



## Extreme Delta Brush Electroencephalography Pattern in Anti-yo Encephalitis: A Case Report

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Autoimmune encephalitis is complex and gradually being recognized. Anti-N-methyl-D-aspartate Receptor (Anti-NMDAR) encephalitis was the most well-known and its unique electroencephalography (EEG) pattern is extreme delta brush (EDB). Anti-Yo encephalitis is far less than common anti-NMDAR encephalitis (anti-NMDARE). A 78-year-old male presented with progressive apathy, hypotension, unsteady gait, and depressed consciousness. EEG revealed an EDB pattern while the serum test was positive for anti-Yo antibodies. The patient then received 10 rounds of plasma exchange, and his blood pressure stability improved. Consequently, urine cytology and abdominal computed tomography revealed atypical cells and linear enhancement in the bladder dome, respectively. However, instead of further pathological confirmation and treatment, the patient's family requested hospice care. As a result, the patient died of desaturation 7 days later after the withdrawal of ventilatory support. First recognized in 2012, EDB is believed to be specific to NMDARE. However, to date, EDB has not been well described, and no description is available regarding its reactivity. To our knowledge, this is the first case of EDB with anti-Yo encephalitis. Similar to the cases of EDB with anti-NMDARE, our patient did not have satisfied prognosis despite no further investigation and treatment of the possible underlying malignancy. As the prevalence and underlying mechanism of this EEG pattern are unclear, further studies are warranted to identify the potentially similar mechanisms and correlation between anti-NMDAR and anti-Yo encephalitis.

**Key words:** Anti-yo encephalitis, encephalitis, extreme delta brush, electroencephalography, anti-N-methyl-D-aspartate encephalitis

### INTRODUCTION

Autoimmune encephalitis is rare disease, characterized by immune-mediated destruction of central nervous system, the neurological manifestations can be either acute or subacute. The common clinical presentations included a change in behavior, autonomic disturbances, psychosis, seizures, cognitive deficits, abnormal movements, and depressed consciousness. Anti-N-methyl-D-aspartate Receptor (NMDAR) encephalitis is one of the most common causes of autoimmune encephalitis.<sup>1</sup>

Extreme delta brush (EDB) of electroencephalography (EEG) abnormalities, consisting of a generalized rhythmic delta activity with a superimposed rhythmic beta activity, in adults is believed to be unique to anti-NMDAR encephalitis (NMDARE) and is highly specific for the patients

with severe anti-NMDARE.<sup>2</sup> It was first recognized in a series of 23 adult patients with anti-NMDARE and has not been described in other neurologic conditions.<sup>3</sup> EDB is also associated with poor outcome.<sup>4</sup>

Anti-Yo antibody is rare and usually identified in paraneoplastic cerebellar degeneration (PCD), which is correlated with ovarian and breast cancers. Therefore, most patients with anti-Yo PCD are women, with <20 cases found in male patients.<sup>5</sup> We reviewed the PubMed and Google databases and were unable to identify any previously reported cases of EDB in anti-Yo encephalitis.

### CASE REPORT

A 78-year-old male has a history of atrial fibrillation,

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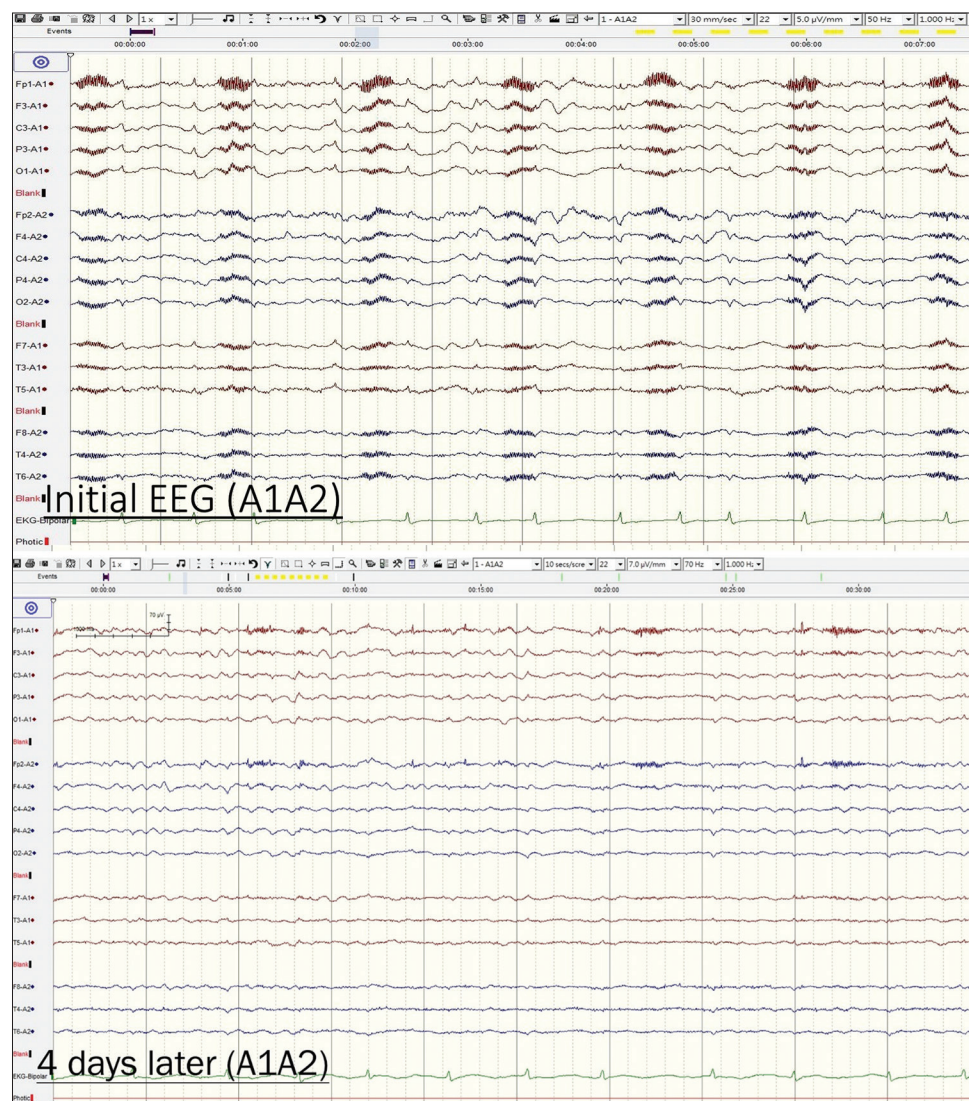
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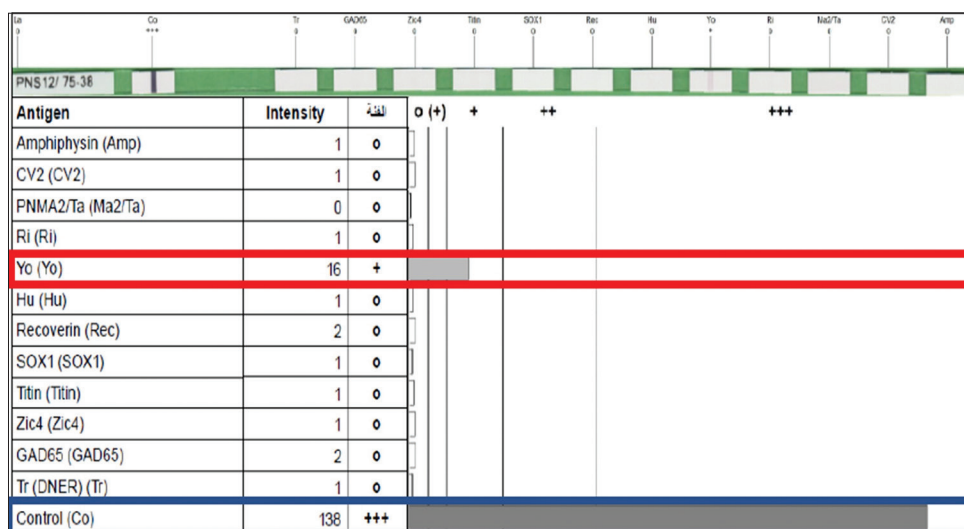
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hypertensive cardiovascular disease, and hyperlipidemia. He presented to our emergency room for low blood pressure measured at home. Associated symptoms were less verbal output, unsteady gait, and apathy, which progressively developed for 2 months. His body temperature was 36.8°C, blood pressure 112/73 mmHg, heart rate 99 beats/min, and respiratory rate 13 times/min. On neurological examination, Glasgow Coma Scale scored E2V2M4 with intermittent upward gazing and jerk nystagmus. Brainstem reflexes were preserved and the Medical Research Council Scale for muscle strength was three in bilateral upper limbs and two in bilateral lower limbs toward pain stimulation. The deep-tendon reflex was decreased and symmetrical in four limbs with bilateral negative Babinski sign. Endotracheal tube was intubated for poor consciousness and suspected nonconvulsive status epilepticus.

After admission, we prescribed levetiracetam, valproic acid, lacosamide, and peramppanel gradually for refractory status epilepticus. Vasopressor was applied temporarily for hypotension and was gradually tapered down. The metabolic data, including electrolytes, hepatic and renal function, thyroid function, folic acid, and thiamine, were in normal range except for the elevation of serum C-reactive protein. Antibiotic regimen for possible infectious process was applied. Cerebrospinal fluid analysis was white blood cell 2/ $\mu$ L and total protein 41 mg/dL. The EEG revealed generalized background slowing and EDB pattern [Figure 1]. Brain magnetic resonance imaging showed brain atrophy with arteriosclerotic encephalopathy and old lacunar infarcts. Anti-Yo antibody was further identified in serum [Figure 2]. The patient then received ten times of plasma exchange.



**Figure 1:** Extreme delta brush pattern was identified in two consecutive EEGs separated by 4 days. There were still some fast activities (brush) on delta waves in the electroencephalogram 4 days later after we turned off all the possible electrical machines such as pump, light, IV set and ventilator (A1A2 montage). EEG: Electroencephalography



**Figure 2:** Anti-yo antibody was identified in immuno-blot of serologic examinations and the signal intensity was scored as 16, which was considered positive

For malignancy evaluation after anti-Yo antibody being identified, urine cytology and abdominal computed tomography revealed atypical cells and linear enhancement over the dome of the bladder, respectively [Figure 3]. The family declined cystoscopy and biopsy in consideration of old age and high risk. After 10 times of plasma exchange, the blood pressure became more stable, which suggested the hypotension attributed to dysautonomia. Nevertheless, there was unremarkable clinical improvement on his neurological deficits. His family asked for hospice care and the patient died of desaturation 7 days later after withdrawal from the ventilator.

## DISCUSSION

The EEG pattern of EDB was first recognized in a case series published in 2012, and then, EDB was regarded as a potential marker for anti-NMDARE. It helps early differentiate other disorders thus leading to early treatment and may predict the poor prognosis or more prolonged illness. Via combining with magnetoencephalography, delta wave and beta activity might originate from different brain regions. Furthermore, there was EDB mimics thus being challenging in clinical practice.<sup>6</sup> However, the precise mechanism of the pattern of EEG still remained unclear.<sup>7</sup> Besides anti-NMDARE, EDB was also observed in a pediatric patient of autoimmune lial fibrillary acidic protein (GFAP) astrocytopathy and anti-gamma-aminobutyric acid (GABA) receptor encephalitis.<sup>8,9</sup> To date, there is limited information describing EDB and we reviewed the PubMed, Google, and Google Scholar databases and were unable to identify any previously reported cases of EDB in anti-Yo encephalitis.

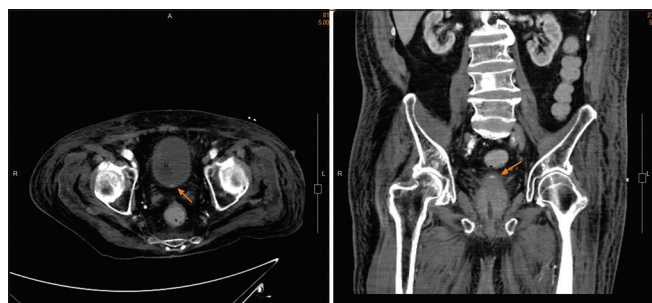
Anti-NMDAR antibodies are antibodies against cell-surface antigens, while Anti-Yo antibodies are antibodies reactive with intracellular antigens. Anti-Yo encephalitis was much less known than anti-NMDA encephalitis and most of the cases reported before were related to PCD, female predominant and is correlated with gynecologic or breast malignancy.

Here, we present a progressive mental status change, ataxia, and dysautonomia 78-year-old male with anti-Yo positive and in suspicion of bladder cancer. EDB was found in EEG. For the consideration of EEG being recorded in an intensive care unit with many potential mechanical artifacts, thus we turned off all the possible electrical machines such as pump, light, intravenous (IV) set, and even ventilator and still EDB present during the second EEG performed 4 days later. The potential causes may relate to electromyogram activities of the orofacial muscles and large potentials of the genioglossus muscle;<sup>6</sup> however, we did not notice this movements during recording.

After prolonged hospitalization and highly suspected bladder malignance, the families declined further IV immunoglobulin and asked for hospice care; also, pulse steroid was not yet administered for infection was in process.

The limitations of our case are, first, incomplete treatments; second, euroline assay produces a high number of false positive; third, without pathology result of linear enhancing bladder wall and the fourth, lacking of electromyography monitoring and EEG reactivity of EDB while passive opening, closing, voice stimulants, etc., Interestingly, previous studies have shown that EDB reactivity may or may not vary with sleep-wake cycles.<sup>3,7</sup>

This rare and atypical case highlights the complexity of autoimmune encephalitis and proposes the novel concept that EDB could developed in anti-Yo encephalitis besides



**Figure 3:** Abdominal computed tomography revealed linear enhancement over the dome of the bladder (arrows), which may indicate malignancy in suspicion

anti-NMDA encephalitis. The components of EDB included fast activity (cortical region) + Delta (subcortical region) while anti-Yo antibodies are known to primarily target cerebellar neurons.

Several possible explanations can account for the involvement of anti-Yo antibodies in subcortical and cortical dysfunction such patients. First, considering the paraneoplastic effects which are due to immune-mediated reactions triggered by the presence of tumors elsewhere in the body. These effects may involve the production of antibodies that target normal neural tissues including subcortical and cortical regions. Second, it is possible that anti-Yo antibodies, by mechanism of cross-reactivity, may also bind to antigens expressed in subcortical and cortical regions in addition to cerebellar neurons and finally lead to dysfunction in these areas. Finally, disruptions caused by anti-Yo antibodies in the cerebellum may influence neural circuits and connectivity patterns, ultimately impacting subcortical and cortical regions that are functionally connected to the cerebellum.

## CONCLUSION

In summary, encountering EDB patterns in EEG monitoring, not only anti-NMDA, but also anti-Yo encephalitis need to be ruled out. Neurologists should continue to share these findings to further investigate the causal relationship between encephalitis and EDB pattern EEG. Further studies are warranted for puzzles of EDB underlying mechanisms and correlation between anti-NMDA and anti-Yo encephalitis.

## Ethical approval statement

This study was approved by the ethical committee of Tri-Service General Hospital, Taiwan (TSGHIRB No.: A202215033). The IRB approves the waiver of the informed consent form.

## Data availability statement

The data that support the findings of this study are available from the corresponding author, CK Tsai, upon reasonable request.

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Nil.

## Conflicts of interest

Dr. Chia-Kuang Tsai, an editor at Journal of Medical Sciences, had no role in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

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