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Case Report

Bilateral facial nerve palsy in a patient with West Nile neuroinvasive disease

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Abstract

Introduction: Bilateral facial nerve palsy (FNP) is a rare condition that is idiopathic in only 20%. FNP is the most common cranial neuropathy in West Nile neuroinvasive disease (WNND) but is usually unilateral and only a few cases of bilateral FNP have been reported. Case: We present a case of a 65-year-old woman with confirmed WNND and simultaneous bilateral FNP. Results: In August 2022, the patient presented with ataxia, gait instability, tremor, fever, and vomiting. Following admission, due to her cerebrospinal fluid analyses she was diagnosed with WNV encephalitis. Her initial symptoms subsided, but on the 17th day of the disease, right FNP was observed. Three days later bilateral FNP developed, predominantly on the right side, with bilateral otalgia. Further diagnostic was performed but no other aetiology that could contribute to FNP was found. The patient was treated with a 3-day metilprednisolone course, followed by 60 mg of prednisone with dose tapering for 12 days. One month later she was discharged with significant regression of the left and slight regression of the right FNP. Subsequent physical therapy was conducted. The patient's neurological status gradually improved and 4 months after the first symptoms onset, her neurological examination was normal.

Conclusions: WNND should be included in the differential diagnosis of acquired bilateral FNP. It can result in full recovery, but unfavorable course is also possible.

Key words: West Nile virus; facial nerve palsy; bilateral; neuroinvasive disease.

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Introduction

Less than 1% of people infected with West Nile virus (WNV) develop neuroinvasive disease (WNND) [1]. Bilateral facial nerve palsy (FNP) is a very uncommon illness that affects 1 in 5 million people [2]. It is idiopathic in about 20% of cases and accounts for less than 2% of all FNP [3]. We present a case of WNND and simultaneous bilateral FNP.

Case report

On 26th August 2022, a 65-year-old woman presented with ataxia, gait instability, and tremor, along with fever and vomiting that started three days earlier. Her endocranial CT scan was unremarkable and SARS CoV-2 antigen and DNA were not detected in the nasopharyngeal swab. Blood analysis revealed thrombocytopenia 94 × 10^3/mL, and biochemical and coagulation analysis were under normal limits. Cerebrospinal fluid (CSF) analysis revealed moderate pleocytosis of 145 cells/μL with lymphocytic predominance, mild hyperproteinorachia 0.62 g/L, and normal CSF glucose and CRP level, suggesting viral encephalitis. The results of the patient's blood and CSF analysis on admission are shown in Table 1 and Table 2.

Her past medical history included hypertension and hypothyreosis. The patient reported spending a long time outside, swimming in the pool, and suffering numerous insect bites before the illness.

There was no evidence of a cognitive disability or consciousness impairment on admission. Neurological examination revealed wide-based gait, instability, dysmetria, and action tremor of the upper limbs. The rest of the neurological and somatic evaluations were unremarkable.

Anti-WNV IgM and IgG antibodies were detected in serum, and specific anti-WNV IgM antibodies were detected in CSF. Furthermore, WNV RNK was detected in CSF using RT-PCR. The patient had no history of flavivirus immunization, had sterile CSF culture and negative CSF PCR analysis for other common causes of viral encephalitis (herpes simplex

Table 1. Patient's blood biochemical analyses on admission.

Biochemical blood analyses	On admission	Normal range	Units
Leucocytes	4.5	3.4-9.7	$\times 10^9$/L
Lymphocytes	1.14	1.2-3.4	$\times 10^9$/L
Neutrofils	2.95	2.1-6.5	$\times 10^9$/L
Erythrocytes	4.14	3.86-5.08	$\times 10^{12}$/L
Hgb	119	119-157	g/L
Platelets	94	158-424	$\times 10^9$/L
C reactive protein	1.9	0-3.0	mg/L
Fibrinogen	3.3	1.8-3.5	g/L
INR	1.04		
D-dimer	0.6	< 0.5	mg/L
urea	3.8	2.5-7.5	mmol/L
creatinine	63	45-84	µmol/L
Na	137	135-148	mmol/L
K	4.4	3.5-5.1	mmol/L
Aspartat aminotransferase	19	0-37	U/L
Alanin aminotransferase	36	14-63	U/L
Lactat dehydrogenase	158	85-227	U/L
Creatin kinase	38	0-150	U/L
fT3	3.06	2.63-5.2	pmol/L
fT4	18.5	9.0-19.1	pmol/L
TSH	2.1	0.35-4.94	mlU/L
Angiotensing converting enzyme (ACE)	14	12-68	U/L
Hytotryosidase	70	1.8-146.6	nmol/ml/h
Tumor markers			
Carcinoembrionic antigen (CEA)	4.2	0.0-5.0	µg/L
Alpha-fetoprotein (AFP)	3.6	1.1-8.0	µg/L
CA 125	26	0-35	kU/L
CA 15-3	25.0	0.0-31.0	kU/L
CA 19-9	30	0-37	kU/L
CA 72-4	0.7	0.0-6.9	kU/L
CYFRA 21-1	1.5	0.0-2.1	µg/l

viruses, varicella zoster virus, human immunodeficiency virus (HIV), cytomegalovirus, Epstein Barr virus (EBV), enteroviruses), as well as negative tick-borne encephalitis and Lyme disease serology tests in serum and CSF (Table 2).

Before WNND was confirmed, the patient was treated with intravenous acyclovir. After admission ataxia and tremor gradually subsided, but on the 8th of September a right peripheral FNP was observed. The patient's neurological impairment worsened during the next three days, resulting in bilateral peripheral FNP, predominantly on the right side, and bilateral otalgia (Figure 1 A, B).

Otorhinolaryngeal examination revealed no other pathology. The patient's thyroid hormones status was normal, and serum workup results were negative for syphilis, hepatitis B, and C. Tumor marker analyses and serum angiotensin-converting enzyme were within normal limits. Chest X-ray showed no evidence of sarcoidosis. Brain magnetic resonance imaging (MRI) with intravenous contrast application was performed and findings are shown in Figure 2. The MRI revealed the presence of multiple punctuate T2W and FLAIR hyperintense changes in the left insular region, left putamen, as well as in pons and bilaterally in frontal and parietal regions of the brain, without restricted diffusion and contrast enhancement. Furthermore, it showed periventricular leucoencephalopathy and cortical reductive alterations. In addition, discrete bilateral contrast enhancement of the distal intrameatal part of the facial nerve (T1w-contrast enhanced) was also

Table 2. CSF cytobiochemical, serological and molecular analyses.

Cerebrospinal fluid analyses	On admission	Normal range (units)
Cytobiochemical analyses		
Leucocytes	145	0-5 × 10^6/L Ly
Lymphocytes	83%	
Polimorphonuclear cells	17%	
C reactive protein	0.1	< 0.5 mg/dl
Glucose	3.3	2.7-4.1 mmoL/L
Protein	0.62	0.15-0.45 g/L
PCR analyses		
Streptococcus pneumoniae	DNA not detected	not detected
Neisseria meningitides	DNA not detected	not detected
Haemophilus influenza	DNA not detected	not detected
Listeria monocytogenes	DNA not detected	not detected
Escherichia coli K1	DNA not detected	not detected
Streptococcus agalactiae	DNA not detected	not detected
Cytomegalovirus	DNA not detected	not detected
Enterovirus	RNA not detected	not detected
Herpes simplex virus 1	DNA not detected	not detected
Herpes simplex virus 2	DNA not detected	not detected
Herpes simplex virus 6	DNA not detected	not detected
Human parechovirus	RNA not detected	not detected
Ebstein-Barr virus	DNA not detected	not detected
Variccela zoster virus	DNA not detected	not detected
West Nile virus	*RNA detected*	not detected
Serological analyses		
Borelia burgdorferi IgM (CSF) ELISA	negative	negative
Borelia burgdorferi IgG (CSF) ELISA	negative	negative
Borelia burgdorferi IgM (serum) ELISA	negative	negative
Borelia burgdorferi IgG (serum) ELISA	negative	negative
Borelia burgdorferi IgM (serum) Western blot	negative	negative
Borelia burgdorferi IgG (serum) Western blot	negative	negative
West Nile virus IgM (CSF) ELISA	*positive*	negative
West Nile virus IgM (serum) ELISA	*positive*	negative
West Nile virus IgG (serum) ELISA	*positive*	negative
Tick-borne encephalitis (TBE) IgM (CSF) ELISA	negative	negative
Tick-borne encephalitis (TBE) IgM (serum) ELISA	negative	negative
Tick-borne encephalitis (TBE) IgG (serum) ELISA	negative	negative

Figure 1. Image presenting the patient with WNND and bilateral peripheral FNP. **A, B.** At bilateral FNP onset; **C, D.** One month after onset; **E, F.** Complete recovery four months later.

detected (Figure 2). On the 13th of September corticosteroid therapy (metilprednisolone 3 days, followed by 60mg of prednisone with dose tapering during 12 days) was initiated, with pregabalin for pain relief. The patient was discharged one month later with significant regression of the left and slight regression of the right peripheral FNP (Figure 1 C, D). Electrostimulation and laser therapy were used in the subsequent physical therapy. The patient was followed for 4 months during which her neurological status gradually improved. On the last visit in January 2023, her examination was completely nonfocal (Figure 1 D, E).

Discussion

Cranial nerve palsies can occur during WNV infection due to inflammation in the region of cranial nerves motor nuclei [4]. According to the literature, FNP is the most common cranial neuropathy in WNND affecting 11–17% of patients, but it typically develops unilaterally [5,6]. There are only a few reported cases of bilateral FNP in WNND. Among 19 patients with acute flaccid paralysis (AFP) and cranial neuropathies reported by Sejvar *et al*, two patients had unilateral and 8 bilateral FNP, while one patient had bilateral FNP during WNV-associated *Guillain- Barre* syndrome (GBS) [7]. Chan *et al.* reported a case of a woman with WNND who developed facial diplegia two weeks after flu-like symptoms and who had an unfavorable clinical course [8]. In our patient, FNP developed on the 17th day of illness. Wahba also suggested that bilateral FNP may occur during the second or third week of WNND [9].

Pathological process in WNND results from direct infection of neurons and immune-mediated tissue damage [10]. It is expected that in patients who develop paresis/paralysis later in the course of illness, viremia has subsided and that immune-mediated inflammation is responsible for the neurological deficit. Thus, corticosteroid therapy may be beneficial in that phase, without risk of exacerbating viral infection.

As opposed to unilateral FNP, bilateral FNP is often a presentation of serious underlying conditions like GBS, myasthenia gravis, brain and meningeal tumors, syphilis, HIV, Lyme disease, sarcoidosis, vasculitis, systemic lupus erythematosus, trauma, etc. [2,11]. Cases of EBV-induced bilateral FNP were reported, predominantly in children [12,13]. Differential diagnosis of bilateral FNP is shown in Table 3.

Due to the patient's past medical history, hypothyreosis was also considered a potential cause of FNP. In hypothyreosis, autoimmune-mediated response

Figure 2. MRI findings in patient with WNND and bilateral peripheral FNP. Subtle punctuate signal abnormality in: **A.** the left frontal region (FLAIR); **B.** the left insular region (FLAIR); **C.** pons (hyperintensity on T2W without restricted diffusion and contrast enhancement); **D.** Discrete bilateral contrast enhancement of the distal intrameatal part of the facial nerve (T1w-contrast enhanced).

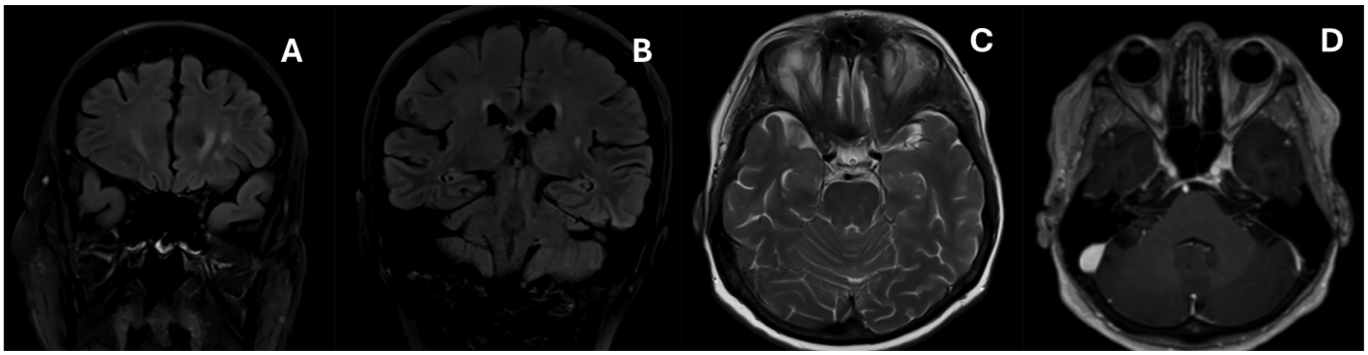

Table 3. Differential diagnosis of the possible causes of bilateral FNP.

Infectious causes of bilateral facial nerve palsy
Viruses
Ebstein-Barr virus
Herpes simplex virus
Varicella zoster virus
Poliomyelitis
Human immunodeficiency virus
Spirochaetae
Borrelia burgdorferi
Treponema pallidum
Bacteria
Mycobacterium tuberculosis
Fungi
Cryptococcus neoformans
Non-infectious causes of bilateral facial nerve palsy
Inflamatory diseases
Sarcoidosis
Polyarteritis nodosa
Wegener's granulomatosis
Systemic lupus erythematosus (SLE)
Guillain-Barre syndrome
Neuromuscular disorders
Myastenia gravis
Bulbospinal neuronopathy
Malignancies
CNS leucaemia/lymphoma
Brain tumors
Other causes
Amyloidosis
Idiopathic/ Bell's palsy
Benign intracranial hypertension
Head trauma

triggers fluid accumulation in tissues, and therefore, can cause entrapment of the facial nerve. However, our patient's thyroid hormone status was normal.

Our patient fully recovered during 4 months. Sejvar *et al.* also reported that all patients with FNP had complete or almost complete recovery during short-term follow-ups [7]. On the contrary, in the study by Hart *et al*, 4 patients with FNP in WNND still had some degree of palsy at 90 days of visit [14].

Conclusions

In conclusion, WNV infection should be included in the differential diagnosis of bilateral FNP, even in patients without symptoms of meningitis/encephalitis. Since it usually occurs later during the course of illness, corticosteroid therapy might be beneficial. This condition can result in full recovery, but unfavorable course is also possible.

Ethical Approval

The work was approved by the Ethical committee of Clinic for Infectious and Tropical Diseases and was performed according to the Declaration of Helsinki and subsequent revisions.

Informed Consent

The patient described in the report provided a written informed consent for case presentation and publication, as well as for picture publication in the format submitted.

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