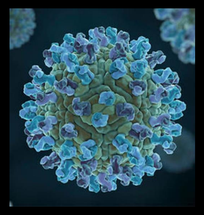
Monday-21

PERSISTENT WEST NILE VIRUS VIREMIA IN A KIDNEY TRANSPLANT RECIPIENT



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Background

- West Nile Virus (WNV) is commonly transmitted by mosquito bite
- ~80% of infections are asymptomatic and <1% develop neuroinvasive disease
- WNV infections have occurred in all 48 contiguous US states (Figure 1)
- WNV occasionally causes donor-derived infection in solid organ transplant recipients, with a high incidence of neuroinvasive disease[1]

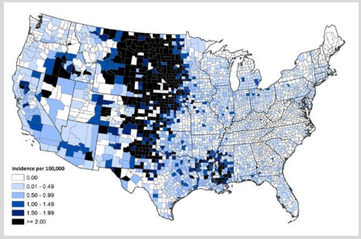

FIGURE 1: Average annual incidence of West Nile virus neuroinvasive disease reported to CDC by county, 1999-2017. Source ArboNET, Arboviral Diseases Branch, Centers for Disease Control and Prevention.

- The possibility of WNV infection should be considered when investigating post-transplant infections during times of high WNV prevalence.
- We describe a kidney transplant case, where the recipient developed fever, lethargy, hiccups, slight speech and vision impairment, and generalized weakness, 10 days after transplant. WNV testing was requested because of the neurological symptoms.
- Experience with Zika virus and published information on WNV, prompted a request for urine and whole blood specimens in addition to serum, for WNV real-time RT-PCR.

Methods

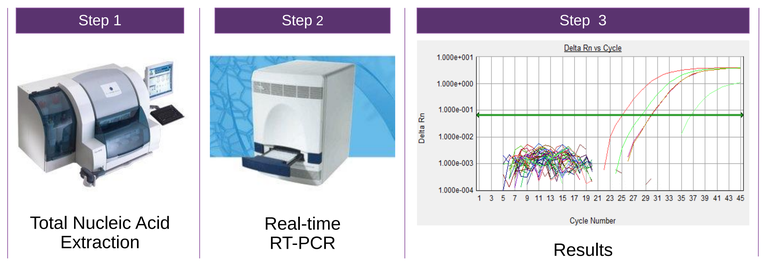

Table 1: easyMAG Extraction Information

Specimen Type	Extraction Volume	Elution Volume
serum	1 mL	60 uL
urine	1 mL	60 uL
whole blood	200 uL	60 uL

- Total nucleic acid extraction was performed using a bioMérieux easyMAG
- Amplification and detection was done on an ABI 7500FAST
- A WNV-specific real-time RT-PCR targeting the envelope gene[2] (Figure 2) was performed with AgPath-ID One-Step RT-PCR reagents on serum, urine and whole blood.
- Green Fluorescent Protein RNA transcript, spiked and detected by real-time RT-PCR, was used as an extraction and PCR inhibition control[3].
- Qualitative results were used for monitoring and patient care.

Methods (con't)

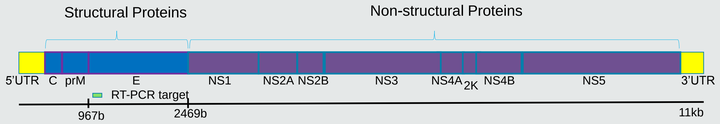

Figure 2: West Nile virus gene map and location of the real-time RT-PCR assay target (▭).

- Nucleic acid from WNV-positive specimens was quantitated against a standard curve, generated from 10-fold dilutions from 1,000,000 to 10 GC/uL of whole virus control.
- Viral loads in original specimens were calculated based on extraction, elution and template addition volumes.

Results

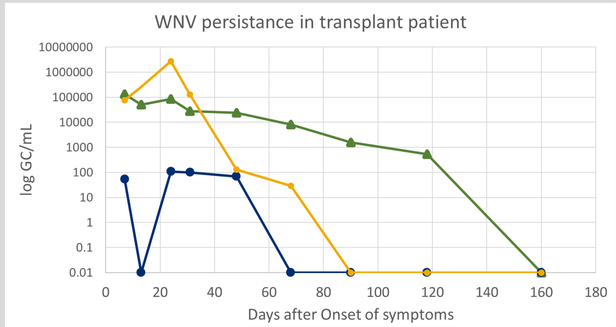

FIGURE 3: Quantitation of West Nile virus Viral Load in patient's specimens. Transplant was on Day -10 and Day 0 is onset of symptoms. serum, urine, whole blood. Negative results are included in the graph as 0.01 Log GC/mL.

- WNV was detected in serum, urine and whole blood 7 days after onset of symptoms
- Urine and whole blood contained higher titer WNV RNA than serum
- Serum, urine and whole blood remained positive post-onset of symptoms for 48, 68 and 118 days, respectively
- WNV RNA titer in serum remained low throughout
- WNV RNA titer in urine was initially approximately 3 log higher than in serum, increased by more than a log over the next few weeks, before decreasing and becoming negative
- Viral titer in whole blood was initially as high as that in urine and remained relatively high with a very slow decline

Case Resolution

- All immunosuppression treatment was stopped for two weeks after the initial WNV diagnosis. The patient ultimately made an almost complete recovery with the only residual symptoms being slight issues with speech.
- Another transplant center, where organs were received from the same donor, was alerted to the possibility of WNV transmission. The recipient of the donor liver developed significant weakness, was moved to the Intensive Care Unit for breathing and neurological issues, and subsequently tested positive for WNV by RT-PCR.
- WNV was confirmed in the donor sera retrospectively by molecular testing.

Discussion

Table 2: Solid Organ Transplant-transmitted West Nile virus Infections in United States from 8 Donors, 2002-2018[1,4-5]

Organs	Recipients	WNV Infection	Neuroinvasive WNV infection	Death
Kidney	11	2	7	3
Liver	7	1	4	1
Heart	2	-	2	-
Lung	2	-	2	2

- West Nile Virus infections in solid organ transplant recipients remain rare events (Table 2) but have a high rate of severe consequences.
- The persistence of WNV in the red cell compartment of the blood of infected individuals is believed to increase the risk of transmission to transfusion and transplant recipients[6-9].
- CDC guidelines indicate that laboratory diagnosis of WNV infection is generally by testing for WNV-specific IgM in serum or cerebrospinal fluid (CSF). Testing for viral RNA in serum by RT-PCR early in the course of illness (≤ 7 days) is also confirmatory.
- Early diagnosis by molecular testing may be facilitated by the higher viral loads in specimen types such as whole blood and urine.
- This study and published data from others, indicates that confirmation with molecular testing can also be made for a much longer period of time when other sample types such as urine and whole blood are tested.

Conclusions

- WNV viremia commonly ranges from 3-8 days post-onset of symptoms. The unusually long duration of WNV RNA positivity in serum in this patient was likely due to the post-transplant immunosuppressive therapy.
- Molecular testing of multiple specimen types is important for WNV diagnosis because viral loads may be much higher in urine and whole blood than in serum and positivity may be for longer duration.
- Similar dynamics have been seen with viral loads in Zika virus infections and we believe should be considered in testing algorithms for all Flaviviruses.

References

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