Cancer Medicine

Case Report | Vol 6 Issue 2

Neuro-psycho Disorders and Hyponatremia in a Renal Carcinoma Patient Revealed as Anti-LGI1 Encephalitis and Renal Salt Wasting

Zhichuan Lin[1], Fang Gao[2#], Jing Wang[3#], John K Maesaka[4], Yingliu Huang[1], Guoqiang Wen[1], Qi Qin[5], Shixiong Huang[1*] and Yan Lv[1*]

[1]*Department of Neurology, Hainan General Hospital, Haikou, China*

[2]*Health Management Center, Binzhou People's Hospital, Binzhou, China*

[3]*Department of Neurology, Sanya Central Hospital, Sanya, China*

[4]*Division of Nephrology and Hypertension, Department of Medicine, NYU Winthrop Hospital, Mineola, New York, USA*

[5]*Department of Neurology, Xuan Wu Hospital, Capital Medical University, Beijing, China*

Correspondence should be addressed to Yan Lv, Department of Neurology, Hainan General Hospital, Haikou, China

Received: December 14, 2022; Accepted: December 22, 2022; Published: December 29, 2022

[#]Indicated Co-First Author

[*]Indicated Co-Correspondence Author

ABSTRACT

BACKGROUND

LGI1(leucine-rich-anti-glioma1protein 1) is one of the latest identified voltage-gated potassium channels related antigens. Anti-LGI1 encephalitis is one of the autoimmune encephalitis and characterized with neurological symptoms and hyponatremia. The anti-LGI1 encephalitis was thought to be non-malignancy related. And the hyponatremia of anti-LGI1 encephalitis was considered as inappropriate secretion of antidiuretic hormone.

CASE DESCRIPTION

Here, we firstly report a 71-year-old female diagnosed with anti-LGI1 encephalitis with renal clear cell carcinoma and renal salt wasting. The old female was discovered a renal mass identified as renal clear cell carcinoma. Two months after the renal carcinoma resection, the patient fell frequently and showed discontinuous neuro-psychiatric disorders manifested as memory decline, disorientation, and unintentional upper limb movements as typical faciobrachial dystonic seizure episode. She also had hyponatremia. The combination of her clinical presentations and laboratory assessments supported a diagnosis of anti-LGI1 encephalitis and renal salt wasting. The Immunohistochemistry studies of the kidney resection indicated circulating LGI1 antibodies in sera might be binding to extracellular LGI1 predominantly in the proximal tubule where the major defect in solute transport exists in renal salt wasting.

CONCLUSION

Anti-LGI1 encephalitis with renal carcinoma indicated its paralimbic pathology origin. The early diagnosis and immune-

Citation: Zhichuan Lin, Neuro-psycho Disorders and Hyponatremia in a Renal Carcinoma Patient Revealed as Anti-LGI1 Encephalitis and Renal Salt Wasting. Can Med 6(2): 69-78.

modulation therapy could lead to a good outcome. The hyponatremia in anti-LGI1 encephalitis was renal salt wasting instead of syndrome of inappropriate secretion of antidiuretic hormone.

KEYWORDS

Anti-LGI1 encephalitis; Renal carcinoma; Hyponatremia; Renal salt wasting

ABBREVIATIONS

LGI1: Leucine-Richanti-Glioma1protein; FBDS: Faciobrachial Dystonic Seizure; RSW: Renal Salt Wasting; CRSW: Cerebral/Renal Salt Wasting; FEurate: Fractional Excretion of Uric Acid; SIADH: Syndrome of Inappropriate Secretion of Antidiuretic Hormone; IHC: Immunohistochemistry; MMSE: Minimental State Examination; CSF: Cerebral Spinal Fluid; MRI: Magnetic Resonance Imaging; VGKC: Voltage-Gated Potassium Channels; AMPA1: Glutamate Receptor, Ionotropic, Alpha 1; AMPA2: Glutamate Receptor, Ionotropic, Alpha 2; GABAR: Gamma Aminobutyric Acid Receptors; NMDAR: N-Methyl-D-Aspartate Receptors; IVMP: Intravenous Methylprednisolone; IVIG: Intravenous Immunoglobulin; VPA: Valproic Acid Sodium; OXC: Oxcarbazepine; CRMPs: Amphiphysin, Collapsin Response Mediator Proteins; LRR: Leucine-Rich Repeats; ADAM22: A Disintegrin and Metalloproteinase Domain-Containing Protein 22; ADLTE: Autosomal Dominant Lateral Temporal Epilepsy; LTE: Lateral Temporal Epilepsy; HLA: Human Leukocyte Antigen; SAH: Subarachnoid Hemorrhage

INTRODUCTION

Anti-LGI1 encephalitis affects the limbic systems and presents with subacute onset of progressive neurological, cognitive, psychiatric disturbance and obstinate hyponatremia [1,2]. Anti-LGI1 encephalitis is mostly considered to be non-malignancy related [3,4]. We reported a case of anti-LGI1 encephalitis presented cognitive disorder and FBDS (Faciobrachial dystonic seizure) after resection of her renal carcinoma for the first time. The unique relationship between serum sodium and fractional excretion of uric acid Feurate (Fractional excretion of uric acid) determined that the hyponatremia was due to CRSW (Cerebral/renal salt wasting) or more appropriately RSW (Renal salt wasting) instead of the SIADH (Syndrome of inappropriate secretion of antidiuretic hormone). The IHC (Immunohistochemistry) studies of the kidney indicated that circulating LGI1 antibodies in sera might be binding to extracellular LGI1 predominantly in the proximal tubule where the primary defect in solute transport exists in RSW.

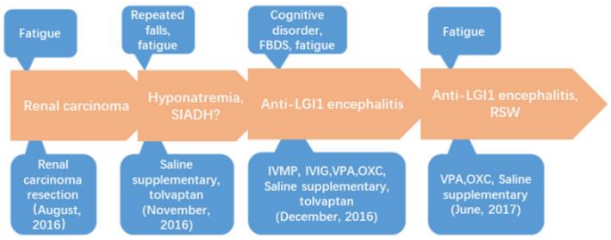
CASE DESCRIPTION AND RESULTS

Clinical Manifestation

A 71-year-old female had a renal mass surgically removed, which was identified as renal clear cell carcinoma by pathological and immunological evaluation. Almost two months after surgery, the patient complained about fatigue, fell frequently, unstable gait, and reported unintentional upper limb movements. Her family also noticed cognitive defects as short-term memory, inability to recognize family members, and being unaware of home circumstances or time in the patient. There was no family history of psychiatric disorders or dementias. She did not take medicines and denied the use of tobacco or alcohol.

The symptom evolution of the patient presented typical neurophysiological symptoms during the development instead of at the very beginning of the disease. She also reported FBDS (Faciobrachial dystonic seizure) episode (Supplementary figure 1 and Supplementary table1 and Supplementary table 2). Her MMSE (Minimental state examination) was 3/30 (Orientation 1, memory 1, language

1). Detailed neurological examination showed a lack of coordination, including normal cranial nerves, predicted IV symmetric strength throughout, active reflexes, incorporated finger-to-nose testing. On physical examinations, she had a normal cardiovascular, respiratory, abdominal, and pulmonary examination during the reported medical history.



Supplementary Figure 1: Evolution of diagnosis and evaluation of the main symptoms.

Na	K	PosmmOsm/KgH2O	UA	Create	Renin	Aldo	AII	Cortisol
mmol/L	mmol/L		µmol/L	µmol/L	ng/ml/Hr	pg/ml	pg/ml	nmol/L
141	3.86	308	224	83	0.15	129.18	39.36	404
FRT3	**FRT4**	**TSH**	**Na (Urine)**	**K(Urine)**	**Uosm**	**UA**	**Create**	**FEurate**
pmol/L	pmol/L	mIU/L	mmol/24 hours	mmol/24 hours	mOsm/KgH2O	µmol/24 hours	µmol/24 hours	%
4.09	9.82	3.98	28.8	25.22	687	3655	5296	26.93

Supplementary Table 1: Patient's laboratory findings of hyponatremia correction.

Note: Posm: Plasma Osmolality; Uosm: Urine Osmolality; AII: Angiotensin II; Aldo: Aldosterone; Create: Creatinine; UA: Uric Acid; FRT4: Free T4; FRT3: Free T3; TSH: Thyroid Stimulating Hormone; FEurate: Fractional Excretion of Uric Acid, FEurate: Serum Creatine X Urine UA (24 hours))/(Serum UA X Urine Creatin (24 hours)) X 100%).

	RSW	SIADH
ECV	↓	N-↑
UNa	N-↑	N-↑
Renin	↑	±↓
Aldosterone	↑	±↓
Serum urate	↓-↓	↓-N
FEurate	↑-↑	↑-N

Supplementary Table 2: Differentiation of SIADH from RSW.

Note: ECV: Extracellular Volume; RSW: Renal Salt Wasting; SIADH: Secretion of Antidiuretic Hormone; Una: Urinary Sodium Concentration.

Table comparing laboratory expectations for RSW and SIADH. UNa can be normal or often >20 mmol/l; Serum urate and FEurate are increased during hyponatremia in both RSW and SIADH but differ when serum is normal. Serum urate and FEurate remain abnormal in RSW and normalize in SIADH when serum sodium is normal.

LABORATORY RESULTS

Serum and CSF from the patient was qualitatively tested for neuropil antibodies associated with autoimmune encephalitis including antibodies to glutamate receptors type NMDA, type AMPA1 and type AMPA2, LGI1, CASPR2 and GABARB1/B2using the indirect immunofluorescence test (IIFT) (EUROIMMUN, FA 112d-1005-1, Germany). Cell based assays (CBAs) for those antibodies were performed using EU90 cells (EUROIMMUN) transfected with cDNAs encoding the relevant proteins. Combinations of substrates were incubated with patient serum (1:10 dilution) or undiluted CSF sample. In a second step, the attached antibodies were stained with fluorescein-labelled anti-human antibodies (EUROIMMUN) and made visible with a fluorescence microscope. Fluorescence intensity level was used to describe the intensity of the specific fluorescence as a numeric value, reaching from "0" or "–" (No specific fluorescence) to "5" or "+++++" (Extremely strong specific fluorescence). The deviation in the fluorescence intensity of the IIFT amounted to no more than ±1 fluorescence intensity level for all samples [5-36]. A cell-based assay showed serum VGKC (Voltage-gated potassium channels) complex proteins (EUROIMMUN, Germany) serum LGI1-Ab to be positive+++ (1:100) while the CSF LGI1-Ab was negative; other autoimmune encephalitis antibodies including AMPA1 (Glutamate receptor, ionotropic, alpha1), AMPA2 (Glutamate receptor, ionotropic, alpha2), Casp2, cerebellum-1, GABAR (Gamma-aminobutyric acid receptors), NMDAR (N-methyl-D-aspartate receptors) in serum and CSF were all negative, which established the diagnosis of anti-LGI1 encephalitis.

CSF (Cerebral spinal fluid) tests for protein, cells, glucose, chloride, and culture were normal. Serum sodium ranged between 118 mmol/L - 148 mmol/L during the reported medical history. The cortisol, FT4 and TSH were normal, which excluded hypothyroidism and Addison's disease. Autoimmune, infectious, endocrinologic, neoplastic and paraneoplastic screenings were unremarkable. FEurate was increased after correction of her hyponatremia (Supplementary Table 1), which is in consistent with RSW and not SIADH [5] (Supplementary Table 2). The increased aldosterone during the period of hyponatremia was in consistent with RSW.

Expression of LGI1 by patient's carcinoma. The IHC staining of LGI1 protein expression in kidney, and renal cell carcinoma to explore the underlying LGI1 related RSW mechanism (Figure 1). Paraffin embedded tumor junction tissue sections of the patient's renal clear cell carcinoma from a patient with serum LGI1 antibodies (A tumor junction, B normal tissue, C carcinoma tissue), another patient with only renal clear cell carcinoma without serum LGI1 antibodies (D tumor junction, E normal tissue, F carcinoma tissue), a commercial antibody against LGI1 (rabbit polyclonal anti-LGI1, Abcam, ab137045, diluted 1:50) was used. Note the expression of LGI1 in normal renal tubule (B,E) and absent in carcinoma tissue (D,F), and the more robust expression pattern in the patient without LGI1 serum antibody (B,E). Note expression of LGI1 in normal renal tubule (C,D) and absence in renal carcinoma tissue (E,F). There was reduced expression of the LGI1 in the patient when the circulating LGI1 antibody was present as compared to the absence of LGI1 antibody (C,D). There was a higher expression of LGI1 in proximal as compared to distal convoluted tubules both in the patients with or without circulating LGI1 antibodies (C,D).

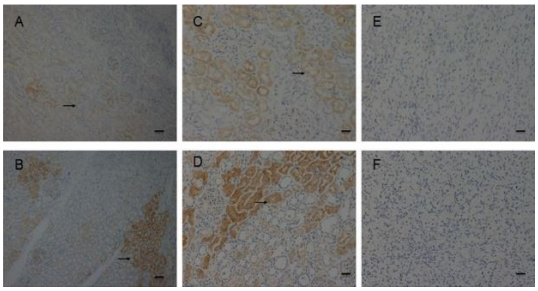


Figure 1: Expression of LGI1 by patient's carcinoma. Tumor junction tissue sections of the patient's renal clear cell carcinoma from a patient with serum LGI1 antibodies (A,C,E), another patient with only renal clear cell carcinoma without serum LGI1 antibodies (B,D,F). A commercial antibody against LGI1 (rabbit polyclonal anti-LGI1, abcam, ab137045, diluted 1:50) was used for IHC. Note the expression of LGI1 in normal renal tubule (C,D) and absent in carcinoma tissue (E,F), and the reduced expression pattern in the patient with LGI1 serum antibody (C,D), and higher expression in proximal than distal convoluted tubules (C,D). (The bar presented 20 µm, 10 µm, 10 µm for A,C,E, respectively).

IMAGING RESULTS

Cerebral MRI (Magnetic resonance imaging) (Figure 2A and Figure 2B) scans, including T2 flare (Figure 2A), DWI (Figure 2B) were normal. EEG (Electroencephalogram) showed accidental sharp and slow wave complex in bifrontal and biparietal leads (Figure 2E) with diffuse theta and delta wave background during FBDS. sLORETA (Standardized low-resolution brain electromagnetic tomography) spike source analysis by ASA 4.9 software showed the sharp and slow wave complex were sourced in frontal lobe (Figure 2C and Figure 2D).

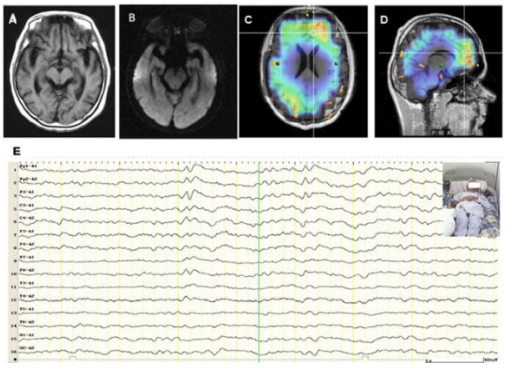


Figure 2: MRI, EEG and spike sLORETA analysis presentations of the patient. The patient presented normal MRI in T2 flare and DWI sans (A,B); slow and accidental sharp and slow wave complex in bifrontal and biparietal leads with diffuse theta and delta wave background during FBDS (E), sLORETA (Standardized low-resolution brain electromagnetic tomography)

spike source analysis by ASA 4.9 software showed the sharp and slow wave complex were sourced in frontal lobe (C,D).

DIAGNOSTIC ASSESSMENT

Diagnosis, Treatment and Prognosis

The treatments were given and modulated according to the evolution of diagnosis and evaluation of the main symptoms (Supplementary Figure 1). When the LGI1 antibody encephalitis diagnosis was established, treatment with IVMP (Intravenous methylprednisolone) 1.0/day for 5 days, 0.5/day for 3 days, 0.125/day for 5 days, followed with IVIG (Intravenous immunoglobulin) at a dose of 0.4 g/kg/day for 5 days 0.4 g/kg/day for 5 days and continued oral prednisolone 40 mg/day treatment for a month declined to 8mg/day maintained. VPA (Valproic acid sodium) 0.5 oral bid combined OXC (oxcarbazepine) 0.3 oral bid were administered to prevent epilepsy recurrence. The patient's neurological dysfunction responded well to immunoglobulin with diminution of facial muscle jerk as FBDS and improved MMSE scores during the IVIG and consisted afterward, which increased to 15/30 (Orientation 6, memory and recall ability 2, attention and calculation 2, language 3, executive function 2, visual spatial 0) after IVIG therapy, and jump to 22/30 (Orientation 8, memory and recall ability 4, attention and calculation 4, language 3, executive function 3, visual spatial 0) at 6-months follow up, 27/30 (Orientation 10, memory and recall ability 6, attention and calculation 4, language 3, executive function 3, visual spatial 1) at 2-years follow up. For hyponatremia, the patient received saline supplementary as 10% sodium chloride solution intravenous 1.5% sodium chloride 250 ml qd-bid plus 20 ml oral bid-qid according to the serum sodium level. Hypersaline supplementary and Toveptan was given in a combination of immunomodulation therapy, and the relationship of sodium level between the therapy showed good effectiveness of IVMP and hyper saline supplementary treatment (Figure 3). The elevated FEurate indicated the diagnosis of RSW instead of SIADH. No hyponatremia and other complaints were observed at the 6 months and 2 years follow up.

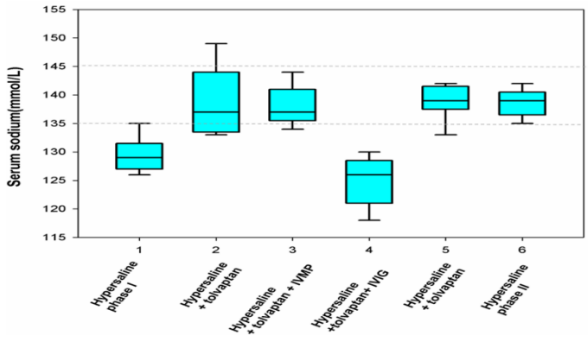


Figure 3: Sodium level with according to treatment.
Note: IVMP: Intravenous Methylprednisolone; IVIG: Intravenous Immunoglobulin.

DISCUSSION

The diagnosis of encephalitis was not initially entertained when the patient presented with fatigue and found to have hyponatremia, but the development of more obvious symptoms such as repeated falls and FBDS episodes were highly suggestive of a paraneoplastic condition associated with LGI1 encephalitis. There has been a growing interest and understanding of paraneoplastic encephalitis and autoimmune encephalitis. Since the 1980s, there has been investigations which identified two major groups of antigens that categorize paraneoplastic autoimmune encephalitis, the classic onco-neuronal antigens that include Yo, Hu, Ri, Tr, CRMPs (Amphiphysin, collapsin response mediator proteins), Recoverin, Ma; autoimmune synaptic antigens including NMDAR, AMPAR, LGI1, Casp2, GABAR and unknown antigens [6].Paraneoplastic autoimmune encephalitis has been reported in patients with lung small cell carcinoma, adenocarcinoma of breast, ovarian teratoma, lung cancer etc. [3]. We present a rare case of renal carcinoma related paraneoplastic encephalitis, which has been reported previously in 3 cases over the last two decades, the diagnosis being hampered in most by a lack of specific antigens [7-9]. For example, a hallucinating 66-years-old with renal cell carcinoma had a diagnosis of limbic encephalitis made based on tests for intracellular autoimmune encephalitis that included Hu, Yo antibody

but failed to identify antibodies in serum or CSF extracellular antibodies including NMDAR, AMPAR, LGI1, Casp2, GABAR [7], which would be possible autoimmune encephalitis antigens. On the other hand, the anti-IGI1 antibody was first reported in 2010 as an extracellular autoimmune factor that targeted the nervous system playing a role in paraneoplastic autoimmune encephalitis [10]. In time LGI1 paraneoplastic encephalitis or anti-LGI1 encephalitis have been reported in lung cancer [11], and thymoma [12]. The diagnosis of this rare condition can thus be challenging for primary care physicians, and we hope that this report will raise awareness and highlight the unique presentation of patients with paraneoplastic anti LGI1 encephalitis. Despite the lack of a clear line to distinguish the paraneoplastic encephalitis and anti-LGI1 encephalitis, the main characteristic presentations of anti-LGI1 encephalitis could be summarized as follows: 1) Serum or CSF LGI1 antibody; 2) Neuropsychic-disorder as memory decline, disorientation or hallucination; 3) Tonic seizure as FBDS; 4) Hyponatremia related symptoms.

The LGI1 gene was discovered in the 1980s, which encodes a protein LRR (Leucine-rich repeats) with conserved flanking sequences. In the LRR domain, LGI1 shares the highest homology with many transmembrane and extracellular proteins, and these proteins act as receptors and adhesion proteins [13]. LGI1 primarily expresses in neural tissues, particularly in the brain, which reduced in low-grade brain tumors as malignant gliomas [14,15]. LGI1 modulates ADAM22 (A disintegrin and metalloproteinase domain-containing protein 22) or ADAM23 as a secretion protein [1]. LGI1 micro-rearrangements were observed in a collection of ADLTE (Autosomal dominant lateral temporal epilepsy) families and sporadic LTE (Lateral temporal epilepsy) patients and investigated novel ADLTE and LTE patients [16]. Anti-LGI1 limbic encephalitis was distinguished from VGKC antibody group encephalitis (Anti-LGI1, Caspr2, or VGKC positive groups) with hyponatremia and typical FBDS [17-19]. In this report, the patient failed to show obvious abnormalities in MRI scans, including T1, T2, DWI scans (Figure 2), thus lacked the characteristic imaging presentations in the hippocampus [20], striatum [21] and mesial temporal lobes [22]. However, EEG based studies showed hippocampal functional dynamics changes beyond structural abnormalities [19,23]. In this report, the sLORETA based source analysis showed frontal lobe sourced epileptic foci (Figure 2 C and Figure 2 D), which could shed light on the positioning diagnosis. There is no congruous treatment strategy for autoimmune encephalitis; the indicated and accepted therapies are immuno-therapies as steroids and sequenced immunoglobulins [24,25]]. In our report, the patient presented with typical features of anti-LGI1 limbic encephalitis, including cognitive defects, FBDS, hyponatremia, and had an excellent response to steroids and IVIG therapy [26,27].

Hyponatremia, another characteristic symptom of LGI1 encephalitis patients, defined as serum sodium <135 mmol/L, is the most common electrolyte abnormality [28]. Differentiating SIADH from RSW has been difficult because of the perception that RSW is a rare condition and even more so because of identical clinical parameters that include hyponatremia, hypouricemia, concentrated urine with urine sodium >30 mmol/L, increased FEurate with normal renal, adrenal and thyroid function [29,30]. There is accumulating evidence to utilize a new algorithm where FEurate is central to our evaluation of hyponatremia. In this algorithm, FEurate increases to >11% during hyponatremia in both SIADH and RSW. However, after the correction of hyponatremia, FEurate returns to normal in SIADH but remains increased in RSW (Supplementary Table 1). Our patient with paraneoplastic LGI1 encephalitis had increased FEurate after correction of hyponatremia when serum sodium was 141 mmol/L to meet the criteria for RSW where treatment with saline is most appropriate [30]. The etiology of RSW is most likely due to the presence of

a circulating natriuretic peptide that is somehow up-regulated in diverse clinical conditions, and is not confined to those with cerebral disease. The natriuretic factor and increased FEurite has its major effect in the proximal tubule where uric acid is exclusively transported [31-33]. In this patient, we traced the LGI1 origin in renal tissues for the clues of this phenomenon. Even there was no reported LGI1 expressions in the literature research, it is in accordance with previously reported mice LGI1 expressions in renal tubule in mice [34] It would be interesting to speculate that LGI1 may play a role in the development of the urology carcinoma, as it has been shown for the development of prostate cancer [35]. According to IHC staining studies of the kidney, LGI1 appears to exist more abundantly in the proximal tubule as compared to the distal tubule (Figure 1). The intensity of the staining is reduced when there are circulating antibodies in serum (Figure 1 A and Figure 1C) as compared to the absence of circulating antibodies to LGI1(Figure 2B - Figure 2D). It is interesting that there was absence of staining in renal carcinoma cells with or without the presence of circulating antibodies (Figure 2E and Figure 2F). These data indicate that circulating antibodies in sera might be binding to extracellular LGI1 predominantly in the proximal tubule where the major defect in solute transport exists in RSW.

PATIENT PERSPECTIVES

Anti-LGI1 encephalitis with FBDS should be assessed not only structural but also functional measures as EEG based analysis. The sLORETA analysis could provide insight into the Anti-LGI1 encephalitis. Also, LGI1 encephalitis is a multisystem disorder that includes the renal tubule, which is manifested as a renal salt wasting syndrome due to a circulating natriuretic peptide and must be differentiated from SIADH because of opposed therapeutic goals. Anti-LGI1 encephalitis should be a syndrome that is not only confined to patients with encephalitis. However, this case report did not obtain FEurate before hyponatremia correction, the etiology of hyponatremia as RSW could be evaluated in a large sample of anti-LGI1 encephalitis with or without renal carcinoma, thus lead to the conclusion besides rare circumstances.

DECLARATIONS

Ethics Approval and Consent to Participate

Written informed consent and ethical approval were obtained from the subject in accordance with the Helsinki Declaration.

Consent for Publication

Written Informed consent to participate and publication including clinical data, images and videos were obtained from the patient at 6-months follow up, when she had no orientation defections and estimated by 2 attending physicians in neurology department and her family to for the acceptable capacity to make decisions.

Availability of Data and Material

All data generated or analyzed during this study are included in this published article [and its supplementary information files]. The raw datasets used and/or analyzed during the current study are also available from the corresponding author on reasonable request.

Competing Interests

All of the authors declare no conflict of competing interests.

Funding

This work was supported in part by grants from the Key Science and Technology Project of Hainan Province (ZDXM2015070) and (ZDYF2018141). The funding supported the collection, analysis, and interpretation of data.

Authors' Contributions

All authors listed have contributed sufficiently to the project to be included as authors, and all those who are

qualified to be authors are listed in the author byline. Dr. YL M.D.& P.H.D. -acquisition of data, analysis and interpretation, critical revision of the manuscript for important intellectual content. Dr. ZCL M.D.-study concept and design, analysis and interpretation of data analysis and interpretation of data analysis and interpretation of data. Pro. JM. - conceptual guidance, anaylysis and interpretation, critical revision of the manuscript for important intellectual content. Dr. YLH M.D.- analysis and interpretation. Dr. XLX M.D.& M.S- acquisition of data. Pro. GQW M.D.- analysis and interpretation. Dr. QQ M.D.& P.H.D. - study concept, analysis and interpretation, critical revision of the manuscript for important intellectual content. Dr. TL M.D.& P.H.D.- study concept and design, analysis and interpretation of data. analysis and interpretation of data analysis and interpretation of data, critical revision of the manuscript and supervision of the study. Dr. SXH M.D.& P.H.D. - study concept, acquisition of data, analysis and interpretation, critical revision of the manuscript for important intellectual content, study supervision.

Acknowledgements

This study was supported by multi-department cooperation. Including Dr. HB Quan, Dr. DH Cai, Dr. DJ Chen for their clinical care of the patient; Dr. Hongwen Zhu; Prof. Wei Qiu; Dr. Yun Zhong for the manuscript preparation.

REFERENCES

1. Lai M, Huijbers MG, Lancaster E, et al. (2010) Investigation of LGI1 as the antigen in limbic encephalitis previously attributed to potassium channels: A case series. The Lancet Neurology 9(8): 776-785.
2. Petit-Pedrol M, Sell J, Planagumà J, et al. (2018) LGI1 antibodies alter $K_v1.1$ and AMPA receptors changing synaptic excitability, plasticity and memory. Brain 141(11): 3144-3159.
3. McKeon A (2013) Paraneoplastic and other autoimmune disorders of the central nervous system. The Neurohospitalist 3(2): 53-64.
4. Seluk L, Taliansky A, Yonath H, et al. (2019) A large screen for paraneoplastic neurological autoantibodies; diagnosis and predictive values. Clinical Immunology 199: 29-36.
5. Maesaka JK, Imbriano LJ, Ali NM, et al. (2009) Is it cerebral or renal salt wasting?. Kidney International 76(9): 934-938.
6. Lee SK, Lee ST (2016) The laboratory diagnosis of autoimmune encephalitis. Journal of Epilepsy Research 6(2): 45-50.
7. Harrison JW, Cherukuri R, Buchan D (2015) Renal cell carcinoma presenting with paraneoplastic hallucinations and cognitive decline from limbic encephalitis. Journal of General Internal Medicine 30(7): 1037-1040.
8. McHugh JC, Murray B, Renganathan R, et al. (2007) GAD antibody positive paraneoplastic stiff person syndrome in a patient with renal cell carcinoma. Movement disorders: Official Journal of the Movement Disorder Society 22(9): 1343-1346.
9. Kararizou E, Markou I, Zalonis I, et al. (2005) Paraneoplastic limbic encephalitis presenting as acute viral encephalitis. Journal of Neuro-oncology 75(2): 229-232.
10. Lai M, Huijbers MG, Lancaster E, et al. (2010) Investigation of LGI1 as the antigen in limbic encephalitis previously attributed to potassium channels: A case series. The Lancet Neurology 9(8): 776-785.
11. Ahn SW, Kim JM, Kim JE, et al. (2014) Development of LGI1 antibody encephalitis after treatment of lung cancer. Canadian Journal of Neurological Sciences 41(5): 669-671.
12. Simabukuro MM, Petit-Pedrol M, Castro LH, et al. (2015) GABAA receptor and LGI1 antibody encephalitis in a patient with thymoma. Neurology-Neuroimmunology Neuroinflammation 2(2): e73.

13. Kegel L, Aunin E, Meijer D, et al. (2013) LGI proteins in the nervous system. ASN Neuro 5(3): AN20120095.
14. Chernova OB, Somerville R, Cowell JK (1998) A novel gene, LGI1, from 10q24 is rearranged and downregulated in malignant brain tumors. Oncogene 17(22): 2873-2881.
15. Jang Y, Lee ST, Bae JY, et al. (2018) LGI1 expression and human brain asymmetry: Insights from patients with LGI1-antibody encephalitis. Journal of Neuroinflammation 15(1): 1-7.
16. Manna I, Mumoli L, Labate A, et al. (2014) Autosomal dominant lateral temporal epilepsy (ADLTE): Absence of chromosomal rearrangements in LGI1 gene. Epilepsy Research 108(3): 597-599.
17. van Sonderen A, Schreurs MWJ, Wirtz PW, et al. (2016) From VGKC to LGI1 and Caspr2 encephalitis: the evolution of a disease entity over time. Autoimmunity Reviews 15(10): 970-974.
18. d'Orsi G, Martino T, Lalla A, et al. (2018) Faciobrachial dystonic seizures expressed as epileptic spasms, followed by focal seizures in anti-LGI1 encephalitis: A video-polygraphic study. Epileptic Disorders 20(6): 525-529.
19. Li LH, Ma CC, Zhang HF, et al. (2018) Clinical and electrographic characteristics of seizures in LGI1-antibody encephalitis. Epilepsy & Behavior 88: 277-282.
20. Hanert A, Rave J, Granert O, et al. (2019) Hippocampal dentate gyrus atrophy predicts pattern separation impairment in patients with LGI1 encephalitis. Neuroscience 400: 120-131.
21. Plantone D (2018) Striatum involvement in lgi1 limbic encephalitis. Clinical Psychopharmacology and Neuroscience 16(4): 508-509.
22. Yang X, Li AN, Zhao XH, et al. (2019) Clinical features of patients with anti-leucine-rich glioma inactivated-1 protein associated encephalitis: A Chinese case series. International Journal of Neuroscience 129(8): 754-761.
23. Nantes JC, Thomas AG, Voets NL, et al. (2018) Hippocampal functional dynamics are clinically implicated in autoimmune encephalitis with faciobrachial dystonic seizures. Frontiers in Neurology 9: 736.
24. Blachère NE, Orange DE, Santomasso BD, et al. (2014) T cells targeting a neuronal paraneoplastic antigen mediate tumor rejection and trigger CNS autoimmunity with humoral activation. European Journal of Immunology 44(11): 3240-3251.
25. Kim TJ, Lee ST, Moon J, et al. (2017) Anti-LGI1 encephalitis is associated with unique HLA subtypes. Annals of Neurology 81(2): 183-192.
26. Feyissa AM, Lamb C, Pittock SJ, et al. (2018) Antiepileptic drug therapy in autoimmune epilepsy associated with antibodies targeting the leucine-rich glioma-inactivated protein 1. Epilepsia Open 3(3): 348-356.
27. Shin YW, Ahn SJ, Moon J, et al. (2018) Increased adverse events associated with antiepileptic drugs in anti–leucine-rich glioma-inactivated protein 1 encephalitis. Epilepsia 59: 108-112.
28. Dineen R, Thompson CJ, Sherlock M (2017) Hyponatraemia-presentations and management. Clinical Medicine 17(3): 263-269.
29. Sterns RH (2015) Disorders of plasma sodium-causes, consequences, and correction. New England Journal of Medicine 372(1): 55-65.
30. Maesaka JK, Imbriano LJ, Miyawaki N (2017) Application of established pathophysiologic processes brings greater clarity to diagnosis and treatment of hyponatremia. World Journal of Nephrology 6(2): 59-71.
31. Lipkowitz MS (2012) Regulation of uric acid excretion by the kidney. Current Rheumatology Reports 14(2): 179-188.
32. Maesaka JK, Venkatesan J, Piccione JM, et al. (1993) Plasma natriuretic factor (s) in patients with intracranial disease, renal salt wasting and hyperuricosuria. Life Sciences 52(23): 1875-1882.

33. Hayslett JP, Kashgarian M (1979) A micropuncture study of the renal handling of lithium. Pflugers Archiv European Journal of Physiology 380(2): 159-163.
34. Head K, Gong S, Joseph S, et al. (2007) Defining the expression pattern of the LGI1 gene in BAC transgenic mice. Mammalian Genome 18(5): 328-337.
35. Cowell JK, Head K, Kunapuli P, et al. (2010) Inactivation of LGI1 expression accompanies early stage hyperplasia of prostate epithelium in the TRAMP murine model of prostate cancer. Experimental and Molecular Pathology 88(1): 77-81.
36. Zhang L, Lu Q, Guan HZ, et al. (2016) A Chinese female Morvan patient with LGI1 and CASPR2 antibodies: A case report. BMC Neurology 16(1): 1-6.