2017 CST-Astellas Canadian Transplant Fellows Symposium

Case Study: Pediatric Kidney Transplantation

Tom Blydt-Hansen, MD

Dr. Tom Blydt-Hansen received his Medicinæ Doctorem et Chirurgiæ Magistrum from McGill University in 1992. He trained in pediatrics and nephrology at the Montreal Children's Hospital, and went on to receive further training in transplantation and research at the University of California, Los Angeles. He started his nephrology career at the University of Manitoba in 2001 and went on to become Division Head of Nephrology from 2005-2014. Since 2014, he has been the Director of the Multi-Organ Transplant Program at BC Children's Hospital and a Senior Scientist at the BC Children's Hospital Research Institute. His clinical and translational research program is focused on characterizing kidney allograft injury using urine metabolite profiling and other biomarkers. He is Lead Investigator in the PROBE study, a Canadian Institutes of Health Research (CIHR)funded multi-center cohort study to identify non-invasive urine biomarkers of allograft rejection in pediatric kidney transplant recipients. He is also engaged in collaborations to identify urinary biomarkers (metabolomics) associated with chronic kidney disease, acute kidney injury, type 2 diabetes and cisplatin nephrotoxicity. He is Co-investigator on several nationally funded transplant research studies including CKiD, iCARE, CAN-RESTORE and, the Canadian National Transplant Research Program (CNTRP).

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Case Study:
Pediatric Kidney Transplantation

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Tom Blydt-Hansen, MDCM, FRCPC
Associate Professor of Pediatrics, UBC
Director, Multi Organ Transplant, BCCH

Disclosure

- Grant/Research Support:

- Consultant/Speaker Fees: Astellas Canada

Objectives

- To appreciate the long-term complications
- To identify management issues that are particular to pediatric kidney recipients
- To discuss a framework for adherence and transition to adult care

Long-term outcomes

Case #1 – Long-term outcomes

- 11.5 years old, now 6 years post-transplant for FSGS
- Family/social history
  - Only child, both parents have type 2 diabetes, live on farm
- Pre-transplant history
  - Well until 3 years old – onset of steroid-dependent nephrotic syndrome, MCNS on biopsy
  - Treated with TAC, cyclophosphamide and eventually rituximab as became steroid-resistant
  - Eventually underwent unilateral NX, and progressed to PD at age 4 years.
  - Pathology now showed FSGS.
  - Underwent contralateral NX in preparation for kidney tx

Peri-Transplant History

- Age: 3 years and 2 months
- cPRA = 0
- Deceased Donor, MM 1A, 1B, 1DR, 2DQA, 2DQB, negative crossmatch
- Immunosuppression: Daclizumab, MP, MMF, Tac
- Antiviral: Valganciclovir prophylaxis for CMV: D+ R+
- EBV: D+ R-
- Good early function, no recurrence of disease

First few years post Transplant history

- TCMR (subclinical) on 3 month surveillance biopsy – responded to IV MP, increased TAC. Repeat 6 weeks later showed no TCMR
- EBV viremia (max 8000 VL) at 8 months, with lymphadenopathy; resolved with IS reduction.
- Two-year surveillance: No TCMR, IFTA 1, 20% GGS
- Late TCMR at 4 years (Banff 1B), steroid-resistant (x2) but ultimately responded to thymoglobulin. No AMR, no DSA.
- Subsequently had persistent, but intermittent low-titre EBV viremia

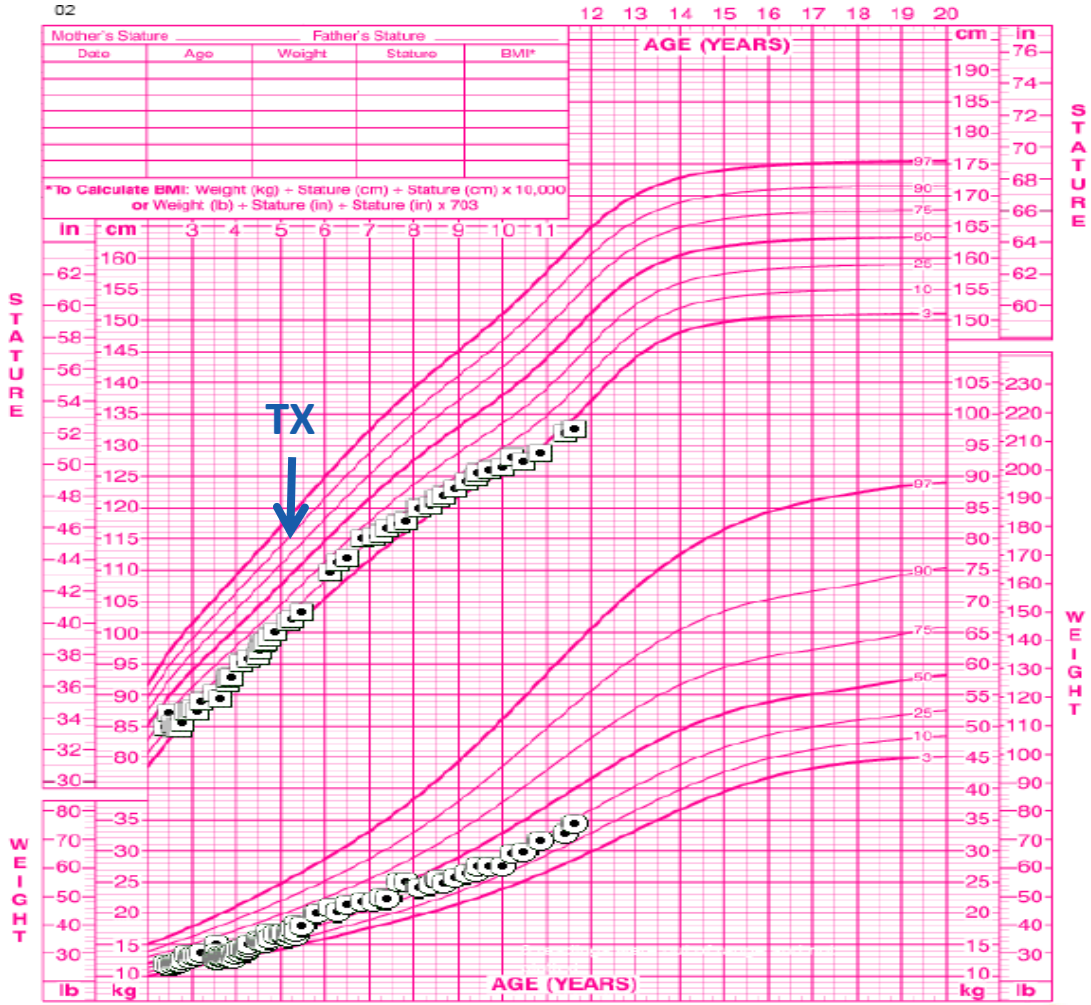
Now 6 years post transplant

- Creatinine is 130 umol/l (nGFR 45 ml/min/1.73m2)
- Minimal proteinuria: PCR = 29 and ACR = 8.2
- Persistent low EBV loads (<1000)
- 1-2 episodes each year of AKI, needing saline
- Hypertensive, on amlodipine
- Hg = 111, not on ESA

What are we worried about in terms of comorbidity?

What about her growth?

- Both parents ~10th %ile height
- Tanner Stage 1
- Mild hyperPTH, on alphacalcidol
- Acidosis, on NaHCO3
- Nutrition appears good
- Asking about rGH…



What about her metabolic risk?

- Transient **am hyperglycemia** peri-transplant; also when treated for late TCMR
- Still on low-dose daily pred
- TAC levels >5 since late TCMR
- High BMI
- Vitamin D normal
- Mg = 0.59
- What about statins, insulin, other treatment??

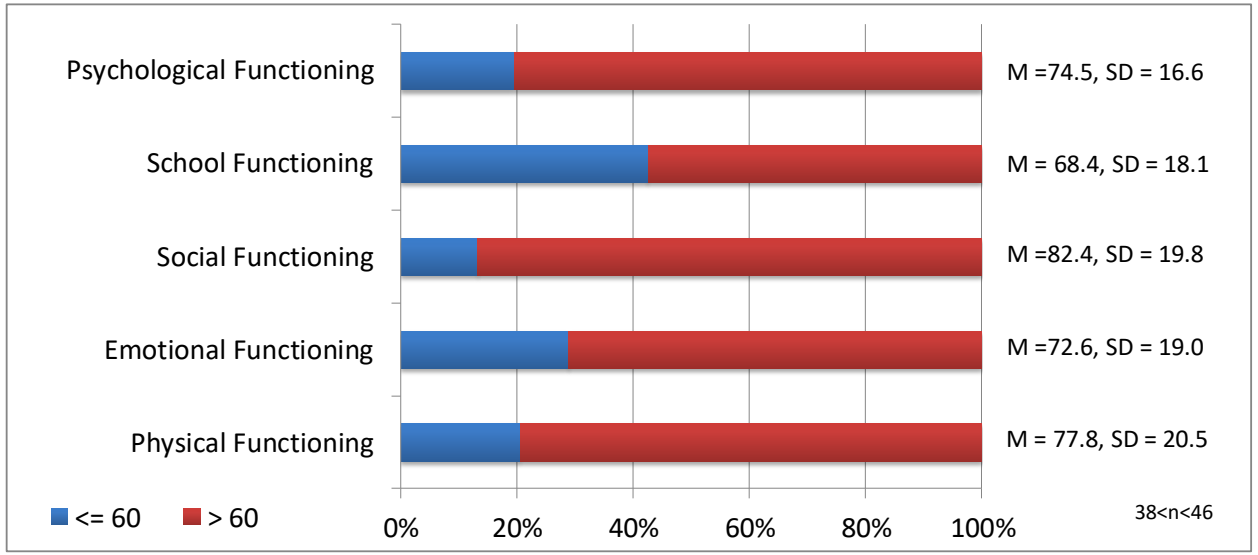
Testing results

- OGTT result
  - Fasting glu 6.6
  - 2hr PC glu 11.9
- Fasting insulin = elevated
- Fasting c-peptide = elevated
- HgA1C = 6.7
- LDL 3.6, HDL 1.5
- ALT = 70

What about her quality of life?

- Not functioning at grade level
- Trauma symptoms
- Needle fear
- Mood dysthymia
- Anxiety, but has many vague somatic complaints
- Impact on home life, parents, siblings

Peds QL (child report)
N=56, not previously seen by psychology



BCCH data, 2017

What long-term complications post-kidney transplantation impact survival?

- Infection
- Cardiovascular disease
- Cancer

What are her infection risks?

- Lymphocyte depletion history: ATG, cyclophosphamide, rituximab
- Chronic immunosuppression
- Infection prophylaxis – PJP?
- Vaccinations – pneumovax, meningococcal, HPV, varicella?
- Reactivation of latent viruses – HSV, CMV, BKV, EBV
- Treatment of recurrent UTI – Multi-drug resistant infection
- Parasitic infections – well water, endemic travel

What is her cardiovascular risk?

- Allograft CKD
- LVH
- Anemia
- Hypertension
- BMI
- Diabetes
- Hyperlipidemia
- What types of cardiovascular events are you most concerned about?

What are her risks for malignancy?

- Chronic IS
- Lymphocyte-depleting therapies
- Chronic EBV viremia (Burkitts)

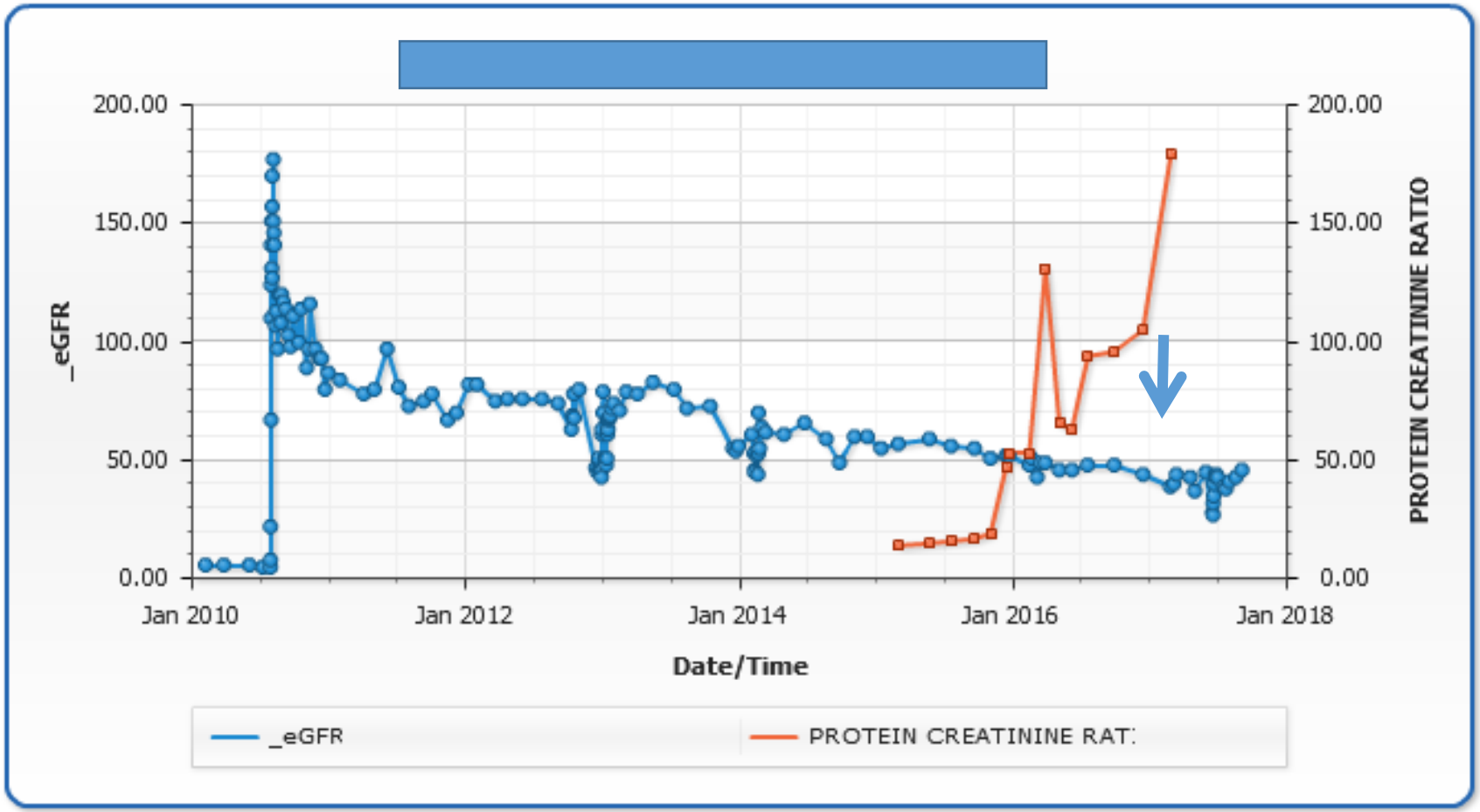
Risk factors for allograft failure

Case #2 – risk of allograft failure

- 12 year old boy, 4 years post-transplantation for posterior urethral valves and dysplasia
- Parents separated, goes in between homes
- Nocturnal enuresis; mild-moderate allograft hydronephrosis
- UDS 1 year ago for fluctuating Cr and diagnosed with voiding dysfunction
- Started ACEi for mild proteinuria x3 months ago
- Slowly rising Cr

Case #2: Kidney function since transplant

Any other info/tests? What would you recommend?



Case #2: Biopsy and further test results

- Haplo-match to donor (father)
- HLA antibody testing showed a DR and DQB dnDSA (MFI >10,000)
- Biopsy day Cr = 158
- Banff: i3, t3, g2, ptc3, v1, ci1, ct1, cv0, cg3, ti3, c4d1. GGS 5%

How do you interpret these findings?

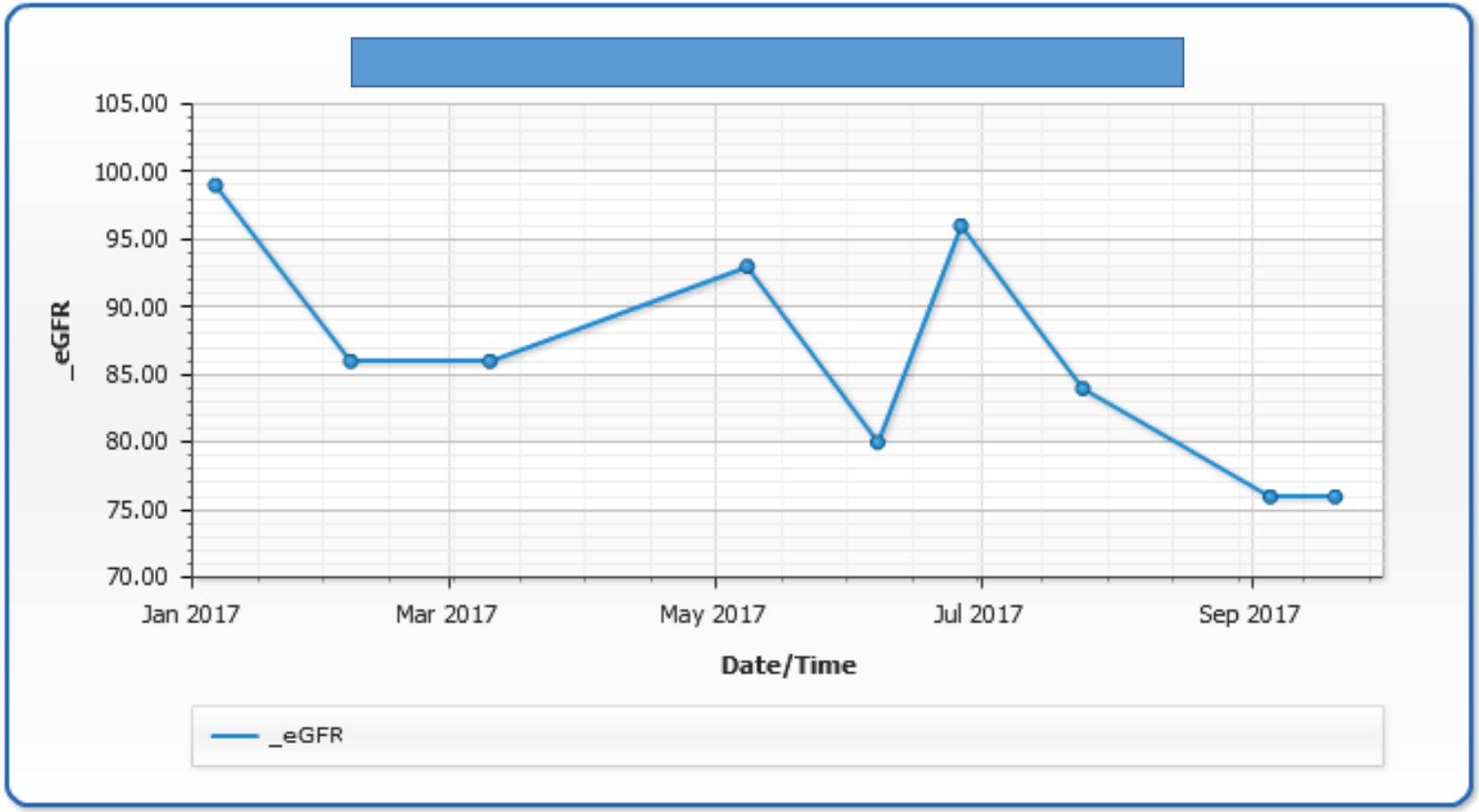
Why did this happen?

Case #3 – Risk of allograft failure

- 12 year old girl, transplanted age 4 with renal dysplasia
- Complicated by CVA with residual mild hemiplegia, developmental delay
- No surveillance biopsies, no clinical rejection episodes
- Prior history of recurrent UTI, but none x2 years
- Creatinine creep over last 2 years, but more in last 4 months
- No intercurrent illness and no response to increased hydration

Case #3: Kidney function since transplant

Any other info/tests? What would you recommend?



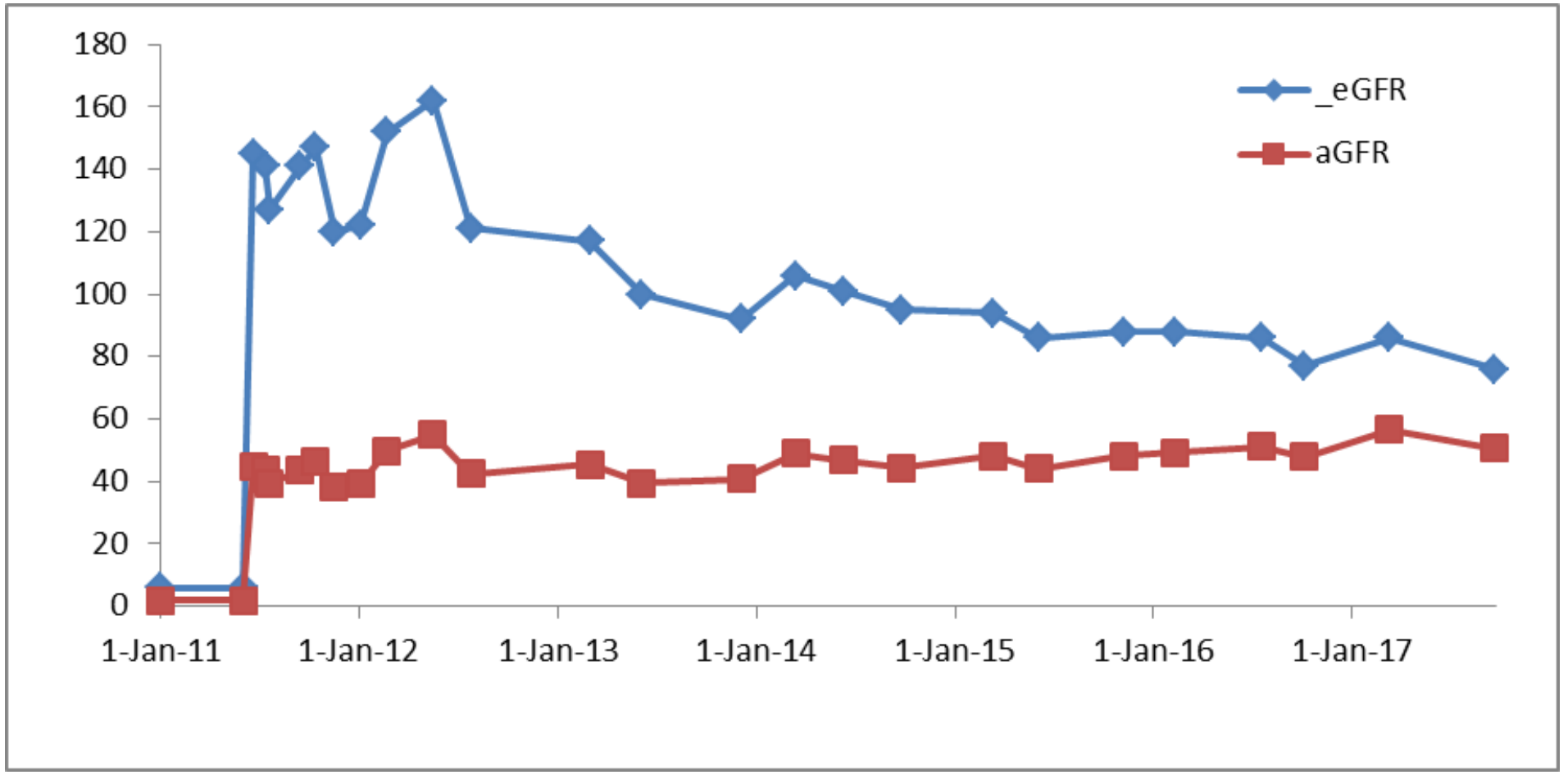
Case #3: Biopsy and further test results

- LD (father), MM at class II 0DR, 0DQA, 1DQB
- HLA antibody testing – no DSA
- Biopsy day Cr = unchanged
- Banff: i0, t0, g0, ptc0, v0, ci1, ct2, cv0, cg0, ti0, c4d0; GGS 26%

How do you interpret these findings?

Why then is her eGFR declining?

Case #3: Absolute GFR over time

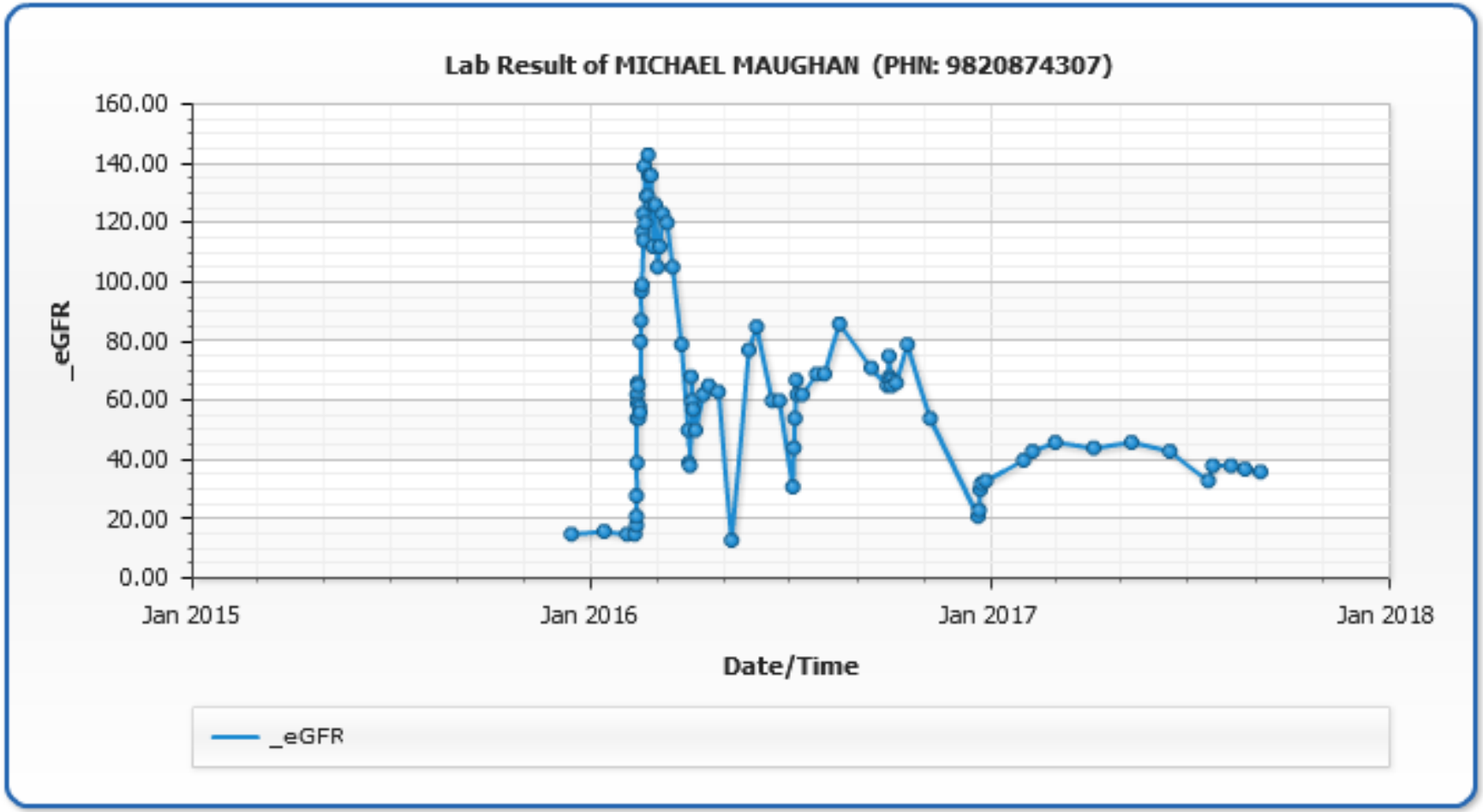


Case #4 – Risk of allograft failure

- 14 year old boy, 13 mo post-LD transplant from father for dysplasia
- Genetic syndrome: ectodermal dysplasia, anhydrosis, pancreatic insufficiency and deafness. Small stature, weight at Tx 31 kg.
- Early episodes of AKI, responded to IV rehydration – 3-4L per day H2O
- Mild TCMR (borderline), treated x1 with steroids. Last biopsy at 12 month, persistant mild ti2, t1, i0 at last follow-up biopsy. IFTA grade 1.
- No UTI, no HTN, nighttime enuresis persists
- eGFR fell from 110 to 55 over 1st year.
- Presents again with elevated Cr, slowly over 2-3 months.

Case #4: Kidney function since transplant

Any other info/tests? What would you recommend?



Case #4: Additional labs & findings

- TAC levels stable, adherent – biopsy not repeated
- High-normal potassium, despite low K feeds by GT
- Metabolic acidosis – 2 mmol/kg/day NaHCO3
- 0.5 mcg alphacalidol for HyperPTG
- Darbepoietin for anemia
- BP at/below 50th %ile persistently

Any other testing to consider?

Case #4: Urinary & ancillary findings

- pH = 7
- FENa = 1.6%
- TTKG = 3.4

- Trial of florinef – unresponsive to adult dose
- Serum renin = high normal; Aldosterone = 2x normal

Case #5 – Risk of allograft failure

- 18 year old male, 5 years post-transplant for ESRD from Alport syndrome
- Post-transplant course complicated by morbid obesity, insulin resistance.
- Periodically undetected drug levels, little parental supervision. Swears he takes his meds. Converted to Advagraf.
- Kidney function stable
- Mild proteinuria (ACR=35), DSA testing shows weak DQB antibody

Non-adherence and adult transition

YOUTH QUIZ

I AM #ONTRAC

A LIST OF QUESTIONS TO HELP YOUTH LEARN TO MANAGE THEIR HEALTH AND GET READY FOR ADULT CARE

PUT A SYMBOL IN EACH BOX TO COMPLETE THE QUIZ

☑ GOT IT! ☒ NEEDS WORK

Voice

	I ask health care providers questions about my health
	I meet with health care providers on my own
	I can describe my health conditions to others
	When my symptoms are getting worse, I contact the clinic for help
	I visit my family physician, at least once a year, for check-ups, referrals, prescription refills, birth control or emotional concerns
	I know what my long-term health problems might be
	I know what patient's rights and confidentiality mean
	I understand the risks and benefits of health care treatments before consenting
	I know who my adult care providers will be, how often to see them and for what

Action

	I know what I am allergic to (food, medication or other)
	I know the names of my medications and what each is for
	I know the side effects of the medications I take
	I take my medications on my own
	I know how to fill my own medication(s) prescriptions
	I do my own home treatments or therapies
	I get my blood test results on my own
	I know the reasons for my tests
	I have an emergency plan - who to call for what
	I carry emergency information with me - care card, phone numbers and/or medic alert
	I know how to order and use my equipment and/or supplies
	If I have home care, I am talking to my care providers about how these services will change as I get older
	I can make and get to my health care appointments on my own
	I know how to get my medical/health records

Connections

	My family supports me in managing my health and plans for transition
	I talk to my family/ friend(s) about my problems and worries
	I participate in clubs, groups, sports or activities outside of school
	I keep myself safe by telling someone if I am being bullied in person or online
	I talk to others when I am feeling sad, depressed, anxious, hopeless or having difficulty sleeping
	I connect with others who have the same health conditions as me
	I talk to others about my feelings and concerns about transferring to adult care

Future Planning

	I have teachers/others I talk to about my school strengths and problems
	I know how my health condition might affect my career choices
	I have a Social Insurance Number (SIN)
	I talk to my family about medical and extended health insurance after high school
	I work for service hours, volunteer and/or have a paid job
	I have ideas about after high school and plans for school and/or work
	I know how to get information about scholarships, bursaries and/or career counselling
	I know how and why to register for College/ University special accommodation
	I know there is planning to do around my health before I go away for school, work or travel

Sexual Health

	I know how my condition/treatments might affect my physical development
	I know where to get information about healthy relationships, sexual orientation, gender identity and birth control
	I know how to prevent sexual health risks such as pregnancy and sexually transmitted infections (STIs)
	I know how my condition might affect my sexual functioning and ability to produce children
	I understand why I might need genetic counselling

Safety

	I participate in physical activities that are safe for me
	I make good nutritional choices and am at healthy weight
	I know how alcohol, drugs and tobacco affect my medications and health
	I know if I have any driving restrictions

MY NOTES & QUESTIONS

OnTrac online using REDCap

https://rc.bcchr.ca/redcap/surveys/

Dummy code:K3PMXCLK4

Helping kids shine.