Refractory Anemia in a 2-year-old Peritoneal Dialysis-dependent Patient

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- H.C is a 2 year old female, ex 36 weeker with ARPKD, Caroli’s disease, portal hypertension s/p bilateral nephrectomies early in life and is on peritoneal dialysis.

- In January/2020 was found to have hemoglobin of 7.7 g/dl .
- A repeat CBC showed it to be 7 and she had a positive fecal occult blood (FOBT).

HPI

- No vomiting or diarrhea, no melena, no abdominal pain.
- No increased fatigue or change in appetite or SOB.
- Had switched from Elecare to Puramino Jr 2 weeks prior due to poor weight gain and had since then gained 0.7 kg.
- No new medications.

Past Surgical and Medical history

- Nephrectomies at age 1 week
- PD catheter insertion at age 1 week
- BL inguinal hernias, GERD and Pulmonary hypoplasia
- Discovered to have biliary duct dilatation and a cystic liver “mass” on a routine follow up ultrasound at age 15 months.
- At age 23 months she underwent a magnetic resonance cholangiopancreatography imaging.
- She was found to have splenomegaly with varices and portal hypertension. She also had intrahepatic biliary dilatation with regions of saccular dilatation in the right hepatic lobe which was consistent with her diagnosis of Caroli’s disease.

Meds

- Nephronex
- Zyrtec 1.3 mg/day
- Sevelamer 6000 mg/day
- Amlodipine 1.5 mg /day
- Clonidine 0.03 mg BID
- Calcitriol 0.4 mcg/day
- Cholecalciferol 2000 units/day
- Calcium phosphate 14 cc/day
- Cyproheptadine 2 mg BID
- Epoetin alfa 2000 units SC twice a week
- Ferrous sulfate 30 mg BID
- Miralax 4.25 g PRN/day
- Kayexalate 3.5 g /day

Vitals

- Pulse 126 bpm
- BP 103/75
- Resp 22 bpm
- Ht 80 cm (0.32 %ile)
- Wt 11.2 kg (7.76%ile)

Physical exam

- General: smiling, playing, small for age, thin hair.
- Eyes: pallor, no periorbital edema
- ENT: No lesions, moist mucous membranes
- Resp: Clear lungs, no increased work of breathing
- CVS: Normal s1, s2, no murmur
- Abd: soft and lax abdomen, hepatosplenomegaly, no guarding or tenderness. PD cath site clean.
- MSK: normal ROM, bruising present on lower limbs
- Neuro: Normal exam

Lab Results

- Repeat hg 7.0 gm/dl. Trend was from 10.4 to 7 gradually over the course of 5 months.
- MCV 89
  - MCH 29
  - MCHC 32
- Platelets 132
- Retic 4.6%
- Iron 42
- TIBC 248
- Tsat 17%
- INR 3.3
- PTT 62.9
- ALT 23
- AST 39
- Total bilirubin <0.2
- LDH 210 U/L
- Direct bilirubin <0.1

Lab Results

- Weekly KT/V 2.41
- Lead level <2
- Aluminum Level 14 (0-15 ug/L)
- Folate 15.4 ng/ml (>5.38 ng/ml)
- B 12 2165 picogram/ml (220-1125 picogram/ml)
- Methylmalonic Acid 0.85 ng/ml (0-4 umol/l)
- 25-hydroxy vit D 23 (20-80 ng/ml)
- Ca 9.2, Phos 4.1
- PTH 127 pg/ml (10-65 pg/ml)
- Hemoglobinopathies screen : normal
- FOBT positive
- BUN 25, Creatinine 5.6, K 3.8, Na 142, CO2 32, Albumin 2.2

Imaging

- Abd US: Similar intrahepatic biliary ductal dilatation compared to previous mages in the patient with history of Caroli Disease and Splenomegaly

What do you think is the cause of the anemia?

Carnitine profile

- Total carnitine 64 micromole/L (38-73 micromole/L)
- Acyl carnitine 25 micromole/L (7-24 micromole/L)
- Acyl/free carnitine 0.6 (0.1-0.8)
- These were obtained in 2017

What is the next step in your management?

- GI consult
- IV Vit K x 3
- Blood transfusion
- Plan for Upper GI endoscopy and liver biopsy as outpatient.
- Discharged on oral vit K.

- FINAL DIAGNOSIS: Vit K deficiency, Occult GI bleeding

- Two months later, hgb decreased gradually to 7 g/dl despite increasing Epoetin to 3000 units 3 days a week and receiving IV iron every two weeks.
- In addition, she had begun to lose weight despite adequate caloric intake. A fecal occult blood test was positive again, but INR was 1.1. She was suspected of having GI bleeding.

- She was admitted and transfused with the plan of upper GI endoscopy and possible sclerotherapy of varices.

What was the finding on endoscopy?

MEDLINE
non calibrated

- A hair bezoar was identified occupying 30% of the gastric lumen. It extended beyond the pyloric channel and tranversed as far as the scope could be safely advanced in the proximal jejunum. It occupied 50% of the duodenal lumen.
- It was not amenable to endoscopic therapy and the need for surgical evaluation and intervention was discussed with the family.

- An explorative celiotomy for removal of gastric duodenal jejunal tricho-bezoar was done without complications

One month later…

- Hgb 10.8 g/dl
- Iron 129
- Ferritin 103.5
- Tsat 50%

- Gaining weight steadily and adequately

Reason for hair bezoar formation?

- She had been started on amlodipine for blood pressure control in October/2019 (4 months prior to presentation).

- Amlodipine is known to cause alopecia,

Stump the Consultants

Annual Dialysis Conference, March 7th 2021

Dr. Priya Saini, MD, FRCPC
The Hospital for Sick Children
Toronto, Ontario, Canada

Case Presentation -1-

- 11 year old male
- Recent left elbow injury, receiving ibuprofren Q4 hours x 1 week
- PMHX: non-medicated ADHD, height & weight 90th %le
- Family Hx: early major vascular events in mother and maternal grandparents

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Case Presentation -2-

- 1 week after his elbow injury, presented with area of white discharge from his elbow
- Also, fever, vomiting, diffuse maculopapular rash, and petechiae
- BP 90mmHg requiring bolus

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Case Presentation -3-

Blood work

Lab	Value
WBC	24.6 x10^9/L
Hemoglobin	108 g/L (10.8 g/dL)
Platelets	494 x10^9/L
Neutrophils	15.6 x10^9/L
Eosinophils	0.62 x10^9/L
Creatinine	1900 umol/L
Urea	52.8 mmol/L
Sodium	133 mmol/L
Potassium	3.5 mmol/L

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Case Presentation -4-

Urine

Lab	Value
Urine ACR	35 mg/mmol
Urine PCR	127 mg/mmol
Urine Eosinophils	Positive

- Shortly after admission, noted to be anuric

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Initial Management

- Ceftriaxone, vancomycin, and clindamycin x 14 days
- Temporary femoral CVL insertion with renal biopsy
- Intermittent HD initiated: 2 hours, 2 mL/min clearance -> 3 hours, 4 mL/min clearance
- IV pulse methylprednisone x 3 days
- Started to void on 4th day -> HD 3 times/week

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Further Workup -1-

- Normal ANA, ANCA, C3, C4, anti-GBM.
- Kidney ultrasound: right kidney 11.5 cm, left kidney 11cm. Slightly increased echogenicity but normal renal parenchyma, resistive indices, and bladder.
- Renal biopsy: evidence of ATN. Also 11/18 globally sclerosed glomeruli at the corticomedullary junction. Mild interstitial fibrosis and tubular atrophy (20%). No arteriosclerosis. Immunofluorescence staining negative. No eosinophilic infiltrate.

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Further Workup -2-

- CKD Investigations:
  - Normal ECHO
  - Normotensive on no anti-hypertensive medications
  - Renal osteodystrophy scan: normal skeletal maturation, appropriate for age
  - Mild anemia, initiated on darbepoetin and iron supplementation

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Question #1

How long would you expect a patient with AKI to be on dialysis?

Length of Dialysis for AKI -1-

CJASN® Clinical Journal of the American Society of Nephrology

Recovery of Kidney Function in Children Treated with Maintenance Dialysis

Marjolein Bonthuis,[1] Jérôme Harambat,[2] Etienne Bérard,[3] Karlien Cransberg,[4] Ali Duzova,[5] Liliana Garneata,[6] Maria Herthelius,[7] Adrian C. Lungu,[8] Timo Jahnukainen,[9] Lukas Kaltenegger,[10] Gema Ariceta,[11] Elisabeth Maurer,[12] Runolfur Palsson,[13] Manish D. Sinha,[14] Sara Testa,[15] Jaap W. Groothoff,[16] Kitty J. Jager,[1] and on behalf of the ESPN/ERA-EDTA Registry

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Length of Dialysis for AKI -2-

What is the likelihood that children starting maintenance dialysis therapy will recover kidney function?

CJASN
Clinical Journal of American Society of Nephrology

Methods and Cohort

ESPN/ERA-EDTA Registry
36 European countries

N= 6574
Age <15 years
Maintenance dialysis initiation 2000-2014

Outcome:
Dialysis recovery = discontinuing dialysis for 30 days or more

Recovery (entire cohort)

Recovery at 2 years
2%

Median time to recovery
5 months
(IQR 2-9.6)

Recovery (by cause of kidney failure)

	CAKUT	Vasculitis	Ischemia	HUS
	0.8%	11%	12%	13%
Adjusted HR (95% CI)	ref	20.4 (9.7-42.8)	11.4 (5.6-23.1)	15.6 (8.9-27.3)

Conclusions There was a recovery rate of 2% within 2 years after initiation of maintenance dialysis in children. There is a clinically important chance of recovery in children with vasculitis, ischemic kidney failure and HUS.

Marjolein Bonthuis, Jérôme Harambat, Etienne Bérard, Karlien Cransberg, Ali Duzova, Liliana Garneata, Maria Herthelius, Adrian C. Lungu, Timo Jahnukainen, Lukas Kaltenegger, Gema Ariceta, Elisabeth Maurer, Runolfur Palsson, Manish D. Sinha, Sara Testa, Jaap W. Groothoff, and Kitty J. Jager. ***Recovery of Kidney Function in Children Treated with Maintenance Dialysis.***
doi: 10.2215/CJN.01500218

Case Continued -5-

- After ~12 months on dialysis, our patient was listed for deceased donor kidney transplant while continuing to investigate the etiology
- Eye exam: chronic papilledema despite well controlled BP on ABPM. Papilledema was asymptomatic with no headaches and 20/20 vision
- MRI/MRV: showed additional signs to support raised ICP, as well as a Chiari 1 Malformation

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Question #2

What are the causes and management of papilledema in a dialysis patient?

Papilledema -1-

- Dialysis disequilibrium syndrome
- Idiopathic Intracranial Hypertension
  - Risk factors:
    - Obesity (present in this patient)
    - Otitis media
    - Head trauma
    - Certain medications – ie tetracycline, Vitamin A
    - Refeeding after malnutrition

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Papilledema -2-

- Acetazolamide
  - Carbonic acid inhibitor
  - Contraindicated in ESRD
- Topiramate
  - Anticonvulsant with weak carbonic anhydrase inhibitor properties
  - Chosen for our patient
- Mechanical reduction of CSF
- Weight loss, low sodium diet

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Case Continued -6-

- With the constellation of ESRD, increased ICP, Chiari 1 Malformation, and a maternal family history of early major vascular events, without a unifying diagnosis, a whole exome sequence was performed.
- WES revealed *CLCN5 mutation in keeping with Dent Disease*
  - Variant p.D692LfsX7 with coding DNA c.2073_2076delTGAC, inherited from his mother

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Question #3

What are the presenting features and the natural history of Dent Disease?

Dent Disease -1-

- X-linked recessive disorder of the proximal tubules
- Presenting features can include: a male patient with short stature, polyuria, microscopic hematuria, asymptomatic proteinuria, hypercalciuria , nephrocalcinosis, or nephrolithiasis

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Dent Disease -2-

- Renal biopsy in Dent disease: non-specific but can include focal global glomerulosclerosis without any basement membrane abnormalities. Also can see tubular atrophy, varying degrees of interstitial inflammation, and interstitial fibrosis (seen with our patient).

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Dent Disease -3-

- 2/3 of males patients with Dent disease -> CKD

- If have CLCN5 mutation (60%) & CKD -> 2/3 will then develop end stage kidney failure, usually around 30-50 years old

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Case Resolution -1-

- Shortly after his genetic diagnosis of Dent disease, our patient was tolerating a reduction in dialysis treatments.
- Eventually stopped dialysis altogether at ***26 months after hemodialysis was initiated.***
- His position on the transplant list was put on hold and eventually he was removed from the list.

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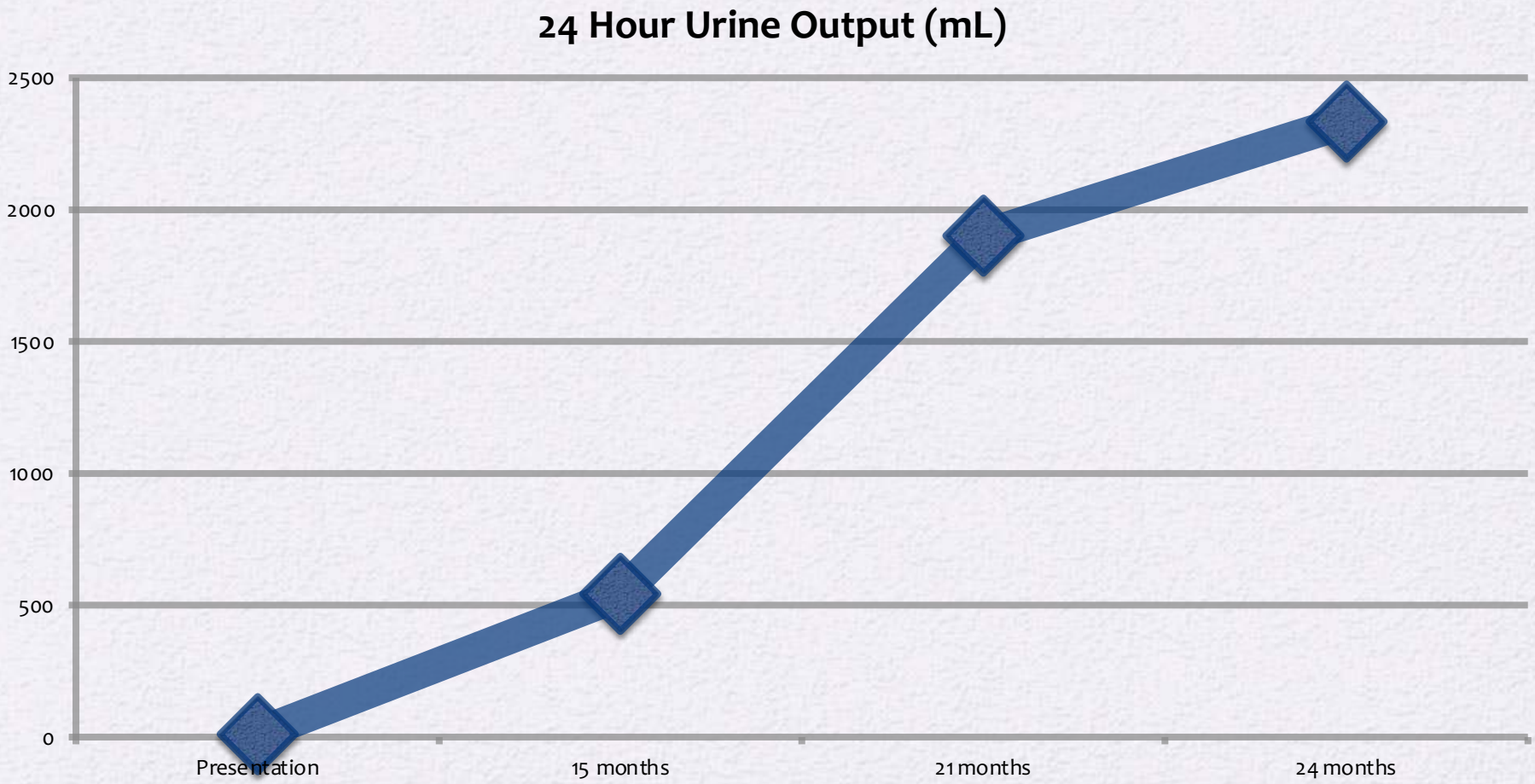
Case Resolution -2-



Case Resolution -3-

- Our patient is now 4.5 years from his initial presentation, and has remained off of dialysis for 2years without a kidney transplant or re-initiation of renal replacement therapy thus far.
- His GFR remains stable at 15 mL/min/1.73m2 and he continues to be followed in our chronic kidney disease clinic.

Thank You!

References

1. Bonthuis M, Harambat J, Bérard E, et al. Recovery of kidney function in children treated with maintenance dialysis. *Clin J Am Soc Nephrol*. 2018;13(10):1510-1516. doi:10.2215/CJN.01500218

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