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WEST NILE VIRUS NEUROINVASIVE DISEASE PRESENTING WITH ACQUIRED FANCONI SYNDROME, WHICH RESOLVED ON RECOVERY

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ABSTRACT

Background: West Nile virus (WNV) is a mosquito-borne flavivirus that can cause neuroinvasive disease. Renal involvement is uncommon and acquired Fanconi syndrome has not been previously described in association with WNV.

Case presentation: An 81-year-old male from Cyprus presented with fever, headache, disorientation, and signs of meningoencephalitis. Cerebrospinal fluid (CSF) analysis and neuroimaging supported the diagnosis of viral encephalitis. Extensive microbiological testing revealed WNV ribonucleic acid in urine and blood, but not in the CSF. The patient developed persistent hypokalaemia, metabolic acidosis, hypomagnesemia, and hypouricemia, with elevated fractional excretion of these solutes—findings consistent with Fanconi syndrome. Acyclovir was discontinued, and supportive treatment was provided. Renal function and electrolyte levels normalized by day 9. At 2-month follow-up, the patient had fully recovered with normal renal parameters.

Conclusion: Renal complications of WNV are rarely documented and this case of WNV associated acquired Fanconi syndrome underscores the importance of evaluating kidney function and electrolyte status in WNV-infected patients. Early recognition of tubular dysfunction may prevent complications and improve outcomes.

KEYWORDS

West Nile virus, Fanconi's syndrome, proximal tubular dysfunction, hypokalaemia

LEARNING POINTS

- While renal complications of West Nile virus (WNV) are documented in rare cases, this is the first reported case of WNV-associated Fanconi syndrome.

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INTRODUCTION

West Nile virus (WNV) is a mosquito-borne flavivirus that can cause neuroinvasive disease. Renal involvement is rare and acquired Fanconi syndrome has not been previously described in association with WNV.

CASE DESCRIPTION

An 81-year-old Cypriot male with a medical history of hypertension, rheumatoid arthritis, prior transcatheter edge-to-edge mitral valve repair , moderate residual mitral regurgitation, and a solitary pulmonary nodule under investigation in the right upper lobe, presented to the emergency department with a 3-day history of fever (up to 38°C), headache, and altered mental status, including disorientation. The patient was a retired farmer who remained physically active and engaged in agricultural work, including crop cultivation.

On presentation, his vital signs were as follows: body temperature 37°C, heart rate 57 beats per minute, blood pressure 144/79 mmHg, and oxygen saturation 95% on room air. Physical examination was notable for neck stiffness, myoclonic jerks involving the upper limbs and facial muscles, mild dysarthria, and dysphagia. Cardiovascular examination revealed a systolic murmur consistent with mitral regurgitation. Pulmonary auscultation was unremarkable, with no crackles or signs of consolidation. A chest X-ray showed a 1.5 cm nodule in the right upper lobe. Laboratory results obtained at admission are summarized in *Table 1*.

Laboratory test on admission	Results
White blood cell count (WBC/µl) Neutrophils (%) Lymphocytes (%)	13.430 81.3 9
C-reactive protein (mg/l)	18
Lactate dehydrogenase (U/l)	418
Creatine kinase (U/l)	1209
Aspartate transaminase (U/l)	71
Urea (mg/dl)	42
Creatinine (mg/dl)	1
Potassium (mmol/l)	3.5
Sodium (mmol/l)	144
CSF laboratory test	
White blood cell count (WBC/µl) Neutrophils (%) Lymphocytes (%)	40 5 95
Red blood cell count (RBC/µl)	1
Proteins (mg/dl)	155
Glucose (mg/dl)	43

Table 1. Laboratory data on admission and CSF test results.

Following admission, two sets of blood cultures were obtained. Neuroimaging, including a non-contrast computed tomography (CT) scan and a gadolinium-enhanced magnetic resonance imaging (MRI) of the brain, revealed a focal area of signal abnormality in the right paracentral lobule, interpreted as a possible area of gliosis of uncertain clinical significance. A lumbar puncture was subsequently performed; cerebrospinal fluid (CSF) analysis is presented in *Figure 1*. Gram staining of the CSF did not reveal any organisms.

Based on the CSF findings, the patient was empirically started on intravenous acyclovir, given the high clinical suspicion of viral meningoencephalitis. The differential diagnosis at this stage included viral central nervous system infection, autoimmune disease flare (e.g., rheumatoid vasculitis), and paraneoplastic syndromes. An electroencephalogram was performed, demonstrating a diffuse, slow encephalopathic pattern, consistent with generalized cerebral dysfunction.

Extensive microbiological testing was carried out to identify the aetiology of the meningoencephalitis. CSF polymerase chain reaction (PCR) assays were negative for enterovirus, herpes simplex virus, varicella zoster virus, cytomegalovirus, human herpesvirus 6, and *Cryptococcus neoformans*. A nasopharyngeal respiratory viral PCR panel, including influenza A and B and severe acute respiratory syndrome coronavirus 2, also yielded negative results. Blood cultures remained sterile throughout hospitalization.

To further investigate possible arboviral infection, CSF, blood, and urine samples were sent to the Cyprus Institute of Neurology and Genetics. WNV ribonucleic acid (RNA) was detected via reverse transcription PCR (RT-PCR) in both the urine and blood samples, while the CSF sample tested negative for WNV RNA.

Based on these microbiological findings, acyclovir was discontinued, despite initial consideration of continuation of treatment empirically for 10 days. The patient was subsequently enrolled in a rehabilitation program, including physiotherapy, with gradual improvement in speech, swallowing, and motor function.

During hospitalization, the patient developed persistent hypokalaemia, refractory to intravenous potassium replacement, with serum potassium reaching a nadir of 3.0 mmol/l on hospital day 4. Evaluation of electrolyte balance revealed a high fractional excretion of potassium (FEK), consistent with renal potassium wasting. Concurrent

$$\text{FEK} = \frac{\text{Urine K} \times \text{Serum Cr}}{\text{Serum K} \times \text{Urine Cr}} \times 100 \qquad \text{FEUA} = \frac{\text{Urine UA} \times \text{Serum Cr}}{\text{Serum UA} \times \text{Urine Cr}} \times 100$$

$$\text{FEMg} = \frac{\text{Urine Mg} \times \text{Serum Cr}}{0.7 \times \text{Serum Mg} \times \text{Urine Cr}} \times 100$$

Figure 1. Equations used to calculate fractional excretions of electrolytes.

Creatinine (Cr)	
Serum Cr (mg/dl)	0.8
Urine Cr (mg/dl)	50.7
Potassium (K)	
Serum K (mmol/l)	3
Urine K (mmol/l	23.9
FEK (%)	12.6
Uric acid (UA)	
Serum UA (mg/dl)	2.2
Urine UA (mg/dl)	31.9
Fractional excretion of uric acid (FEUA) (%)	22.8
Magnesium (Mg)	
Serum Mg (mg/dl)	1.57
Urine Mg (mg/dl)	3.75
Fractional Excretion of Mg (FEMg) (%)	5.4

Table 2. Fractional excretion of electrolytes on day 4 of hospitalization.

laboratory studies demonstrated metabolic acidosis (venous pH 7.36, HCO_3^- 19.6 mmol/l), hypomagnesemia, and hypouricemia, with corresponding elevated fractional excretion of magnesium and uric acid *(Tables 1 and 2)*. These findings were strongly suggestive of renal tubular acidosis (RTA) and acute Fanconi syndrome, likely related to proximal tubular dysfunction.

By hospital day 9, the patient's serum potassium and uric acid levels had normalized, reaching 3.8 mmol/l and 3.9 mg/dl, respectively. On hospital day 14, the patient was discharged to a rehabilitation facility, where they continued physiotherapy to support recovery of motor and cognitive function.

At 2-month follow-up, the patient was fully ambulatory, independent in activities of daily living, and had resumed his usual agricultural routine. Laboratory evaluation demonstrated normal renal function (serum urea: 26 mg/dl, creatinine: 0.69 mg/dl) and stable serum potassium (3.9 mmol/l). The FEK was 8.2% (urine potassium: 29.8 mmol/l; urine creatinine: 64 mg/dl), indicating resolution of prior renal tubular dysfunction.

DISCUSSION

West Nile virus (WNV) infection is predominantly asymptomatic, with clinical illness developing in approximately 20% of cases, and neuroinvasive disease occurring in less than 1%[1]. Viral RNA is frequently detectable in the urine of acutely infected patients, particularly those with neuroinvasive manifestations, and has been associated in some studies with chronic renal sequelae[2]. However, acute renal failure remains an exceedingly rare complication of WNV infection[3].

Among the Flaviviridae family, renal involvement has been more extensively studied in Dengue virus infections (DVI). In DVI, the reported prevalence of acute kidney injury (AKI) ranges from 0.2–10% in children and 2.2–35.7% in adults, depending on severity and clinical setting. AKI in DVI is attributed to direct viral cytopathic effects, hemodynamic instability, rhabdomyolysis, haemolysis, glomerular injury, and a systemic inflammatory response[4,5]. These pathogenic mechanisms suggest that flaviviruses may have a broader capacity for renal tropism than previously appreciated.

Interestingly, Fanconi syndrome—a form of proximal renal tubular dysfunction characterized by impaired reabsorption of electrolytes and small molecules—has been reported in association with certain viral infections. Notably, a study by Kormann et al.[6] from the University Hospital of Nancy identified incomplete Fanconi syndrome in 75% of hospitalized coronavirus disease 2019 patients with no prior kidney disease. These patients presented with proteinuria, hypophosphatemia, hyperuricosuria, and glycosuria, sometimes preceding AKI. The authors proposed that SARS-CoV-2 may induce transient Fanconi syndrome, either as a prodrome to AKI or as an isolated tubular dysfunction during the acute phase[6].

In the context of WNV infection, this is the first reported case of acquired Fanconi syndrome, manifesting with profound electrolyte disturbances—including hypokalaemia, hypomagnesemia, hypouricemia, and metabolic acidosis—alongside elevated fractional excretion values, strongly suggestive of proximal tubular dysfunction. Although the CSF was negative for WNV RNA, the detection of viral RNA in both urine and blood supports the diagnosis of active systemic infection. The reversibility of renal findings and normalization of serum and urinary parameters at follow-up further reinforce the diagnosis of WNV-associated transient Fanconi syndrome.

To our knowledge, this is the first documented case of WNV-associated Fanconi syndrome. However, this entity may be under-recognized, especially in patients with neuroinvasive disease, where the focus is often placed on neurologic deficits.

Clinicians should be aware that electrolyte abnormalities in WNV-infected patients may not solely reflect systemic illness or dehydration but may indicate subclinical or overt renal tubular dysfunction. Recognition of this pattern is critical, as untreated tubular electrolyte losses may lead to significant morbidity, particularly in elderly or comorbid patients.

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