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Cranial Diabetes Insipidus in Neuropsychiatric Systemic Lupus Erythematosus, a Rare but Treatable Association: A Case Report

Nöropsikiyatrik Sistemik Lupus Eritematozusta Kraniyal Diyabet Insipidus: Nadir Fakat Tedavi Edilebilir Bir Olgu

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ABSTRACT

Systemic lupus erythematosus has been rarely reported to be associated with cranial diabetes insipidus. It is a condition clinically manifest as severe polyuria and reactive polydipsia that may lead to electrolyte imbalance or acute kidney injury as a result of arginine vasopressin insufficiency. Here, we report a patient with systemic lupus erythematosus and lupus nephritis previously under control with medication presented with neuropsychiatric symptoms which responded to pulsed methylprednisolone, developed severe polyuria, polydipsia and hypernatremia which persisted after pulsed therapy. Serum and urine osmolarity were suggestive of diabetes insipidus and the polyuria resolved dramatically after trial of oral desmopressin which in keeping with the diagnosis of central cause. The objective of this case report is to share the uncommon occurrence of diabetes insipidus in neuropsychiatric systemic lupus erythematosus.

Key Word: Cranial diabetes insipidus; arginine vasopressin; systemic lupus erythematosus

Received: 12.04.2018

Accepted: 02.17.2020

ÖZET

Sistemik lupus eritematozusun nadiren kraniyal diyabet insipidus ile ilişkili olduğu bildirilmiştir. Arginin vazopressin yetmezliğinin bir sonucu olarak elektrolit dengesizliğine veya akut böbrek hasarına yol açabilen ciddi poliüri ve reaktif polidipsi kliniğiyle ortaya çıkan bir durumdur. Burada, pulse metilprednizolona yanıt veren, pulse tedaviden sonra devam eden şiddetli poliüri, polidipsi ve hipernatremi gelişen nöropsikiyatrik bulgular veren ilaçlarla daha önce kontrol edilen sistemik lupus eritematozus ve lupus nefriti olan bir hastayı sunuyoruz. Serum ve idrar osmolaritesi diyabet insipidusu düşündürdü ve poliüri, santral neden teşhisine uygun olarak oral desmopresin denemesinden sonra dramatik bir şekilde düzeldi. Bu olgu sunumunun amacı, nöropsikiyatrik sistemik lupus eritematozusta nadir görülen diyabet insipidus oluşumunu paylaşmaktır.

Anahtar Sözcükler: Kraniyal diyabet insipidus; arginin vazopressin; sistemik lupus eritematozus

Geliş Tarihi: 04.12.2018

Kabul Tarihi: 17.02.2020

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doi:<http://dx.doi.org/10.12996/gmj.2020.48>

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, autoimmune disorder which characteristically has remitting and recurrent episodes, and has multisystem involvement. The common clinical manifestations include arthritis, dermatitis, photophobia, alopecia, haematological abnormality, genitourinary and also central nervous system involvement. In this case report we share a rare occurrence of a SLE and lupus nephritis patient who develop polyuria, polydipsia and severe dehydration as a result of cranial diabetes insipidus (DI). It is a condition due to arginine vasopressin (AVP) insufficiency [1], and will be the centre of discussion in this case report.

CASE REPORT

A 46-year old non-smoker and a teetotaler gentleman who has underlying systemic lupus erythematosus (SLE) diagnosed in 1999 and subsequently developed Lupus Nephritis class 3a based on renal biopsy in 2008 which currently

treated with oral prednisolone 5mg once every two days, oral hydroxychloroquine 200mg once daily and oral azathioprine 50mg once daily, was presented with complaint of altered behaviour for the past two months. According to his wife, the patient became more withdrawn and spend most of his time daydreaming. He also started to have auditory hallucination whereby he claims to hear a voice telling him to wander around, and to step on the gas pedal while he was driving to hit the roadside pole. He also has a delusion where he believes there is a shadow that trying to posses him. The symptoms worsened two weeks prior to presentation and he have been more talkative but without meaning, although he was still orientated to time, place and person. Otherwise, there was no fever, no headache, no fitting, no joint pain and no skin rash. On arrival to the emergency department, his Glasgow Coma Scale was full and his vital signs were stable. Physical examination reveals no neck stiffness or any meningism signs, no malar rash, no skin lesions, no joint swelling, and no abnormality on cardiorespiratory examination. His abdomen was soft, not tender, and no mass or organomegaly noted. Examination of the fundus noted bilateral mild papilledema. Initial blood investigation was done and shows no abnormal result (as shown in Table 1).

Table 1: Initial blood investigations taken upon arrival to emergency department shows no abnormal results.

Test	Value	Normal range
Haemoglobin	16.0 g/dL	12 – 18 g/dL
White blood cell	9.5 x 10 ⁹ /L	4.0 – 11.0 x 10 ⁹ /L
Platelet	253 x 10 ⁹ /L	150 – 400 x 10 ⁹ /L
ESR	24 mm/hour	0 – 22 mm/hour
Sodium	145 mmol/L	135 – 150 mmol/L
Potassium	4.3 mmol/L	3.5 – 5.0 mmol/L
Urea	3 mmol/L	1.7 – 8.0 mmol/L
Creatinine	86 umol/L	60 – 120 umol/L
Calcium	2.47 mmol/L	2.12 – 2.65 mmol/L
PT	15.5 second	11.8 – 14.5 second
aPTT	38.5 second	30.0 – 44.5 second
INR	1.02	< 1.1

PT: Prothrombin time, aPTT: activated partial thromboplastin time, INR: International Normalization Ratio

Computed Tomography (CT) scan of the brain showed no space occupying lesion. Therefore, proceeded with lumbar puncture and it revealed high opening pressure of 34 cmH₂O, but otherwise no other abnormal parameters.

CT Venography was also done and showed no evidence of dural venous sinus thrombosis. EEG was normal. Magnetic Resonance (MR) imaging with arteriography was done and showed evidence of inflammation over the midbrain and hypothalamus (as shown in Figure 1).

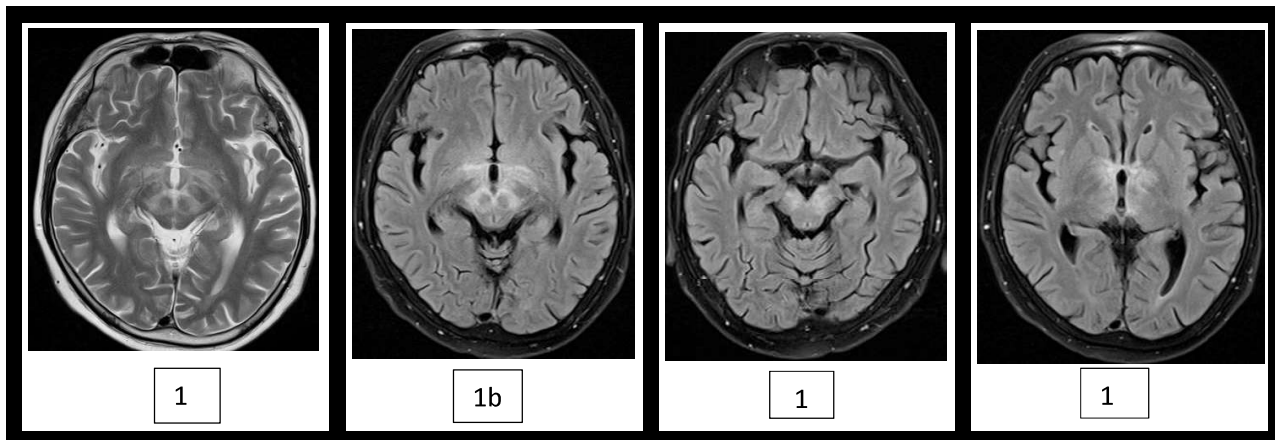


Figure 1. Axial T2WI shows hyperintense signals of the midbrain and hypothalamus (1a) which are not suppressed on FLAIR (1b,1c). There are also hyperintensities of the 3rd ventricle periventricular regions with mild involvement of the globus pallidus, thalamus and internal capsule (1d).
FLAIR: Fluid-attenuated inversion recovery

Based on the findings, he was treated as neuropsychiatric SLE and pulsed intravenous (IV) methylprednisolone 1 gm once daily was given for a total of three days. He responded to the treatment and there were no more psychotic symptoms, and the papilledema reduced. However, on the third day after completion of pulsed treatment, he developed hypernatremia with the plasma sodium of 149 mmol/L. His random blood glucose and other electrolytes was otherwise normal. According to his wife, he actually has been having polyuria since admission with the total urine output at the range of 5L to 6L per day. He also had marked polydipsia in the ward where he drank a few big bottles of water every day. He was initially given IV dextrose 5%, but the plasma sodium went up to 158 mmol/L. Urine sodium was less than 20 mmol/L. Diabetes insipidus (DI)

was suspected but unfortunately, water deprivation test was not able to be done due to unavailability of the test modality at that time. Therefore, a trial of oral desmopressin 0.1mg was given and urine output reduced dramatically to 2.6L. Urine output then went back to 7L the next day after the effect of desmopressin wean off. Regular dose of desmopressin was then started and the urine output has been normalized to 1.3 to 1.5 L per day. The plasma sodium was also normalized below 145mmol/L. As Cranial DI was suspected in view of patient responsiveness to desmopressin, MR imaging with angiography of the brain was repeated. There was residual hyperintensities over the midbrain, hypothalamus and periventricular region of third ventricle (as shown in Figure 2 and Figure 3).

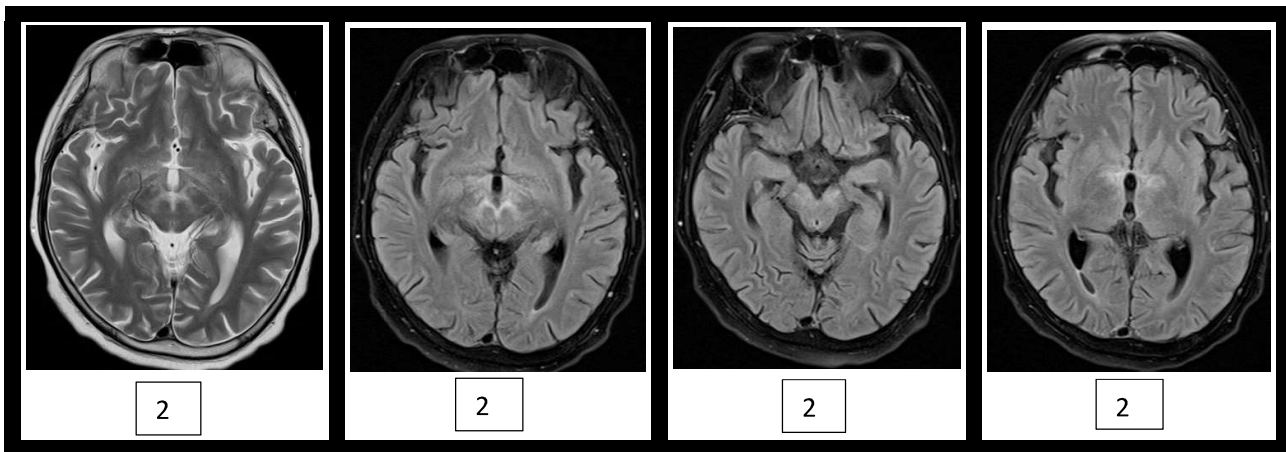


Figure 2. Repeat MRI; axial T2WI (2a) and axial FLAIR (2b, 2c and 2d) show residual hyperintensities of the midbrain, hypothalamus and periventricular region of third ventricle.

T2WI: T2-Weight Image, FLAIR: Fluid-attenuated inversion recovery



Figure 3. Sagittal FLAIR shows hyperintensities of the midbrain, lamina terminalis (straight arrow) and tuber cinereum (notched arrow).

Neuromyelitis Optica Spectrum Disorder was one of the differentials considered, but anti-Aquaporin-4 IgG and anti-myelin oligodendrocytes glycoprotein antibody was negative. In view of the symptoms and the response toward oral desmopressin, cranial DI was diagnosed. He was then managed with regular oral desmopressin 0.1mg once daily on top of the oral prednisolone and azathioprine.

DISCUSSION

Diabetes Insipidus (DI) is a distressing and potentially life-threatening condition characterized by severe polyuria with the urine production in excess of 2 L/m² over 24-hour. It is usually accompanied by reactive polydipsia to compensate the water loss and eventually will be complicated by acute kidney injury if the compensatory mechanism failed. DI can be either due to arginine vasopressin (AVP) deficiency which also called cranial DI, or due to AVP resistance which causes nephrogenic DI. Cranial and nephrogenic DI can be differentiated by the response to desmopressin administration which will dramatically reduce the amount of urine production in cranial DI, and is not seen in nephrogenic DI [1]. The pathology of cranial DI which either due to the deficiency of AVP synthesis from the hypothalamus or secretion from the neurohypophysis can be due to many causes. Systemic lupus erythematosus (SLE), which is a chronic autoimmune disorder with multi-system involvement, is listed as one of the recognize causes [2]. The occurrence of cranial DI in SLE is very rare. There is no solid data available of the occurrence of cranial DI in SLE and only a few isolated cases have been reported. One of the reported cases relate the presence of autoantibodies to AVP secreting-cells (AVPcAb) in cranial DI patients with SLE. Interestingly, it was characterized by the presence of AVPcAb before the treatment and disappearance after intravenous cyclophosphamide and steroid therapy with restoration of normal post pituitary function [4]. According to one study, 23.3% of the patients with cranial DI was associated with AVPcAb. Other literature reported that cranial DI has been linked with vascular central nervous system damage, with which vascular impairment of the inferior hypophyseal artery system suggests that abnormal blood supply to the posterior pituitary gland is associated [5]. However, in over one-third of cases, the aetiology of cranial diabetes insipidus is unknown. Therefore, further study is warranted to explore this limitation.

In our patient, although the DI was only diagnosed later, the symptoms actually present earlier prior he was given the pulsed methylprednisolone, and it persisted even after that. He actually responded to the pulsed treatment as evidence by resolution of the papilledema and psychotic symptoms, and also the reduction of the hyperintensities from the repeated magnetic resonance imaging and angiography of the brain. Therefore, we are unsure if the DI was as a part of neuropsychiatric SLE manifestations, or as a totally different pathology outside SLE. However, the patient responded to desmopressin to date and currently under regular clinic follow up.

One of the limitations in this case report was that water deprivation test was unable to be done as there was no modality available at that time. However, in view of the severe polyuria with the urine output of 6 to 7L per day and associated with reactive polydipsia and severe dehydration, which resolved after given desmopressin, makes the diagnosis of cranial DI very likely. Another limitation was that AVPCAb level was not measured as there was no modality available in the centre.

CONCLUSION

In conclusion, the objective of this case report is to share the occurrence of a rare association between cranial DI and SLE, which may occur as a part of neuropsychiatric manifestation. SLE patient has more tendency to develop nephrogenic DI rather than cranial DI due to variety of reasons, namely as a consequences of lupus nephritis, hypokalaemia, and many others, but it is worth the while to rule out cranial in origin as the condition is treatable with desmopressin. And in event where water deprivation test cannot be done, a trial of desmopressin can be given to differentiate between cranial and nephrogenic DI, as in this patient.

Conflict of interest

No conflict of interest was declared by the authors.

Acknowledgement

The authors would like to thank the patient for giving his consent and cooperation in relation to the writing of this case report. The author would also like to thank the Director General of Ministry of Health of Malaysia for his permission to publish this article.

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