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Community of Practice: COVID Updates

Here's how Natera is helping you in the world of COVID-19

2nd Edition; March 2021

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As the second installment of our bimonthly newsletter, Natera has compiled our perspective on new research and case studies to share with the community.

The complexities of patient care in the transplant and nephrology clinical communities are vast from the effects of the Severe Acute Respiratory Syndrome 2 virus (SARS-CoV-2).

We hope this series provides the latest information on novel patient management strategies and commentary from your peers to optimize patient care together.

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Views from our Medical Director

Collapsing glomerulopathy (CG) was first described in the 1980's and is associated with a marked dysregulation of podocytes that has been described as a "transdifferentiation" towards a macrophage-like cell. This lesion usually leads to a rapid loss of kidney function and is often resistant to therapy. First described in association with HIV infection (HIV-associated nephropathy, or HIVAN), it has subsequently been seen with other types of viral and mycobacterial infection, malignancy, autoimmune diseases, and drug exposure.

Heterozygous polymorphisms in the APOL1 allele may be seen in up to 13% of Americans with African ancestry. Two gain-of-function mutations, G1 and G2, have been identified and individuals who are homozygous for a gain-of-function polymorphism are at markedly increased risk for chronic kidney disease (CKD.) In particular, the variants seem to be highly associated with focal-segmental glomerulosclerosis (FSGS,) HIVAN, and lupus glomerulonephritis with collapsing features. The mechanism by which these polymorphisms cause kidney disease is unclear but there are two leading hypotheses. First, the risk variants may create pores in kidney cell membranes in a manner similar to what is seen with tryposomal organelles; in fact, the APOL1 polymorphisms seem to be protective against tryposomal disease, which explains their prevalence in endemic areas such as West Africa. Second, it has been postulated that the variants lead to mitochondrial dysfunction and injury. APOL1 variants seem to largely explain the higher rate of CKD seen in the African-American population, although they also contribute to the incidence of CKD around the world including in countries in which many people are of mixed ancestry such as Brazil. The observation that many if not most patients with homozygous variants do not experience CKD suggests that other environmental or infectious factors remain important.

CASE STUDY

This case report presents a patient with mild kidney disease not associated with albuminuria. After a SARS-CoV-2 infection she experienced acute kidney injury with heavy proteinuria and CG on what was described as a "high-risk" biopsy. Subsequent genetic testing showed that she had both the G1 and G2 APOL1 variants. AKI in association with COVID-related systemic inflammatory response syndrome (SIRS) as well as direct viral infection of renal tubules has been described. In fact, AKI may be seen in almost half of patients admitted to the hospital for COVID-19. **This case is one of several demonstrating a correlation with SARS-CoV-2 infection and CG and advances our understanding of the pattern of renal injury seen due to the pandemic.**

This case illustrates the clinical utility of genetic testing for APOL1 variants. Had this information been available earlier in her course she may have been able to avoid a high-risk biopsy. Further, the identification of these variants may inform their prognosis and treatment option. For example, people with hypertension and homozygous APOL1 variants may respond better to angiotensin-converting enzyme inhibitors (ACE-I.)

Thus, it seems that during the pandemic and going forward, more wide-spread genetics testing to identify those with APOL1 risk variants is imperative.

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FEATURED CASE STUDY:

Real-world cfDNA in the Era of COVID-19

Monitoring transplant patients during the COVID-19 resurgence has become more difficult and risky.

This case study[1] highlights a transplant center's evaluation of kidney recipients diagnosed with COVID-19 aimed to:

- Determine if background cfDNA levels were elevated in severe COVID-19 cases
- Assess if background cfDNA levels correlated with COVID-19 severity and outcome
- Map kinetics of background cfDNA in patients as they recover

Case Study[1]

PATIENTS HISTORY

9 patients with the average age of 61 years
Sex: 5 males and 4 females
Race: 2 Blacks and 7 Hispanics
Median Body Mass Index (BMI): 24.9
Median time from transplant: 0.72 years

The Journey

- **Median time from transplant to COVID-19 symptoms:** 8.6 months
- **Median Serum Creatinine after COVID-19 Diagnosis:** 1.35
- **Acute Kidney Injury:** 6 patients
- **2 patients required ventilation:** 2 patients expired

Clinical Assessment with Prospera

- **Time from onset of COVID-19 symptoms to Prospera draw:** 2.4 weeks
- **Median Prospera result:** 0.54%
- **Elevated cfDNA levels (>8x median):** 4 patients

Key Takeaway: Four of the nine patients with COVID-19 exhibited very elevated levels of background cfDNA. In both cases of severe COVID infection that led to death, background cfDNA levels were markedly elevated compared to those who recovered. In both surviving patients with elevated background cfDNA, background levels returned to baseline by 75 days post-infection.

Exploratory Questions:

1. Do you have transplant patients with COVID-19 who might benefit from Prospera?
2. How have you managed immunosuppressive therapies in your kidney transplant patients who have COVID-19?
3. What might you do differently after reading this case study?

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A Call for Stories:

Share your learnings with our community

Natera wants to thank all the healthcare professionals who have been on the frontlines of this crisis. Your dedication, determination, grit, resilience, and sacrifice over the last few months have been inspiring and invaluable to our community.

We extend our call for stories, research, and experiences to our transplant and nephrology partners so we can continue to learn together and improve patients' lives during these uncertain times.

Please contact **prospera@natera.com** to discuss with the Natera Clinical Team.

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