Acknowledgments

This study was supported by Biomedical Research Institute Grant (2014-14), Pusan National University Hospital – South Korea. Authors have no conflict of interest to disclose.

References

[1] Marler JR, Price TR, Clark GL, et al. Morning increase in onset of ischemic stroke. Stroke 1989;20:473–6.
[2] Lago A, Geffner D, Tembl J, et al. Circadian variation in acute ischemic stroke: a hospital-based study. Stroke 1998;29:1873–5.
[3] Elliott WJ. Circadian variation in the timing of stroke onset: a meta-analysis. Stroke 1998;29:992–6.
[4] Chaturvedi S, Adams Jr HP, Woolson RF. Circadian variation in ischemic stroke subtypes. Stroke 1999;30:1792–5.
[5] Fink JN, Kumar S, Horkan C, et al. The stroke patient who woke up: clinical and radiological features, including diffusion and perfusion MRI. Stroke 2002;33:988–93.
[6] Kocer A, Ilhan A, Ince N, et al. The related causes in very early morning onset of stroke. Prog Neuropsychopharmacol Biol Psychiatry 2005;29:983–8.
[7] Todo K, Moriwaki H, Saito K, et al. Early CT findings in unknown-onset and wake-up strokes. Cerebrovasc Dis 2006;21:367–71.
[8] Roveri L, La Gioia S, Ghidinelli C, et al. Wake-up stroke within 3 hours of symptom awareness: imaging and clinical features compared to standard recombinant tissue plasminogen activator treated stroke. J Stroke Cerebrovasc Dis 2013;22:703–8.
[9] Costa R, Pinho J, Alves JN, et al. Wake-up stroke and stroke within the therapeutic window for thrombolysis have similar clinical severity, imaging characteristics, and outcome. J Stroke Cerebrovasc Dis 2016;25:511–4.
[10] Barreto AD, Martin-Schild S, Hallevi H, et al. Thrombolytic therapy for patients who wake-up with stroke. Stroke 2009;40:827–32.
[11] Natarajan SK, Snyder KV, Siddiqui AH, et al. Safety and effectiveness of endovascular therapy after 8 hours of acute ischemic stroke onset and wake-up strokes. Stroke 2009;40:3269–74.
[12] Stampfl S, Ringleb PA, Haehnel S, et al. Recanalization with stent-retriever devices in patients with wake-up stroke. Am J Neuroradiol 2013;34:1040–3.
[13] Hacke W, Kaste M, Fieschi C, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II): second European-Australasian Acute Stroke Study Investigators. Lancet 1998;352:1245–51.
[14] Adams Jr HP, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of ORG 10172 in Acute Stroke Treatment. Stroke 1993;24:35–41.
[15] Hair JF, Anderson R, Tatham RL, et al. Multivariate data analysis. Upper Saddle River, NJ: Prentice Hall; 2006.
[16] Adams Jr HP, Leira EC, Torner JC, et al. Treating patients with 'wake-up' stroke: the experience of the AbESTT-II trial. Stroke 2008;39:3277–82.
[17] The national institute of neurological disorders and stroke rt-PA stroke study group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995;333:1581–8.
[18] Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 2015;372:1019–30.
[19] Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2016;387:1723–31.
[20] Becker K, Fruin M, Gooding T, et al. Community-based education improves stroke knowledge. Cerebrovasc Dis 2001;11:34–43.
[21] Alberts MJ, Perry A, Dawson DV, et al. Effects of public and professional education on reducing the delay in presentation and referral of stroke patients. Stroke 1992;23:352–6.
[22] DEFFUSE 3: Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3. Available from: https://clinicaltrials.gov/ct2/show/NCT02586415.
[23] POSITIVE: Perfusion Imaging Selection of Ischemic Stroke Patients for Endovascular Therapy. Available from: https://clinicaltrials.gov/ct2/show/NCT 01852201.
[24] DAWN: Trevo and Medical Management Versus Medical Management Alone in Wake Up and Late Presenting Strokes. Available from: https://clinicaltrials.gov/ct2/show /NCT02142283.

http://dx.doi.org/10.1016/j.jocn.2017.02.021

Anti-N-methyl-D-aspartate receptor encephalitis associated with hepatic neuroendocrine carcinoma: A case report

Ee Wei Lim *, Chun Wai Yip

National Neuroscience Institute, Singapore General Hospital Campus, 20 College Road, Academia 169856, Singapore

ARTICLE INFO

Article history:
Received 6 December 2016
Accepted 12 February 2017

Keywords:
Anti-NMDAR encephalitis
Neuroendocrine carcinoma
Paraneoplastic encephalitis

ABSTRACT

Anti-N-methyl-D-aspartate receptor (Anti-NMDAR) encephalitis can present with and without tumor. Tumor associations are less common in older patients. We report a 65-year-old gentleman who presented with one week history of cough, chills, rigor and altered behavior, followed by florid visual and auditory hallucinations. Mini mental status examination score was 16/30. Both cerebrospinal fluid and plasma anti-NMDA receptor antibodies were detected. A course of intravenous methylprednisolone was given with partial symptom improvement. A hepatic neuroendocrine carcinoma was detected and confirmed on biopsy. Unfortunately, he developed several medical complications: non-ST elevation myocardial infarction, infected foot gangrene and peripheral vascular disease, which made him unsuitable for both surgery and chemotherapy. He passed away 6 months later due to the progression of the malignancy. This case illustrated that NMDAR encephalitis may be associated with an uncommon hepatic neuroendocrine carcinoma in an older person, which is responsive to early treatment.

1. Introduction

Anti-N-methyl-D-aspartate receptor (Anti-NMDAR) encephalitis most commonly affects young adults and children as multiple different stages of illness that progress from psychosis, memory deficits, seizures, and language disintegration into a state of unresponsiveness associated with abnormal movements, autonomic and breathing instability. Ovarian teratoma is the most commonly reported in young females while older persons tend to have less tumor associations.

* Corresponding author.
E-mail addresses: lim.ee.wei@singhealth.com.sg (E.W. Lim), yip.chun.wai@singhealth.com.sg (C.W. Yip).

2. Case report

We report a 65-year-old gentleman who presented with one week history of cough, chills, rigor and altered behavior. He then developed both visual and auditory hallucinations. He was known to have hypertension, hyperlipidaemia and diabetes mellitus, but had no history of psychiatric disorder.

On examination, he was alert and orientated. The mini mental state examination (MMSE) scoring was 16/30. His mood was elated and he was cheerful all the time. He had grandiose delusion and kept talking about his great plans in his career whenever he was approached. The rest of neurological examination was unremarkable.

The lumbar puncture showed normal cerebrospinal fluid (CSF) biochemistry and absence of infection. Both CSF and plasma anti-NMDAR antibodies were detected. Anti-voltage-gated potassium channel antibody was absent. MRI brain (Fig. 1) showed a small focus of T2 hyperintensity in the left lentiform nucleus. The electroencephalography (EEG) showed intermittent generalized 4–6 Hz slowing.

A course of intravenous methylprednisolone (1 g daily for 5 days) was given. His affect normalized and the hallucinations ceased. His MMSE score improved gradually from 16/30 to 21/30 a week after treatment. There was further improvement to 24/30 after one month.

A solitary solid heterogeneous liver mass was discovered in the segment 4 of his liver on abdominal CT scan (Fig. 2). An initial ultrasound guided liver biopsy suggested possible hepatocellular carcinoma with a neuroendocrine component or a neuroendocrine tumor/carcinoma. A second biopsy from the hepatic hilar lymph node showed poorly differentiated neuroendocrine carcinoma (small cell carcinoma).

Unfortunately, his disease course was complicated with non-ST elevation myocardial infarction, infected food gangrene requiring below knee amputation and peripheral vascular disease. With all these co-morbidities, he was considered to be unsuitable for both surgery and chemotherapy. He passed away 6 months after the disease onset due to malignancy progression.

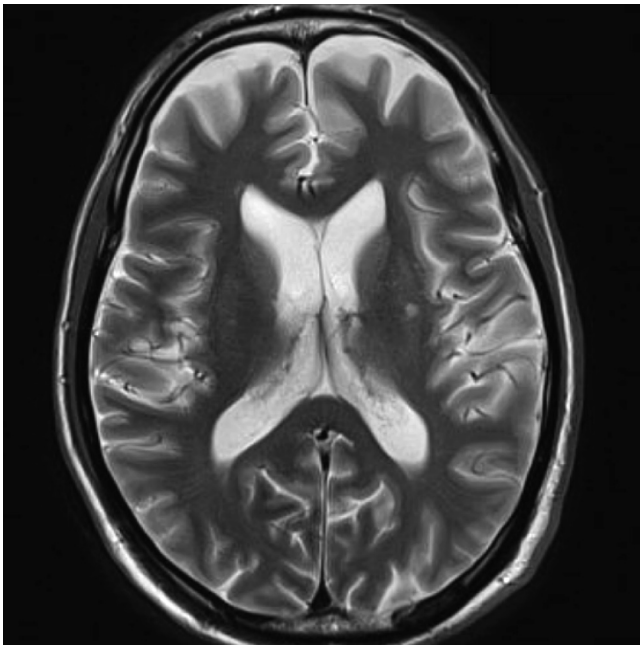

Fig. 1. MRI T2-weighted sequence (axial view) showed T2 hyperintensity in the left lentiform nucleus.

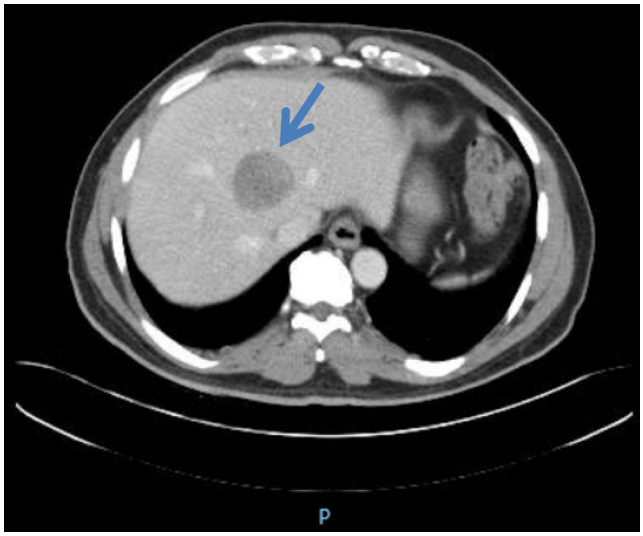

Fig. 2. CT abdomen showed a solitary solid heterogeneous liver mass in the segment 4 of liver measuring 3.5 cm × 3.5 cm.

3. Discussion

Anti-NMDAR encephalitis was first described in 2007 by Dalmau et al. in a case series of 12 young women with mostly ovarian teratoma [1]. Since then, there have been reports involving men, children and patients with no underlying malignancy [3,4,6,7].

Anti-NMDAR encephalitis is an autoimmune and paraneoplastic encephalitis. It is believed that immune-mediated attenuation of cell surface NMDAR function by anti-NMDAR antibodies, leads to neuronal dysfunction. The presence of a tumor which expresses NMDA receptors is believed to be the contributing factor to breaking immune tolerance. However, Anti-NMDAR encephalitis can occur without an underlying tumor. Therefore, other unknown immunological triggers must also be contributory. Although ovarian teratoma is the most commonly associated malignancy, other malignancies e.g. small-cell lung carcinoma, thymic carcinoma, pancreatic cancer, breast cancer, Hodgkin's lymphoma etc have been reported [2–5]. Our case illustrates a rare association with hepatic neuroendocrine carcinoma in an older person.

There are variable clinical presentations of anti-NMDAR encephalitis. Dalmau et al. have proposed different phases of the illness, starting with a prodromal symptoms, followed by prominent psychiatric manifestations within 2 weeks and later neurological symptoms such as memory impairment, seizure, movement disorder, loss of consciousness and autonomic dysfunction [2]. Two other separate studies reported that seizures as initial symptoms was more frequent in adult male patients than adult women [6,8]. Our patient presented with predominantly neurocognitive disturbances which improved with early immunotherapy, but he still had residual memory deficits. We believe that our case did not progress to motor manifestations or seizures because either he expressed a milder form of the disorder or that he was diagnosed at an earlier stage of the disease with access to early treatment.

Titulaer et al. studied 31 affected patients 45 years or older [3,7]. It was found that older patients were more often male, with lower frequency of tumors, had longer median time to diagnosis (8 weeks) and to treatment, as well as less favourable outcome. Our patient differed from this trend. Although being an older male, he was diagnosed and treated early.

In conclusion, this case adds to the current literature of yet another tumor association of anti-NMDAR encephalitis in an older

person: that of a hepatic neuroendocrine carcinoma. Initiating treatment when the presentation symptoms are still mild may result in better response. Therefore, screening for anti-NMDAR antibody could be useful in the evaluation of older patients diagnosed with first episode of psychosis.

Conflicts of interest/disclosures

The authors declare that there is no conflict of interest regarding the publication of this paper.

References

[1] Dalmau J, Tuzun E, Wu HY, et al. Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. Ann Neurol 2007;61:25–36.

[2] Dalmau J, Lancaster E, Martinez-Hernandez E, et al. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. Lancet Neurol 2011;10(1):63–74.

[3] Titulaer MJ, McCracken L, Gabilondo I, et al. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. Lancet Neurol 2013;12(2):157–65.

[4] Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol 2008;7(12):1091–8.

[5] Hara M, Morita A, Kamei S, et al. Anti-N-methyl-d-aspartate receptor encephalitis associated with carcinosarcoma with neuroendocrine differentiation of the uterus. J Neurol. 2011;258(7):1351–3.

[6] Viaccoz A, Desestret V, Ducray F, et al. Clinical specificities of adult male patients with NMDA receptor antibodies encephalitis. Neurology 2014;82:556–63.

[7] Titulaer MJ, McCracken L, Gabilondo I, et al. Late onset anti-NMDA receptor encephalitis. Neurology 2013;81:1058–63.

[8] Titulaer MJ, Dalmau J. Seizures as first symptoms of anti-NMDA receptor encephalitis are more common in men. Neurology 2014;82:550–1.

http://dx.doi.org/10.1016/j.jocn.2017.02.038

Watershed spinal cord infarction developing after a hypotensive episode secondary to massive rectus sheath hematoma

Adviye Ergun [a,*], Oktay Akalın [b], Mehmet Sukru Sahin [c], Kosdere Serkan [d]

[a] Departments of Physical Therapy and Rehabilitation, Pamukkale University, Denizli, Turkey
[b] Baskent University, Department of Neurology, Alanya Teaching and Medical Research Center, Alanya, Turkey
[c] Baskent University, Department of Orthopaedics and Traumatology, Alanya Teaching and Medical Research Center, Alanya, Turkey
[d] Baskent University, Department of Neurosurgery, Alanya Teaching and Medical Research Center, Alanya, Turkey

ARTICLE INFO

Article history:
Received 28 December 2016
Accepted 14 February 2017

1. Introduction

Acute spinal cord infarction (SCI) is an extremely rare events with high mortality and morbidity. It comprises less than 1% of all strokes and 5–8% of acute myelopathies. Although the majority of SCI is associated with atherosclerosis and thoracoabdominal surgery. Generally (in approximately 95%), it occurs in the region supplied by anterior spinal artery [1]. Watershed infarction of the spinal cord is even rarer.

We presented here the watershed infarction of the spinal cord that developed after a hypotensive episode based on massive rectus sheath hematoma on a 77-year-old patient with end-stage renal failure.

2. Case report

A 77-year-old woman with history of end-stage renal disease on hemodialysis, heart valve replacement and subsequent warfarin use at a dose of 10 mg/day and dyslipidemia presented to the emergency department with acute abdominal pain that started 8 h before and the loss of strength in her legs for the past 2 h. Her vital signs revealed a temperature of 36.5 °C, pulse of 130/min, blood pressure of 70/45 mm/Hg. On physical examination, the patient was confused. A mass starting from the abdominal umbilical area and filling the pelvis was detected. Hemoglobin was 8.1 g/dL, hematocrit was 25.7%, leucocytes were 10,300, prothrombin time was 14.8 sn, and INR value was 5.4. A contrast-enhanced abdominal computed tomography scan revealed hematoma with 15 cm diameter that originated from the right rectus sheath and filled the pelvis (Fig. 1). Aggressive fluid resuscitation, erythrocyte suspension, and dopamine infusion were administered. Four hours after the medical management commenced she recovered consciousness and complained of unable to move both of her lower limbs. On neurological examination, lower limbs were flaccid with loss of motor power, sensory appreciation was impaired to the modalities of touch, pain and temperature below T4. Posterior column function was preserved. She was areflexic in the lower extremities with negative Babinski testing bilaterally. There was no sensation or control of bladder or bowel function. Magnetic resonance imaging (MRI) of the spine demonstrated pencil-like centromedular hyperintensity and cord expansion with prominent diffusion restriction extending from the inferior T4 level to the conus (Fig 2). The patient was diagnosed with watershed zone infarction secondary to hypotensive episode with clinical presentation and typical imaging findings. The patient was started on aspirin, clopidrogrel, simvastatin, and low-molecular-weight heparin for thromboprophylaxis. The patient started the rehabilitation

* Corresponding author at: Pamukkale Üniversitesi, Fizik Tedavi ve Rehabilitasyon Bolumu, Kınıklı Kampüsü/Denizli, Turkey. Fax: +90 258 2962338.
E-mail address: adviyesalman@yahoo.com (A. Ergun).