaptic protein complexes. Anti-NMDAR antibodies are the most prevalent, followed by anti-leucine-rich glioma inactivated-1 antibodies (LGI1) [1]. This article provides a concise overview of several treatment options.

Treatment Strategies

Empiric Antimicrobial Treatment

Prior to CSF investigation, it may be difficult to distinguish infectious from autoimmune etiologies in many encephalitis patients; empiric antimicrobials with CNS coverage are typically indicated until infection is excluded. Typically, CNS dosages of intravenous acyclovir and routine coverage for bacterial meningitis are initiated. Antibiotics and acyclovir may be dropped down if CSF bacterial and HSV/VZV tests are negative [2].

First Line Immunotherapy

Corticosteroids, intravenous immunoglobulins (IVIg), and Plasma exchange are frequently used as first-line

immunotherapeutic treatments (PLEX). Although there is insufficient evidence to suggest that any one regimen is preferable, corticosteroids are often the first line of defence, followed by IVIg and PLEX. When a combination of first-line medications is provided, corticosteroids with either IVIg or PLEX are the conventional treatment [1].

Second Line Therapy

Observational studies have demonstrated that second-line therapy improves functional outcomes and reduces recurrence rates while posing manageable side effects. The choice to start second line immunotherapy is determined depend on the seriousness of the disease, the response to first line immunotherapy, the occurrence of relapse, and other clinical factors. The most often utilized second-line medicines in the treatment of AE are rituximab and cyclophosphamide. Cyclophosphamide is an alkylating drug that inhibits both B and T cell growth. Due to the possibility of major adverse effects such as myelosuppression, infertility, hemorrhagic cystitis, and an increased risk of cancer, its usage is not prioritized [1]. Tofacitinib is a Janus kinase inhibitor with effective blood-brain barrier penetration that is already approved for the treatment of refractory rheumatoid arthritis and ulcerative colitis. Tofacitinib was generally well tolerated in seven out of eight patients, with six demonstrating a partial or favorable response. This is an encouraging preliminary report on the use of JAK inhibitors in a variety of refractory autoimmune neurological disorders [3].

Alternative Methods of Treatment

Around 20%–50% of people with AE have insufficient responses to second-line therapy and continue to have neurological problems. Re-administration of first-line immunotherapeutic drugs, prolonged use of second-line immunotherapy, and long-term maintenance on prednisolone or steroid-sparing medicines such as azathioprine or mycophenolate mofetil are all alternatives that have been explored thus far [1]. Mycophenolate mofetil, in example, has demonstrated superior efficacy in generating remission and a more acceptable side effect profile than cyclophosphamide in various autoimmune disorders, supporting its use as a safer alternative to cyclophosphamide for second-line immunotherapy in AE. Tocilizumab is a monoclonal antibody directed against the interleukin-6 (IL-6) receptor. IL-6 enhances the proliferation and differentiation of B cells into antibody-producing cells, stimulates the differentiation of CD8+ cytotoxic T cells, drives the differentiation of naive CD4+ helper T cells into IL-17-producing T-helper cells, and inhibits the differentiation of those cells into regulatory T cells, all of which contribute to autoimmune tissue damage [1].

Mycophenolate mofetil (MMF), methotrexate, and azathioprine have been utilized in pediatric anti-NMDAR encephalitis as steroid sparing medicines. In a systematic assessment of retrospective cohort data, MMF/ methotrexate/ azathioprine were associated with a lower risk of recurrence when begun after the first episode rather than after subsequent ones, and were rather safe [4].

Future Prospects

Autoimmune encephalitis is a rare clinical condition, for which randomized controlled trials related to evaluation of treatment options have not been done. Also the immunotherapeutic medicines currently utilized in AE lack a clear indication due to a paucity of supporting evidence. There are various more considerations that should be made in order to develop more effective treatment options. To begin, an optimal regimen and dose schedule have not been established. Acute care regimens vary amongst practitioners, and there is no universally accepted standard for determining therapy failure and whether to commence other immunotherapeutic drugs. Additionally, the time of immunotherapy required for maintained remission must be determined. Whereas treatment response, duration of treatment, and prognosis are all variable depending on the kind of associated antibody, current immunotherapeutic regimens for AE are not. The fraction of patients who do not respond adequately to first- or second-line immunotherapy is not negligible, and yet some new immunotherapeutic drugs are still not used to treat AE. Additional therapeutic options must be investigated to broaden the therapeutic armamentarium for the treatment of AE.

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