

GUEST EDITORIAL

Autoimmune encephalitis

When we started out on our neurology careers about 20 years ago, the notion of an autoimmune encephalitis (AE) did not exist. We clearly remember young patients who presented with a psychosis followed by unexplained neurological symptoms – and we, after excluding all known causes of an infectious aetiology, often postulated a toxic substance underlying this puzzling and mostly fatal condition. Today, with hindsight, we believe that these patients may have suffered from one of the forms of AE.

AE is not uncommon, yet it is often an unknown, under-recognised and serious condition, which can result in high morbidity and mortality. Prolonged hospitalisation and admission to intensive care units are often necessary, and associated with complications and high costs.^[1] Timely identification of AE is crucial to initiate appropriate treatment and avoid a negative outcome.

Although AE often presents with distinctive syndromes and sequences of psychiatric and neurological symptoms, it may sometimes manifest as a predominant psychiatric syndrome with only subtle neurological findings.^[2] A close co-operation between psychiatrists and neurologists is helpful to discuss and identify such patients. In addition, diagnosing AE in children and adolescents can be especially challenging due to an overlap with developmental changes in behaviour and other psychiatric disorders occurring in these age groups.^[3]

The purpose of this two-part CME series is to assist the broader South African medical community in identifying patients with AE so that prompt and effective therapy can be facilitated. Part 1 describes the epidemiology, pathophysiology and clinical presentation of AE. Our focus will thereby be on anti-NMDA receptor encephalitis because it is the most common form of AE encountered in clinical practice. Part 2 will discuss the diagnostic criteria, investigations and management of AE in more detail.

Inflammatory processes in the brain characterise all forms of encephalitis, including AE. Inflammation distinguishes an encephalitis from an encephalopathy in which the underlying, non-inflammatory aetiologies include metabolic causes (e.g. uraemic or hepatic encephalopathy), toxic causes (e.g. carbon monoxide or heavy metal exposure), as well as hypoxic or chronic traumatic injuries as seen in boxers and professional football and rugby players.

The autoimmune encephalitides comprise a group of autoimmune inflammatory disorders caused by distinctive antibodies against central nervous system antigens, affecting white and grey matter of the brain. The association of antibodies with brain inflammation is quite recent. In 2007, Dalmau *et al.*^[4] reported 12 young female patients with a distinctive encephalitis and teratomas (11 ovarian, 1 mediastinal) associated with newly detected antibodies against the N-methyl D-aspartate receptor (NMDAR). This was groundbreaking work, opening up the area of research into antibodies in central nervous system disorders.

Until Dalmau *et al.*'s seminal research, infective causes, especially viral infections, such as *Herpes simplex virus 1*, were the most common identifiable causes of encephalitis, but in many cases, the cause could not be established.^[5] With better awareness and accessibility to antibody testing, the number of cases reported with this specific condition increased rapidly. Only 5 years after the initial description, Gable *et al.*^[6] in 2012, for example, reported that anti-NMDA-receptor encephalitis was more frequent than any individual viral aetiology in a cohort of young patients with encephalitis. Since then, the list of identified antibodies associated with autoimmune-mediated encephalitis and the spectrum of its clinical presentations has become more extensive.^[7] As a result, the proportion of patients with an unknown cause of encephalitis has decreased, and is likely to decrease even further in future.

If the diagnosis of AE is made in time and appropriate treatment provided, long-term disability can be avoided. Treatment is targeted towards antibody elimination, and, in cases with a paraneoplastic AE, tumour removal. If achieved, the outcome is favourable. A large case series of patients with anti-NMDA receptor encephalitis reported good clinical outcome in 81%, with 12% of patients suffering a relapse and a mortality rate of 7%.^[8]

With this CME review, we hope to raise awareness of this important and curable neurological condition, leading to better care for all our patients.

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