

CASE REPORT

Tentamen suicidii, examen neurologiae: Attempted suicide with neurological symptoms. A case report

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Abstract

A 31-year-old woman was admitted to our intensive care department after a violent suicide attempt. There was no evidence of drug ingestion and no prior psychiatric history. Collateral history provided by her parents revealed unusual and abnormal behaviour in the preceding month. The patient tested positive for N-methyl-D-aspartate-receptor antibodies in serum and cerebrospinal fluid and was treated with immunoglobulins, steroids and rituximab. After a lengthy stay in hospital and a rehabilitation clinic, she recovered almost fully. It is essential to consider a neurological disease in the event of attempted suicide, in particular in the absence of prior medical or psychiatric history.

Introduction

Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is the most common autoimmune encephalitis. Although this complex neuropsychiatric syndrome was first described only 15 years ago and its incidence is estimated at only 1.5 per million per year, it has made a noteworthy impact in both neurology and psychiatry.^[1,2]

The NMDAR plays an important role in human cognition and behaviour. Hypofunction of the NMDAR has been postulated in the pathophysiology of schizophrenia. Anti-NMDAR antibodies cause hypofunction of the NMDAR through neuroinflammation, which results in reduced synaptic NMDAR clusters.^[3]

Patients usually present with psychiatric or behavioural symptoms, which can be similar to those in primary psychiatric disease (such as schizophrenia), combined with neurological symptoms. These neurological symptoms consist of cognitive dysfunction, memory deficits, epileptic seizures, autonomic instability such as orthostatic hypotension, speech disorders and orofacial dyskinesias.^[4] With psychiatric symptoms often being prominent at presentation, it can be difficult to differentiate between anti-NMDAR encephalitis and primary psychiatric disease.^[5-7] However, diagnosing anti-NMDAR encephalitis is critical as it concerns a treatable disease. About 70% of cases are admitted to ICU during the course of the

disease.^[5] Here we describe an impressive clinical presentation of this disorder.

Case

A 31-year-old woman with no prior medical history presented to the emergency department after a violent suicide attempt. She had slit her wrists and stabbed her thorax and abdomen multiple times with a large kitchen knife before jumping from a first-floor balcony. During initial assessment she was alert and cooperative, without signs of either respiratory or cardiovascular compromise. She had, however, multiple lacerations of the thorax, abdomen and forearms. Initial laboratory tests showed no abnormalities and toxicology screening was negative for common drug ingestions. After a CT scan of the cranium, thorax and abdomen, damage to the intra-abdominal organs was ruled out by exploratory laparotomy and abdominal wall haemorrhage was controlled by coagulation. The treatment of a subsequent comminuted acetabular fracture was deferred until later (*figures 1 and 2*).

Postoperatively, the patient was admitted to our ICU. She was extubated before arrival and her respiratory and haemodynamic status was stable. Initially she was alert and cooperative, although slightly disoriented, without any focal neurological deficits. Collateral history provided by her parents revealed unusual and abnormal behaviour in the preceding month. She was unable to continue her daytime work and moved back in with her parents days before presentation to the emergency department. She had been experiencing episodes of confusion, agitation and speech disturbances. She also seemed to have auditory hallucinations, suffered from insomnia and several times she briefly lost consciousness. The occurrence of these episodes of confusion and agitation seemed to have a relation with heat exposure, such as periods of sun exposure, or after a hot shower. There were no signs of a preceding fever. After several hours in the ICU the patient became agitated, suffered from visual hallucinations, and



Figure 1. Perforation of the abdominal wall and intra-abdominal pneumatosis



Figure 2. Blush of arterial contrast in the abdominal wall: comminuted acetabular fracture

removed the bandages from the wounds on her arms. Intravenous midazolam was given, after which the agitation waned.

Based on the aforementioned information provided by her parents, and the absence of a history of psychiatric illness, encephalitis was considered a possible explanation for her abnormal behaviour and subsequent suicide attempt. Cerebral MRI scan and EEG showed no abnormalities. A lumbar puncture was performed, which showed an opening pressure of 16 cmH₂O, white cell count of 7.0 x 10⁶/l (ref: 0-5 x 10⁶/l), total protein of 0.35 g/l (ref: <0.50 g/l), and glucose level of 3.7 mmol/l (serum: 6.6 mmol/l). Serum and cerebrospinal fluid (CSF) were sent for autoimmune antibody testing.

Within several days the diagnosis anti-NMDAR encephalitis was made, with strongly positive antibodies to NMDAR in both serum and CSF. Intravenous immunoglobulin therapy was directly initiated. Steroids were started nine days after admission, after fixation of the acetabulum fracture had been performed in order to avoid problems with wound healing and to minimise the risk of surgical site infection. In the following three to four weeks, she improved slowly. Second-line treatment with rituximab was then commenced.

Apart from a few episodes of orthostatic hypotension, there were no other signs of autonomic dysfunction in the course of the admission. Severe episodic agitation was present in the first weeks, but waned in the weeks thereafter. Ultrasonography of the pelvic region was performed to rule out ovarian teratoma. Both ultrasonography, and a later performed MRI scan, showed no signs of underlying disease.

After seven weeks in hospital, the patient was discharged to an inpatient rehabilitation clinic and has since recovered almost fully. She currently lives independently and notices no significant changes in her personality. Her parents, however, find her to be less talkative and with a slight loss of initiative.

Discussion

The patient described here presented to the emergency department after a dramatic suicide attempt. As initially no collateral information was known, auto-intoxication or psychosis was considered a likely cause of her extensive self-harm. Doubts arose, however, after toxicology screening turned out to be negative, and additional information provided by her parents raised suspicion of an underlying encephalitis. This suspicion was mainly based on behavioural changes with episodes of confusion and agitation in the month preceding presentation in an otherwise healthy patient without a history of psychiatric disease. Further analysis indeed confirmed that the patient suffered from an anti-NMDAR encephalitis.

As this case exemplifies, suicidality is a serious and potentially lethal manifestation of anti-NMDAR encephalitis. Current literature only provides limited reports on the association between anti-NMDAR encephalitis and suicidality or (attempted) suicide in the course of the disease. A retrospective analysis that included 133 anti-NMDAR encephalitis patients focussed specifically on suicidality.^[8] The authors found that some form of suicidality was present in 13% of patients in the course of the disease. Of these patients, 82% had depressive symptoms at initial presentation. Attempted suicide was seen in 6% of patients, with a median interval of one month between the start of initial symptoms and attempted suicide, and two patients committed suicide. The authors found that psychiatric symptoms at initial presentation and their severity were risk factors for suicidal behaviour. Patients who had suicidal ideations, attempted or even committed suicide, more frequently presented initially with insomnia, aggression, depression or delusions. There were no significant differences between the groups (with and without suicidality) with respect to

age or gender. Only two suicidal patients (12%) had a neoplasia. A higher rate of recurrence of encephalitis was found in patients with suicidality, although no multivariate analysis could be performed due to the relatively small sample of patients. The results from this study, however, hint towards the need for increased awareness of relapse of disease. Another review that mentioned suicidality, which included a phenotypic analysis of individual data, included 464 patients with anti-NMDAR encephalitis. Suicidal thoughts, self-harm and suicide attempts were reported in 7%, whereas depressive symptoms were present in 47% of the total studied population.^[9] Although mood disorders or depression seem to be quite common in anti-NMDAR encephalitis, suicide attempt appears to be a relatively rare symptom.

With an incidence of 1.5 patients per 1 million people per year, anti-NMDAR encephalitis is a rare diagnosis, which translates to approximately 26 new cases per year in the Netherlands. Given that the incidence of patients who present to the emergency room with attempted suicide in the Netherlands is 14,000 per year,^[10] the proportion of these patients that suffer from anti-NMDAR encephalitis is very low. However, despite the rarity of occurrence it is important to consider the diagnosis, specifically in patients without a prior history of psychiatric illness, since it concerns a treatable disease and quickly commenced treatment is warranted. The combination of psychiatric symptoms with neurological symptoms in our patient prompted the diagnostics towards (anti-NMDAR) encephalitis. Since its first description in 2005, a complex, polymorphic neuropsychiatric syndrome has been identified.^[1] Psychiatric symptoms are commonly seen at initial presentation, although primary presentation with isolated psychiatric symptoms is rare (around 5%).^[5,6,9] Young women are predominantly affected. Among the patients with proven anti-NMDAR encephalitis, sex and age distribution is predominantly centred around women (80%) below the age of 40 years, and approximately 37% are children.^[2,5] A relation with ovarian teratoma, which can contain nervous tissue and express anti-NMDAR antibodies, has been described. Several large cohort studies reported an incidence of ovarian teratoma of 40-47% in female patients with anti-NMDAR encephalitis.^[2,5,6,11] Besides teratoma, herpes simplex encephalitis is another known trigger, which is found in 2-5% of anti-NMDAR encephalitis.^[2,12] Treatment consists of immunotherapy. Steroids and intravenous immunoglobulin therapy are used as first-line therapy and second-line therapies comprise rituximab or cyclophosphamide.^[2] Lower severity of symptoms (no admission to an ICU) and early initiation of treatment were found to be predictors of a good outcome.^[5] In a study of 472 patients receiving first-line treatment, 53% improved within four weeks after initiation of therapy. Of the non-responders who subsequently received second-line treatment, another 57% significantly improved. Early combined immunotherapy with intravenous immunoglobulins and steroids, as well as low white blood cell count in CSF at ICU admission, are associated with good outcome at six months.^[5,11]

Due to the presentation, this patient was immediately admitted to ICU and was thus diagnosed with anti-NMDAR encephalitis during her admission. About 70% of anti-NMDAR encephalitis patients are admitted to ICUs for airway protection, dyskinesia, persistent dysautonomia or epileptic seizures.^[5] When patients are admitted to the ICU, the prognosis is generally still good despite long stays during which patients receive prolonged courses of sedatives, antiepileptics, and neuroactive or psychoactive medications. The main reasons for ICU admission are coma (41%), seizures (39%) and agitation (10%). Common ICU predictive scores (such as SOFA) and the Glasgow Coma Scale were not found to be predictive of neurological outcome.^[11]

Conclusion

It is essential to consider neurological diseases when patients present with attempted suicide, especially in cases without prior psychiatric or medical history. In anti-NMDAR encephalitis specifically, early recognition of the disease with its multiple clinical presentations and subsequent rapid initiation of treatment may not only improve outcome, but in some cases even be life-saving.

Disclosure

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Informed consent was obtained from the patient for the publication of this case report and the accompanying images.

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