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CASE STUDY

Rehabilitation following anti-NMDA encephalitis

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Abstract

Background: Anti-NMDA (N-methyl D-Aspartate) encephalitis is an autoimmune disorder of the central nervous system which presents acutely with seizures, disturbances in consciousness and behavioural change. Although there is an increasing amount of information about the diagnosis and acute treatment strategies, little is known about rehabilitation needs and outcomes for this patient group.

Case report: This study presents a 52-year old woman who initially presented with generalized seizures and drowsiness. She was admitted to hospital where autoimmune encephalitis was diagnosed based on a positive serum anti-NMDA antibody titre. When medically stabilized, she was transferred to a specialist neurorehabilitation unit for ongoing care. Her main clinical issues were around behavioural disturbance, communication, continence, mobility and cognition. A multi-disciplinary approach was taken to her problems and she was eventually discharged back to community living having made substantial improvements in all domains of functioning. The clinical challenges encountered throughout her rehabilitation and the approach to ameliorating these is described.

Conclusion: Although having a relatively rare diagnosis, the specific rehabilitation needs of this patient were met through an existing specialist neurorehabilitation service. A broader case series is required to determine needs and effective approaches across this patient group as a whole.

Keywords

Impairment, outcome measures, neurological rehabilitation

History

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Introduction

Anti-NMDA (N-methyl D-Aspartate) encephalitis was first described in 2005 as a paraneoplastic disorder in the context of ovarian teratoma [1, 2]. Since then, an increasing number of cases have been identified, including those without associated tumours [3, 4]. Typically, patients with anti-NMDA encephalitis develop psychotic disturbances [5, 6], often preceded by viral infection-like illness with fever and headache. After the psychotic symptoms have developed, disturbances of consciousness and autonomic dysfunction can all be seen [7]. Seizures are a commoner early feature in males who develop the disease, but are less frequently seen at this stage in females [8]. There is a wide variety in the range of clinical features, with a number of unusual presentations being described including total insomnia [9]. Large cohorts of these patients have been described in terms of their longer term outcomes [4, 10]. These suggest that recovery can take up to 18 months and a good outcome is strongly associated with early immunotherapy and not needing to be admitted to an intensive care unit. The gross functional outcome used for this patient series was the modified Rankin scale. Although this has been validated as correlating with quality-of-life after stroke [11], little is known about its applicability to other types of acquired brain injury, such as that caused by encephalitis. There is limited information around more detailed outcomes following anti-NMDA encephalitis, especially relating to the provision of rehabilitation in the post-acute phase.

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Case

A 52-year old woman was referred to hospital having developed seizures. These came on over a 2-week period following a short prodromal phase of feeling generally unwell. The seizures were managed with institution of levetiracetam at a dose of 250 mg bd. This was titrated up to 500 mg bd over the following 2 weeks. The patient displayed very disturbed behaviour, demonstrating physical and verbal aggression alternating with periods of becoming withdrawn and not interacting. Initial investigations included a CT scan of the brain which did not demonstrate any abnormal features. A series of blood tests including full blood count, inflammatory markers, electrolytes, liver function, vitamin b12, syphilis serology, white cell enzymes and serum copper were all within normal limits. Cerebrospinal fluid analysis demonstrated $27\,\mathrm{wc\,mm^{-3}}$, protein $0.31\,\mathrm{g\,l^{-1}}$, glucose $4.5\,\mathrm{mmol\,l^{-1}}$. A tentative diagnosis of encephalitis was made and treatment with acyclovir was commenced pending

the results of further investigations. Anti-NMDA antibody titres later came back as positive and a diagnosis of anti-NMDA encephalitis was made. An ultrasound scan and, later, CT scan of the pelvis were performed, but there was no evidence of associated teratoma.

Immunosuppression with steroids and intravenous immunoglobulin was commenced. Over the following week, the patient improved with fewer episodes of aggressive or very withdrawn behaviour. Because of her behaviour and issues around compliance, therapy including mobilization and assisted standing were challenging to manage on the acute medical ward prior to transition to inpatient rehabilitation.

After a further 3 weeks, she was transferred to an inpatient neurorehabilitation unit. At this point, she demonstrated impairments within the following domains;

(1) *Behaviour*: The patient was generally withdrawn and not responsive to social or verbal cues. After a few days following transfer, she developed acutely disturbed episodes where she would hit out at members of staff and throw objects. These episodes were precipitated by delusional beliefs of having recently given birth or been sexually assaulted.
(2) *Cognition*: Because of communication difficulties, this was challenging to assess formally. She did not appear to recognize family members and friends or react any differently to those who she was and was not familiar with. There was evidence of appropriate object use (a comb, a knife and fork), although sustained attention to a task was limited to a few minutes. She would become overloaded very quickly if too much was going on within the immediate environment. A Cognitive Assessment of Minnesota (CAM) assessment shortly after admission demonstrated severe impairments in complex problem-solving and abstract thinking with relative sparing of orientation, memory and attention. A Behavioural Assessment of Dysexecutive Syndrome (BADS) was performed with scores consistent with impaired executive function.
(3) *Communication*: Although able to follow single-stage commands, she was initially unable to reliably respond to questions verbally or to consistently express ideas or thoughts using language. She was not socially appropriate, did not maintain eye contact or demonstrate any facial expression.
(4) *Continence*: Initially incontinent of faeces and urine at night.
(5) *Mobility*: Had not been out of bed for a 6-week period in the acute hospital setting and, therefore, was hoisted for all transfers with no appropriate seating having been identified.
(6) *Nutrition/swallowing*: Although she was able to eat a normal diet, her nutritional intake was well below her calorific requirements.

Interventions/progress

(1) *Behaviour*: In order to minimize risks of self-injury during psychotic episodes, she was given a low-level bed with protective matting on the floors. The patient was able to work with physiotherapists to sit out in a recliner chair for very short periods of time. External distractions were minimized through having a single-occupancy room with restricted external noise and an accessible toilet. A short course of low dose olanzapine was prescribed. This was associated with modified behaviour within a few days (although a direct effect is difficult to demonstrate with certainty) and was tapered off slowly over the next 3 weeks without any recurrence of delusional beliefs.
(2) *Cognition*: Friends and family were advised to have short visits involving one or two people at a time and to try to avoid visiting after therapy sessions or during meal times. Occupational therapists worked on functional strategies to facilitate independence in activities of daily living through visual cues and sequencing tasks. Regular set routines were helpful in establishing functional abilities without requiring abstract thought or planning.
(3) *Communication*: The use of simple non-abstract yes/no questions was encouraged for all interactions with the patient, both on the part of family members and staff. The use of pictures and drawing was of very limited value. As her ability to communicate improved, increasingly challenging concepts and topics were introduced and variations in verbal output were encouraged through the use of open questions.
(4) *Continence*: The patient responded well to a regular routine of toileting 2-hourly during the day and 4-hourly overnight in the same setting. Eventually, she was able to take this routine on herself and became continent.
(5) *Mobility*: Due to a prolonged period in bed, she was found to have a reduction in passive range of extension at the right ankle to 30° from neutral position. Although her sitting balance improved, as did standing tolerance in a supported frame, she required a weight-bearing cast to correct the position of this ankle. Over the next 6 weeks, this cast was re-set every 2 weeks until both ankles were in a neutral position on weightbearing. A controlled stable walking pattern was achieved through regular supervised use of a wheeled walking frame.
(6) *Nutrition*: Due to the patient's distractibility, she took her meals in a quiet calm setting away from the other patients. This allowed her to focus on finishing her meal. To restore calorific balance, regular nutritional supplements were prescribed during the day. As mobility and independent function improved, the patient began to actively seek out food to the point where she began to exceed her nutritional intake. This behaviour subsequently improved as her steroid dose was tapered off.

Immunosuppressive medical management involved a tapering dose of steroids (reduction by 5 mg prednisolone a month). A repeated assay of anti-NMDA antibodies demonstrated persistently elevated serum levels 8 months after initial presentation. Therefore, mycophenolate was introduced at 500 mg daily, increasing by 500 mg every 2 weeks to a steady dose of 1000 mg od. When the patient had remained seizure-free for 6 months, her levetiracetam was titrated down and stopped.

Having had trial visits to the home environment, she was discharged with ongoing community follow-up after a total of

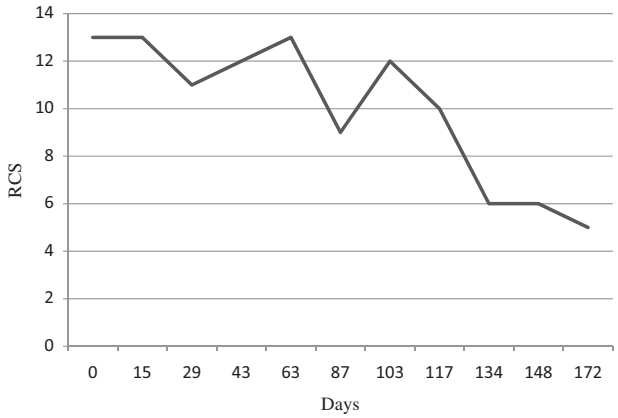

Figure 1. Graph showing the change in Rehabilitation Complexity Scale (RCS) against the time course of admission (days).

5 months in the neurorehabilitation unit and 8 months in hospital altogether.

Reviewing her outcome measures, there was a 68 point (42 to 110) change in her Functional Independence Measure (FIM) score—a scoring system used to record change engendered through rehabilitation across a number of different domains [12], her Barthel score was 5 on admission and 19 on discharge. Her Rehabilitation Complexity Scale was tracked fortnightly during her admission. This is a scale determining levels of input and care from health professionals [13] and shows how her improvements were manifest with a diminishing requirement for medical, nursing and therapy involvement, as shown in Figure 1. Using the Northwick Park Care needs assessment to determine costs of provision of weekly care [14], the projected cost of weekly care at home on discharge was $250 (£150) compared with $3507 (£2100) prior to admission to specialist rehabilitation.

Discussion

Although there are many publications focusing on the presentation, diagnosis and acute treatment of auto-immune encephalitis [15, 16], there is very little information on rehabilitation strategies and outcomes. The psychiatric features found in the early stage of the patient's illness are a common form of presentation [5, 17] and were managed with judicious use of medication and environmental change. The main cognitive impairments previously reported in association with anti-NMDA encephalitis are around memory function and executive function [18]. Although formal functional testing in the patient described was challenging at presentation because of the impairments in communication and behaviour, later assessments confirmed that the domains affected were largely related to abstract thinking and executive function. Language disturbance has been described in the context of anti-NMDA encephalitis [19], but it is unclear how much this is related to the associated cognitive problems. For the patient described, the use of clear non-complex yes/no questions in the early stages allowed preferences to be ascertained. Later, to encourage more the expression and communication of more complex ideas, open questions were employed. A variety of motor impairments have been described in association with anti-NMDA encephalitis including flaccid paraparesis [20], pseudo-piano playing motions [21], dystonia and chorea [22]. Although a secondary motor presentation was not apparent in the patient presented, she developed postural difficulties in association with prolonged non-weight-bearing status due to difficulties in engaging her in a regular standing or seating routine.

Most older patients (> 45 years at presentation) in a large series with anti NMDA encephalitis do not have an associated tumour [23], as for the patient described. The majority of patients in this series (60%) are reported as having a 'full or substantial recovery'. It is becoming acknowledged that early and aggressive immunotherapy may result in a better longer term outcome [24], although the specific role of rehabilitation for this patient group and its likely effect on eventual function is far from clear. The persistence of positive anti-NMDA antibodies for this patient was a very unusual feature given her good outcome, as antibody titre levels have been shown to be lower in patients with better outcomes [25]. Although recovery is typically thought of as occurring over the first 18 months, significant recovery occurring 3 years after presentation has been described in one case [26], indicating a need to be flexible in discussing longer term prognosis and planning rehabilitation and recovery programmes.

While there are clear evidence-based national guidelines for rehabilitation following stroke [27] and traumatic brain injury [28], the interventions and processes involved in the rehabilitation of rarer, clinically heterogeneous conditions such as auto-immune encephalitis, by necessity, are based on experience and a problem-based multi-disciplinary approach.

Conclusion

The specific challenges and impairments experienced by this patient required a number of different specific therapeutic disciplines working through a concerted problem-solving paradigm. Given the heterogeneity of presentations that have been described, it is likely that individual patient-based goals and strategies will be more fruitful in engendering change than a rigid guideline or pathway. A larger descriptive case series focusing on the rehabilitative interventions and outcomes for this patient group would inform this approach.

Declaration of interest

The author reports no conflicts of interest. The author alone is responsible for the content and writing of the paper.

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