Clinical Characteristics and Outcomes of Neuroinvasive West Nile Virus Infection in Immunosuppressed and Immunocompetent Individuals Treated at the Mayo Clinic Hospitals

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BACKGROUND

- Despite the increasing incidence of neuroinvasive West Nile virus (NiWNV) infection in the United States, the spectrum of disease characteristics and neuroimaging findings in immunosuppressed individuals are not adequately described.

OBJECTIVES

- We aimed to compare the clinical characteristics and outcomes of NiWNV infection in immunosuppressed (IS) and immunocompetent (IC) patients.

METHODS

- We extracted relevant data from all NiWNV patients treated between July 2003 and October 2021 at the Mayo Clinic hospitals.
- Cohort was inclusive of patients from the recent historic WNV outbreak in Arizona in 2021.
- Individuals were classified as IS or IC depending on presence of transplant history, active cancer, type 2 diabetes, end stage renal disease or treatment with any immunosuppressive agent.
- Chi-Square or Kruskal-Wallis and logistic regression were used to compare relevant variables and determine predictors of mortality respectively.

RESULTS 1

- We included 115 patients (72 IC and 43 IS), mean age was 63.5 years
- Neurologic syndromes included meningoencephalitis (85.2%), encephalomyelitis (8.7%) and myeloradiculitis (6.1%).
- The most common presenting symptoms were malaise (72%), fever (66%), altered mentation (64%), gastrointestinal symptoms (47%) and myalgia (35.7%).

RESULTS 2

- Magnetic Resonance Imaging (MRI) was abnormal in 62.8% (49/78), demonstrating T2 Fluid Attenuated Inversion Recovery (FLAIR) hyperintensities in 47.4% (brainstem, thalamus, temporal lobes), leptomeningeal enhancement (16.7%) and diffusion restriction (20.5%).
- Altered mental status (76.7% vs 56.9%), myalgia (44.4% vs. 20.9%), myoclonus (18.6% vs. 4.2%) and thalamic MRI T2 FLAIR abnormalities (11.4% vs 0%) were more common in IS patients.
- Higher CSF WBC counts were observed in IC vs IS patients (P<0.05).
- Immunosuppressed patients were more likely to be treated with intravenous immunoglobulin (44.2% vs 8.3% p=<0.001) and/or interferon therapy (32.6% vs 6.9%, p=0.0003) and had increased odds of 90-day mortality on multivariable analysis (Adjusted Odds Ratio, AOR 2.22; 95% CI 1.065-4.627, p=0.0334).
- In the IS subgroup, ICU admission, mechanical ventilation, and Glasgow coma scale of <8 were associated with reduced overall survival/increased 90-day mortality (p<0.005)

TABLE 1: Socio-demographics and Clinical Characteristics

	Immuno-competent N=72	Immuno-suppressed N=43	Total N=115	P-value
Socio-demographic characteristics				
Age, Mean (SD)	63(17)	65(14)	64(16)	0.652[1]
Male gender, n (%)	49(68)	26(61)	75(66)	0.408[2]
Season of Presentation, n (%)				0.293[2]
- Summer	36(50)	20(47)	56(49)	0.388[2]
- Fall	34(47)	22(51)	56(49)	
Duration of symptoms (days), Median (IQR)	5(3,7)	7(4,14)	6(3,9)	0.042[1]
Symptoms and signs, n (%)				
Malaise	55(76)	28(65)	83(72)	0.198[2]
Fever	50(70)	26(61)	76(66)	0.325[2]
Headache	45(63)	18(42)	63(55)	0.031[2]
Altered mental status	41(57)	33(77)	74(64)	0.032[2]
Diarrhea/vomiting	33(47)	21(49)	54(48)	0.807[2]
Myalgias	32(44)	9(21)	41(36)	0.011[2]
Hand tremors	24(33)	13(30)	37(32)	0.731[2]
Skin rash	17(24)	10(23)	27(24)	0.965[2]
Focal motor signs (hemi, mono or quadriparesis)	12(17)	13(30)	25(22)	0.096[2]
Cranial nerve signs	5(7)	6(14)	11(10)	0.216[2]
Myoclonus	3(4)	8(19)	11(10)	0.011[2]
Clinical seizure	4 (8)	6 (19)	10 (12)	0.137[2]
Coma (GCS< 8)	14 (19)	15 (35)	29 (25)	0.065[2]
WNV Specific Laboratory Studies				
Serum WNV IgM, Positive, n (%)	61(78)	33(81)	94(87)	0.113[2]
CSF WNV IgM, Positive n (%)	47(78)	24(62)	71(72)	0.070[2]
CSF WNV PCR, Positive n (%)	5(15)	17(63)	22(37)	<.0012
CSF white blood cell count, cells/mm3, median (IQR)	113 (62, 355)	79 (20, 144)	90 (41, 229)	0.007[1]
CSF protein count, mg/dl, median (IQR)	86 (65, 104)	75 (52, 99)	82 (61, 101)	0.167[1]
CSF glucose, mg/dl, median (IQR)	59 (53, 72)	64 (57, 72)	61 (54, 72)	0.186[1]
Final Diagnoses, n (%)				0.0742
WNV meningoencephalitis	65 (90)	33 (77)	98 (85)	
WNV encephalomyelitis	3 (4)	7 (16)	10 (9)	
WNV Myeloradiculitis	4 (6)	3 (7)	7 (6)	

Abbreviations: GCS: Glascow Coma Scale, WNV: West Nile Virus; CSF: Cerebrospinal Fluid; IVIG: Intravenous Immunoglobulin; IgM: Immunoglobulin M; IgG: Immunoglobulin G; PCR: Polymerase chain reaction

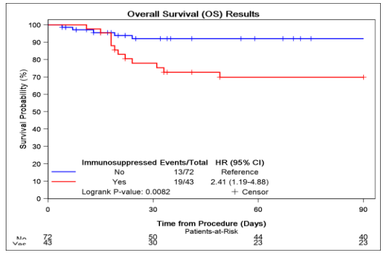
RESULTS 3

TABLE 2: Treatment and Outcomes of Immunosuppressed and Immunocompetent individuals with NIWNV

WNV Specific Treatments, n (%)	Immuno-competent N=72	Immuno-suppressed N=43	Total N=115	P value
None	52(72)	15(35)	67(58)	<.001[2]
Any single agent	16(22)	13(30)	29(25)	
Any combination of agents	4(6)	15(35)	19(16)	
Interferon Treatment Given, n (%)	5(7)	16(37)	21(18)	<.001[2]
IVIG Treatment Given, n (%)	12(17)	24(56)	36(31)	<.001[2]
Other managements				
ICU admission	24(33)	26(61)	50(44)	0.004[2]
Mechanical Ventilation	22(31)	24(56)	46(41)	0.008[2]
Outcomes				
Hospital Length of Stay, Median (IQR)	8(5,20)	16(11,26)	12(6,23)	<.001[2]
90-Day Mortality, Died, n (%)	5 (7)	12 (28)	17(15)	0.002[2]

[1]Kruskal-Wallis p-value; [2]Chi-Square p-value;

FIGURE 1- Overall Survival Among Immunosuppressed and Immunocompetent individuals with NIWNV



Kaplan Meier curves showing the overall survival status of immunocompromised individuals (red line) versus those who are immunocompetent (blue line) over time.

CONCLUSIONS

- Individuals presenting in summer or fall months with the aforementioned symptoms and/or MRI abnormalities should be evaluated for NiWNV infection.
- Compared to the immunocompetent, immunosuppressed patients with NiWNV are at a significantly greater mortality risk.
- Novel and effective antiviral therapies aimed at improving outcomes are warranted.