Cast Nephropathy in Transplanted Kidney

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Case Presentation

- A 58-year-old female
- Complaints: general weakness, increased blood pressure
- Physical examination - Weight – 80 kg, BMI-27.8 kg/ m2, P-89', T/A 140/80 mmHg, t-36.20C, RR- N, no swelling
- Has been diagnosed anemia by family doctor and referred to hematologist
- Lab checkup made by hematologist showed CKD and referred to nephrologist
- Therapy: Ramipril 10 mg, Ferrous (II) sulfate, ascorbic acid

LABs

Crea – 484 umol/l
Urea – 22 umol/l
GFR-8 ml/min/1,73m^2 (CKD-EPI 2021)
Abumin- 31.0 g/l
Total Protein - 66 g/l
CRP-5.0 g/l
UA-5.8 mg/dl
Hb-8.9 g/dl
ESR – 79mm/h
Eosinophiles - 5.3%
WBC - 11.34 10 9/l
PLT- 222 10 12/l
Ferritin – 659 mg/l
TSAT – 33%

Ferritin – 659 mg/l
TSAT – 33%
Anti HCV (-) neg.
HBsAg (-) neg.
Anti HIV- (-) neg.
GOT-12,64 U/L
GGT-19,44 U/L
GPT- 4,32 U/L
Na- 132.0 mmol/l,
K- 4,49mmol/l
Ca++- 1.23 mmol/l
pH-7,4.
Ca- 2.40 mmol/l
P- 1.47 mmol/l
PTH- 211 pq/ml
Urinanalisis : Protein - (+2), Ery - (+1).

US – small echogenic kidneys

Left Kidney – 85X43 mm
parenchyma- 14 mm

Right Kidney – 75X42.5 mm
parenchyma- 13 mm

- Diagnosis: Chronic Kidney Disease

- Preemptive kidney transplantation was planned
  - living related donor (sibling)

- The GFR quickly decreased during the next month
  - creatinine – 759 umol/l

- Hemodialysis was started on 14.06.2019

- Pre-transplant Compatibility Tests NS
  - Cross match - negative (T and B)
  - PRA – 0 %
  - 1 haplotype matching

- KTx was performed on 10.07.2019
  - No surgical complications

- Standard immunosuppression without induction therapy
  - Methylprednisolone + Cyclosporine + MMF

11.07.19 – Post KTx day 1

Crea – 482 mmol/l

Urea- 20 mmol/l

Hb-7.3 g/dl, WBC - 11.79 10 9/l, PLT - 224 10 12 /ϖ, ESR – 28 mm/h

ALT- N, AST- N , GGT- N

Urin Analisis: Protein- (+2), Leu – (+2), Ery/ul - (+1)

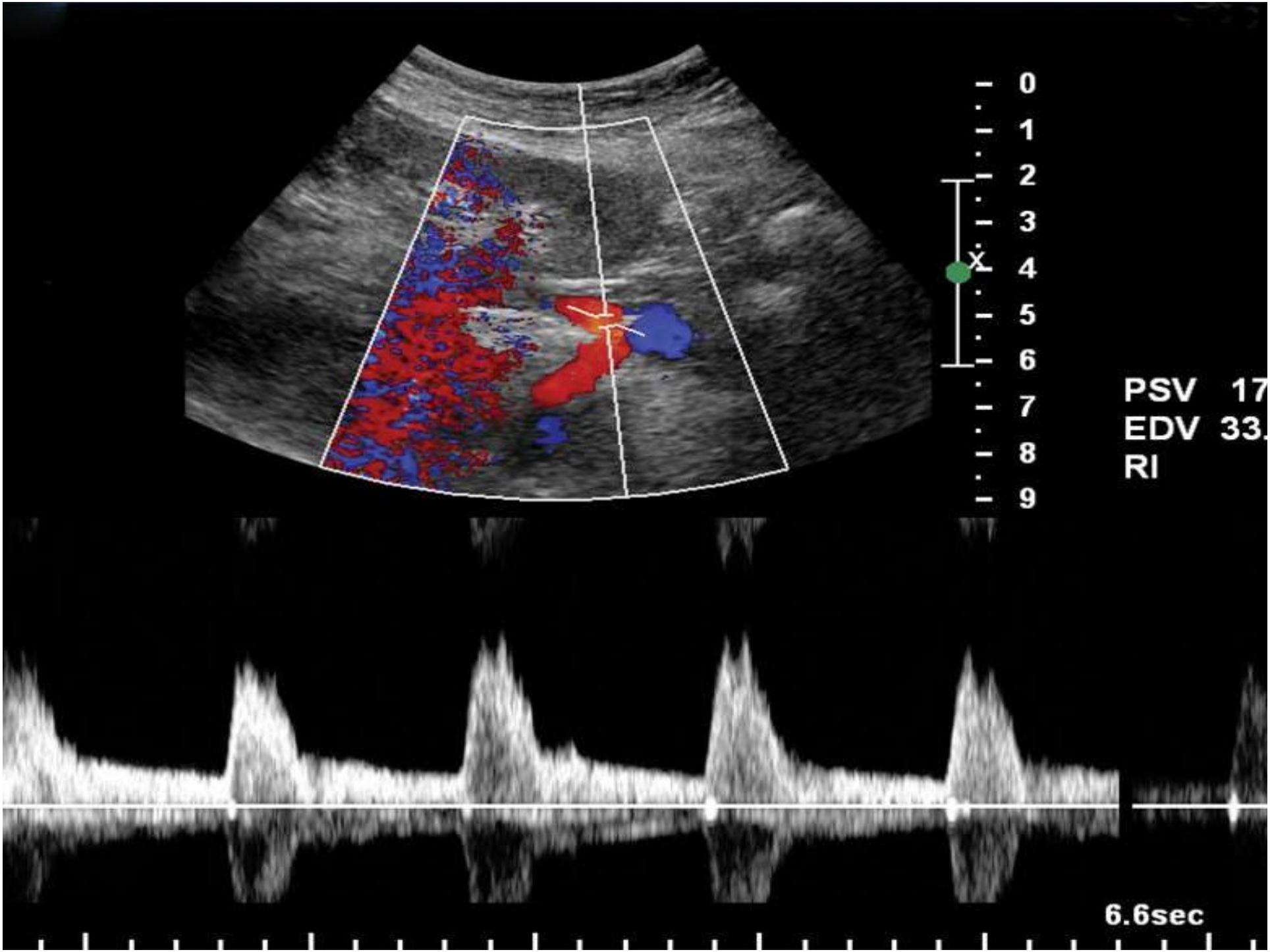
Na- 136.0 mmol/l, K- 4,13mmol/l, Ca++- 1.23 mmol/l, pH-7.41, HCO3- 22.7 mmol/l

Ca- 2.29 mmol/l, P- 1.89 mmol/l, PTH- 215.4 Pq/ml

US/doppler of the kidney - N

Diuresis - 2350 ml

Renal replacement therapy was continued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EDV 33.
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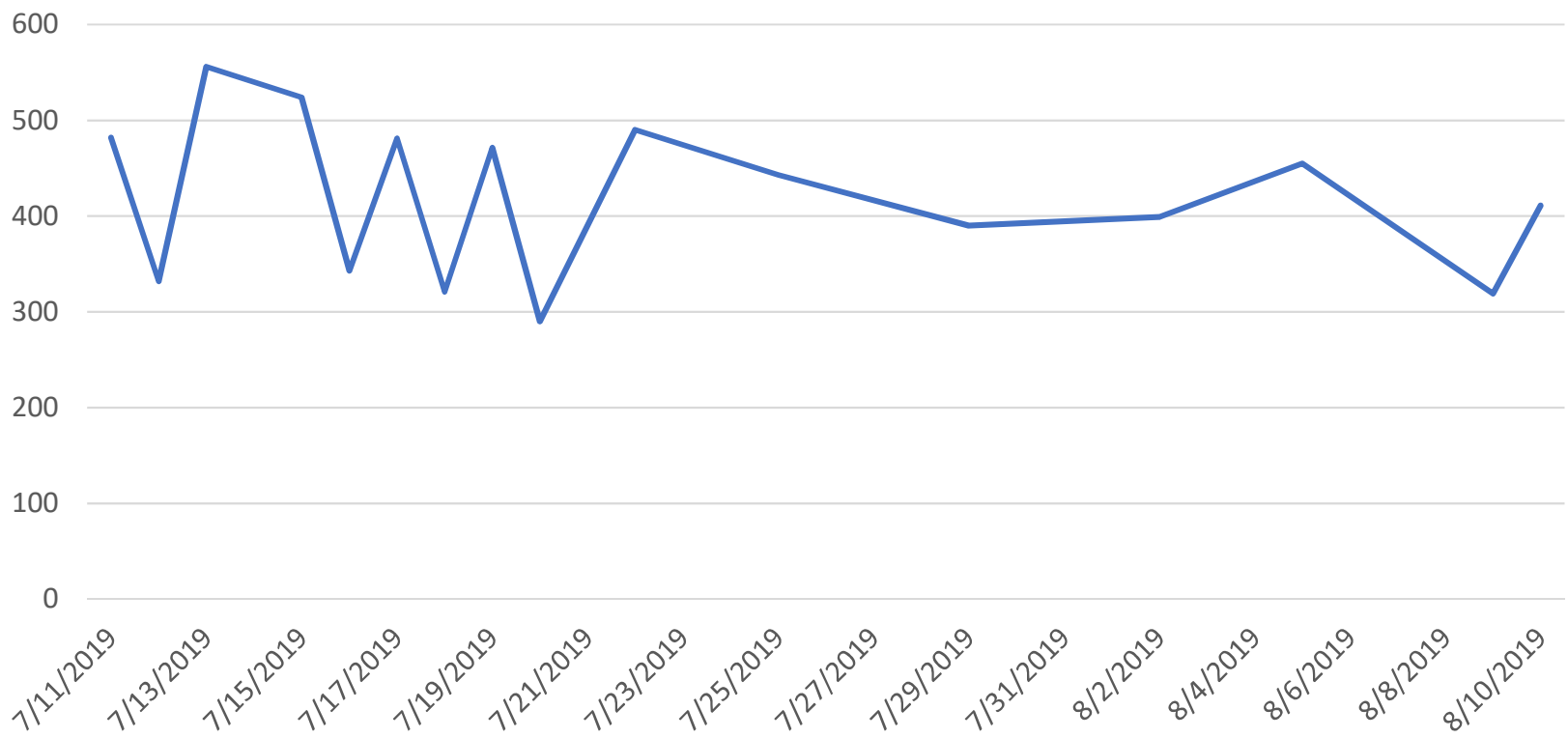
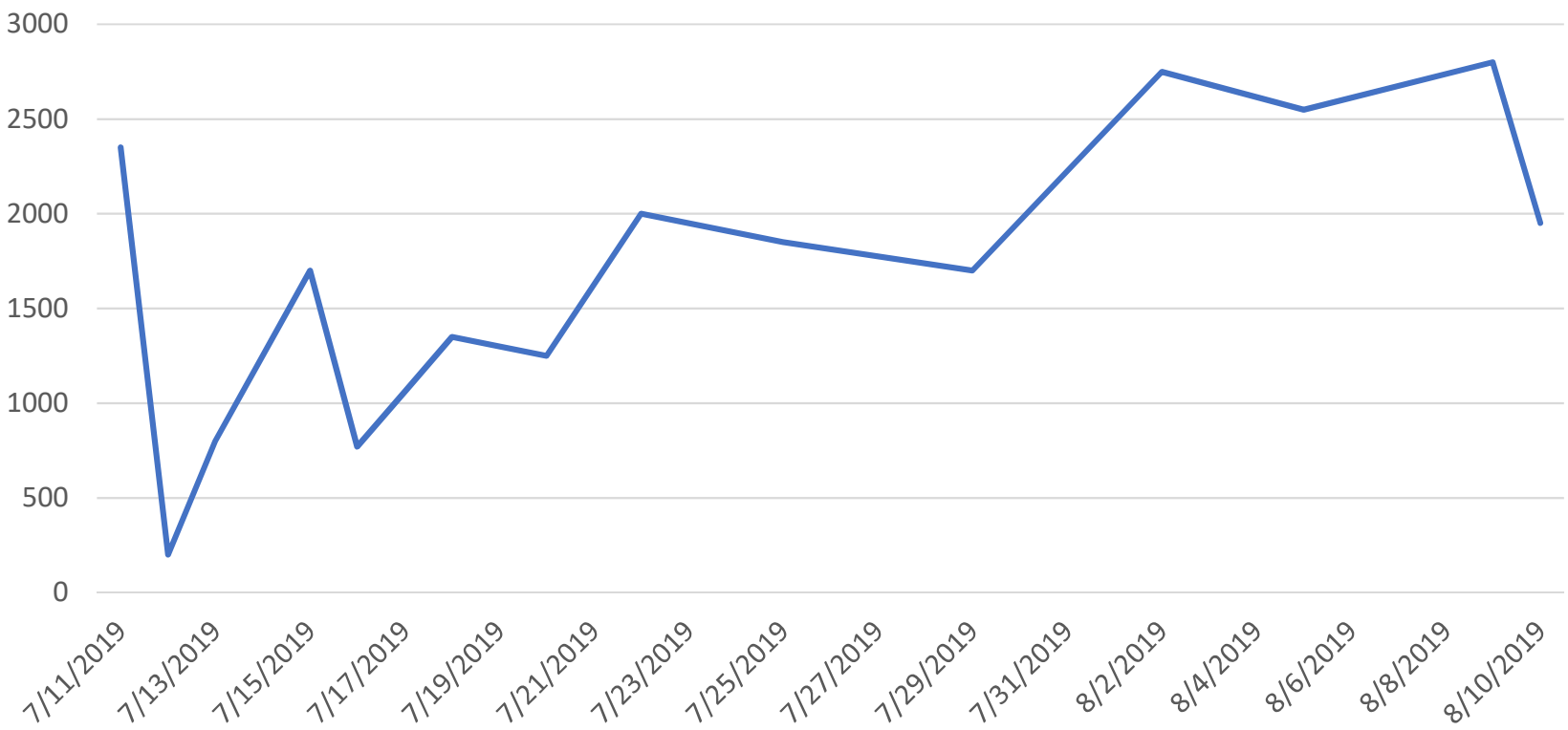
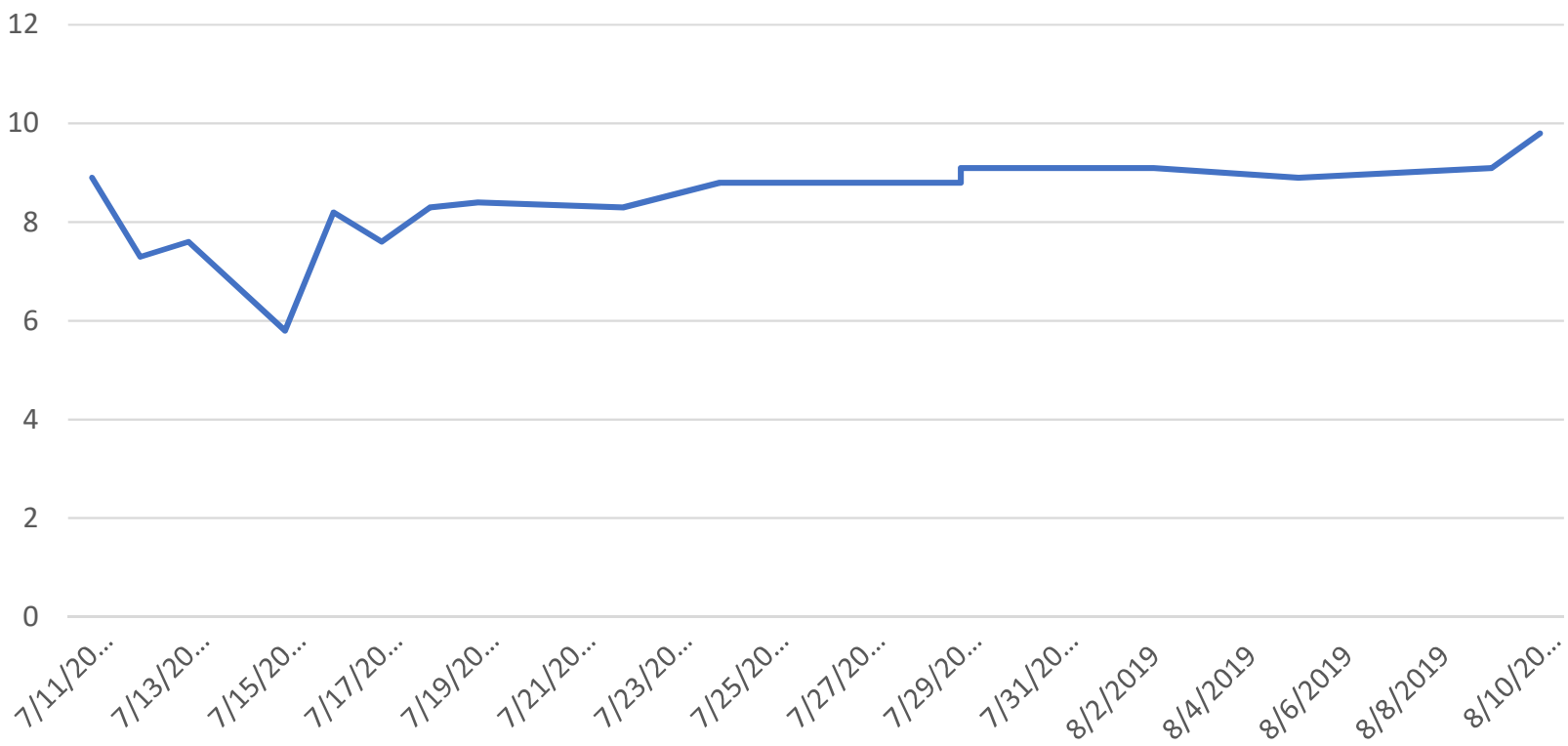
Creatinine level in the early post KTx period



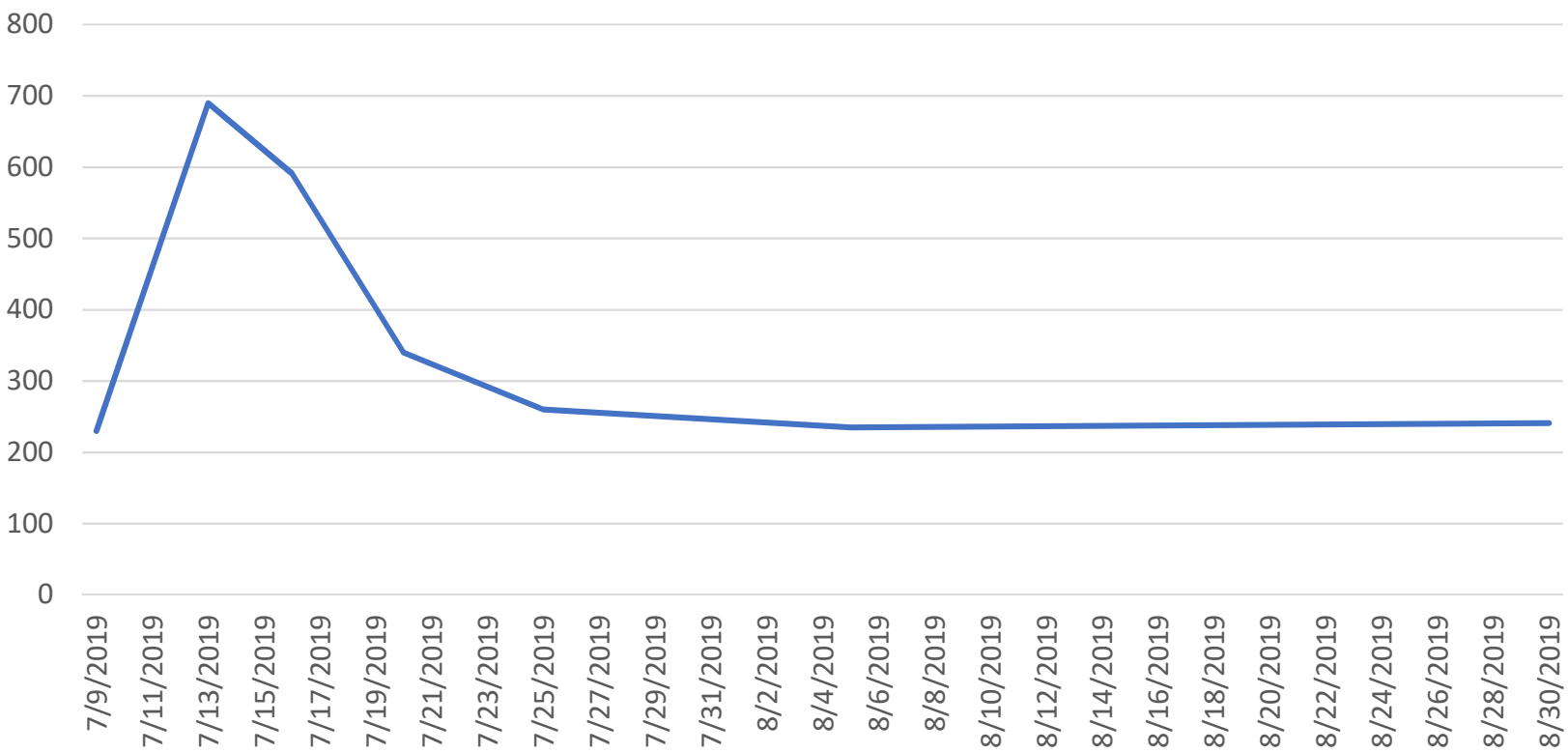
Urine Output in the early post KTx period



Hemoglobin level in the early post KTx period



Cyclosporin level in the early post KTx period



LABs 31 JUL 2019

Crea – 319 mmol/l
Urea – 20 mmol/l
Abumin- 35.0 g/l
Total Protein - 61 g/l
CRP-5.0 g/l
GOT-14,64 U/L
GGT-17,44 U/L
GPT- 7,32 U/L
UA-5.6 mg/dl
Hb-9.9 g/dl
ESR – 40mm/h
Eosinophiles – 4.8%
WBC - 11.95 10 9/l
PLT- 243 10 12/l

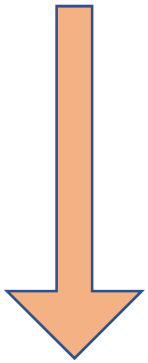
LDH – 259 mg/l
Cyclosporin level- 151 ng/ml
Anti HCV (-) neg.
HBsAg (-) neg.
Anti HIV- (-) neg.
Na- 136.0 mmol/l,
K- 4,50mmol/l
Ca++- 1.22 mmol/l
pH-7,4.
Ca- 2.07 mmol/l
P- 0.90 mmol/l
PTH- 138 pq/ml
Urinanalisis : Protein - (+2), Ery - (+1)
Protein 24h Urin – 526

Differential diagnosis of renal allograft disfunction:

- Acute rejection?
- Cyclosporin nephrotoxicity?
- Delayed graft function?
- Acute tubular necrosis?
- Other?

In order to clarify the diagnosis, the patient underwent a kidney biopsy (transplant biopsy).

Renal replacement therapy was continued



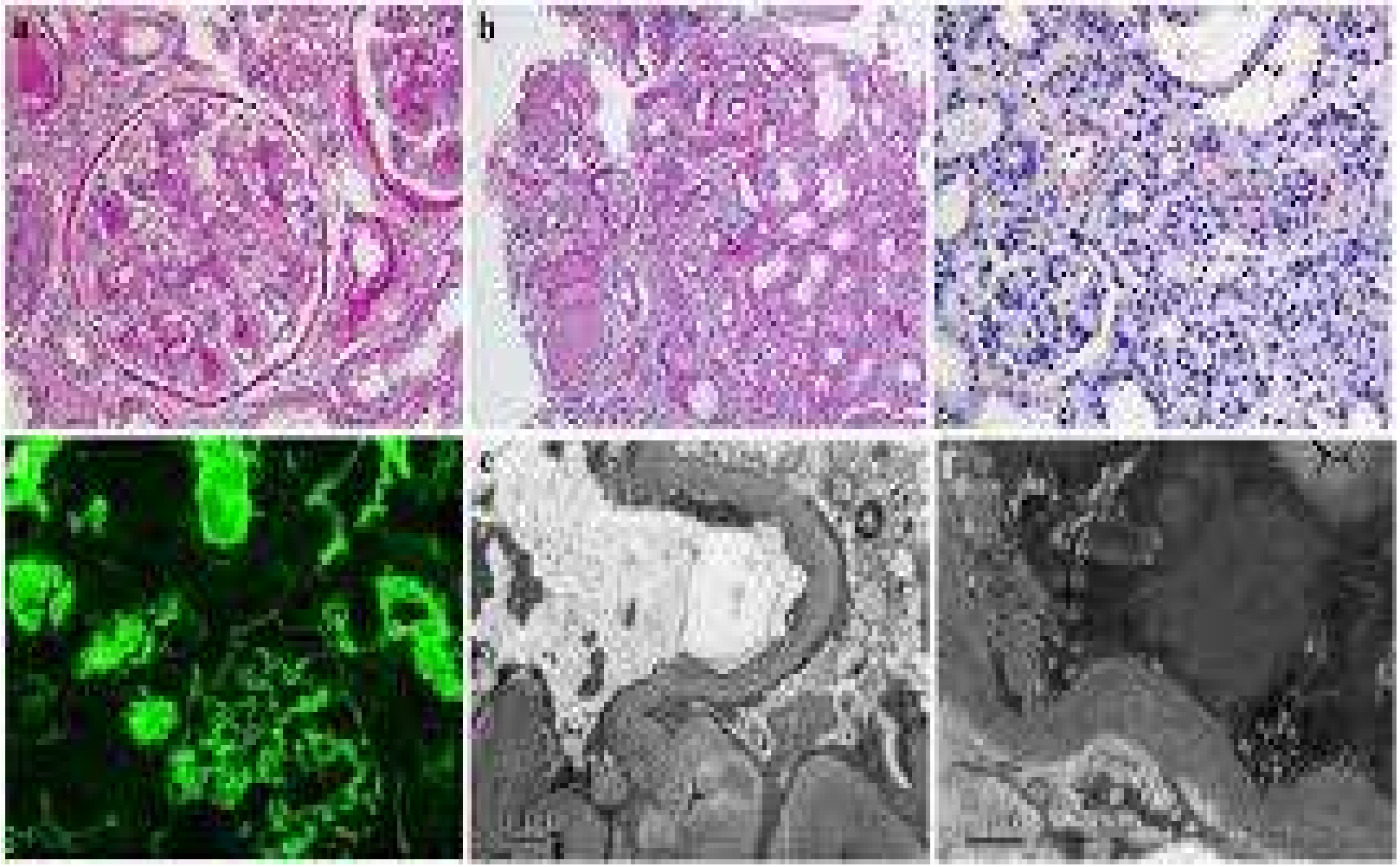
Diagnosis:

- Kidney biopsy for this patient showed definite cast nephropathy and minimal chronic changes, with only one of over 20 glomeruli sclerosed and minimal interstitial deposits.

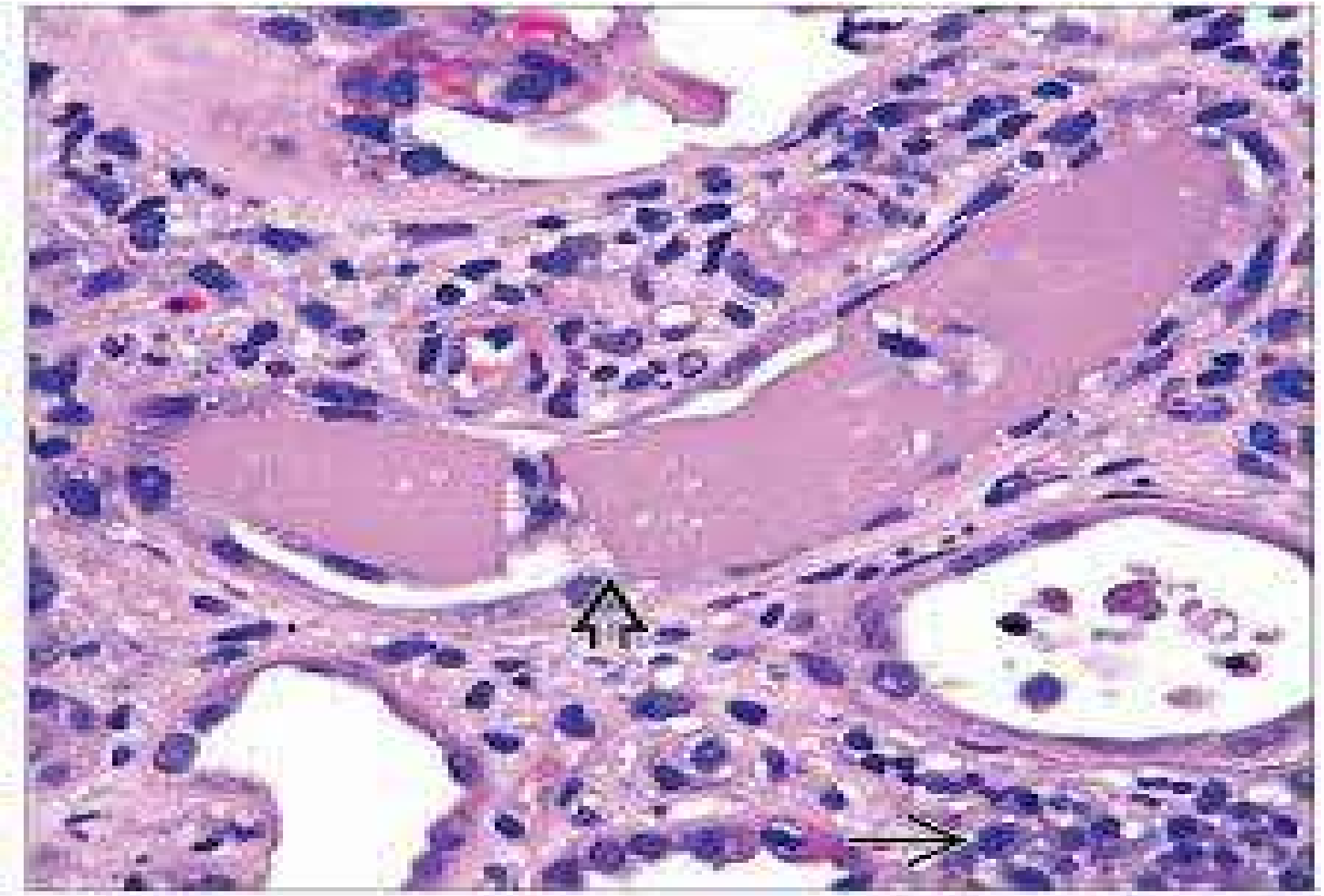
- All glomeruli were a normal structural appearance. The immunofluorescence (IF) microscopy was performed using antisera to human IgG, IgA, IgM, Clq, C3. Tubular casts stained for IgG and C1q. Congo red stain for amyloid was negative. Immunoperoxidase staining using antibodies to lambda and kappa chains showed strong positivity for kappa chains in the casts.

- Myeloma Cast Nephropathy

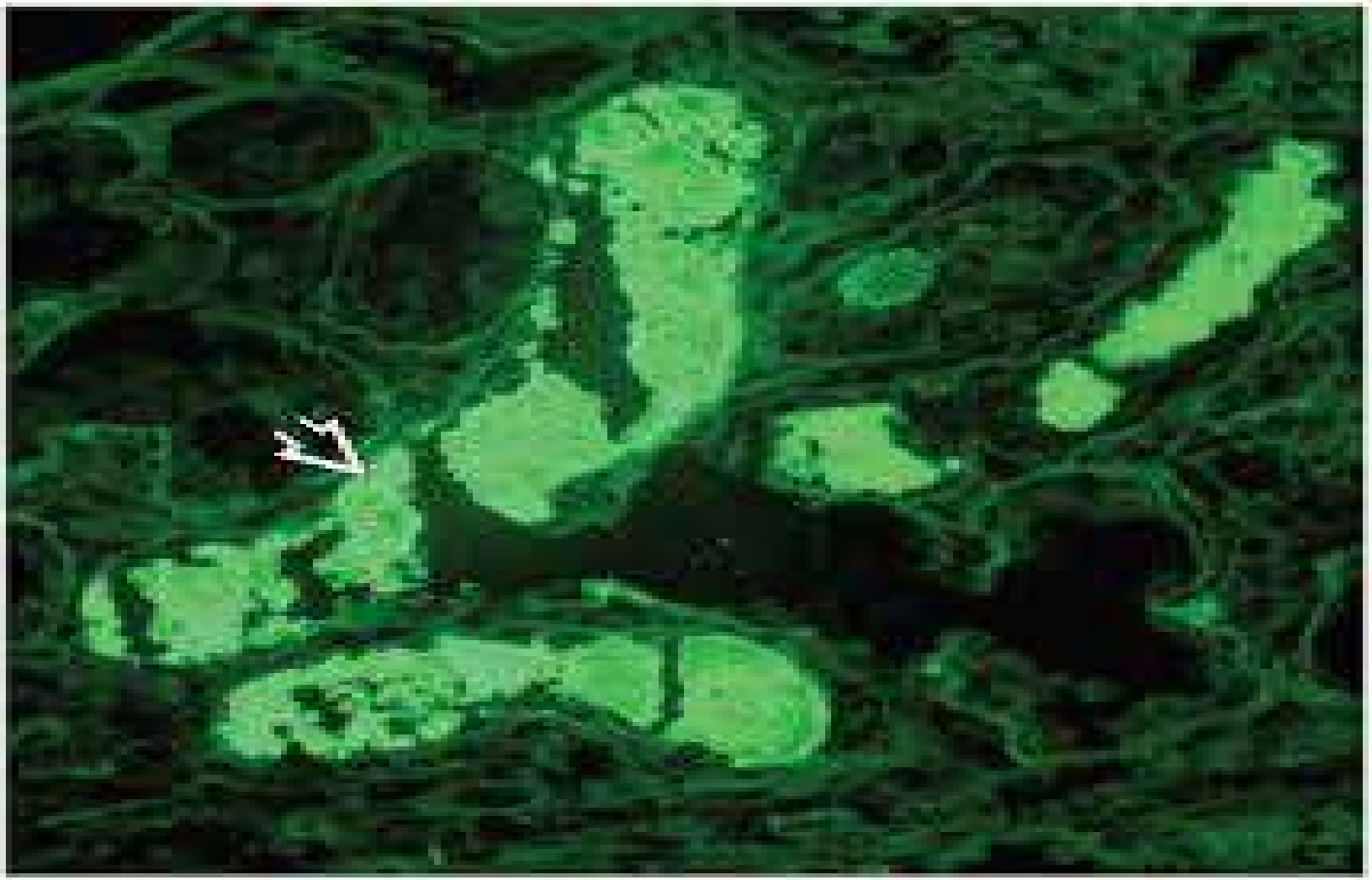
Myeloma Cast Nephropathy

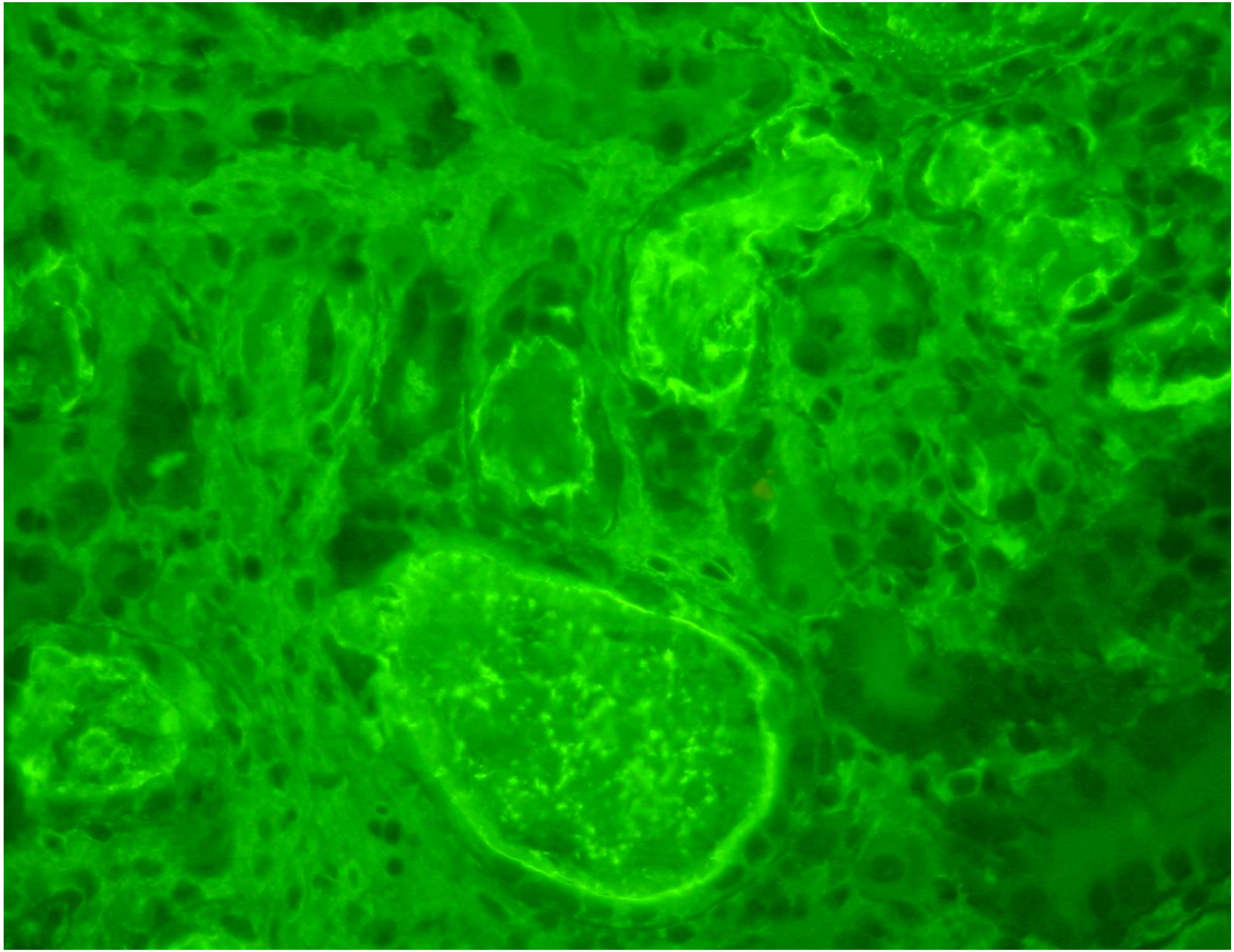


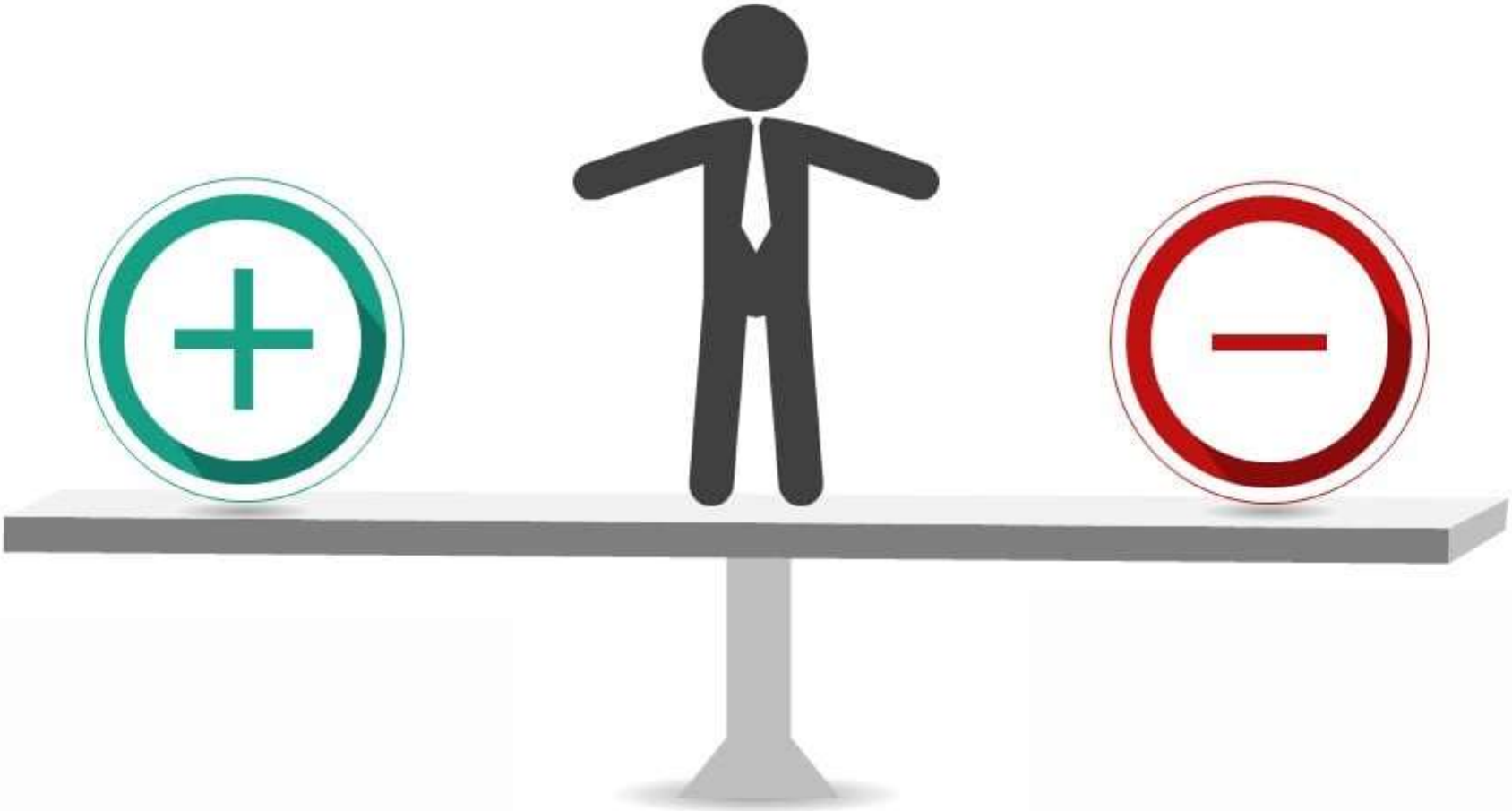
Mieloma Cast Nephropathy



Mieloma Cast Nephropathy



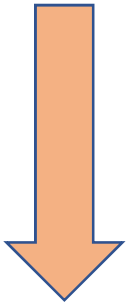




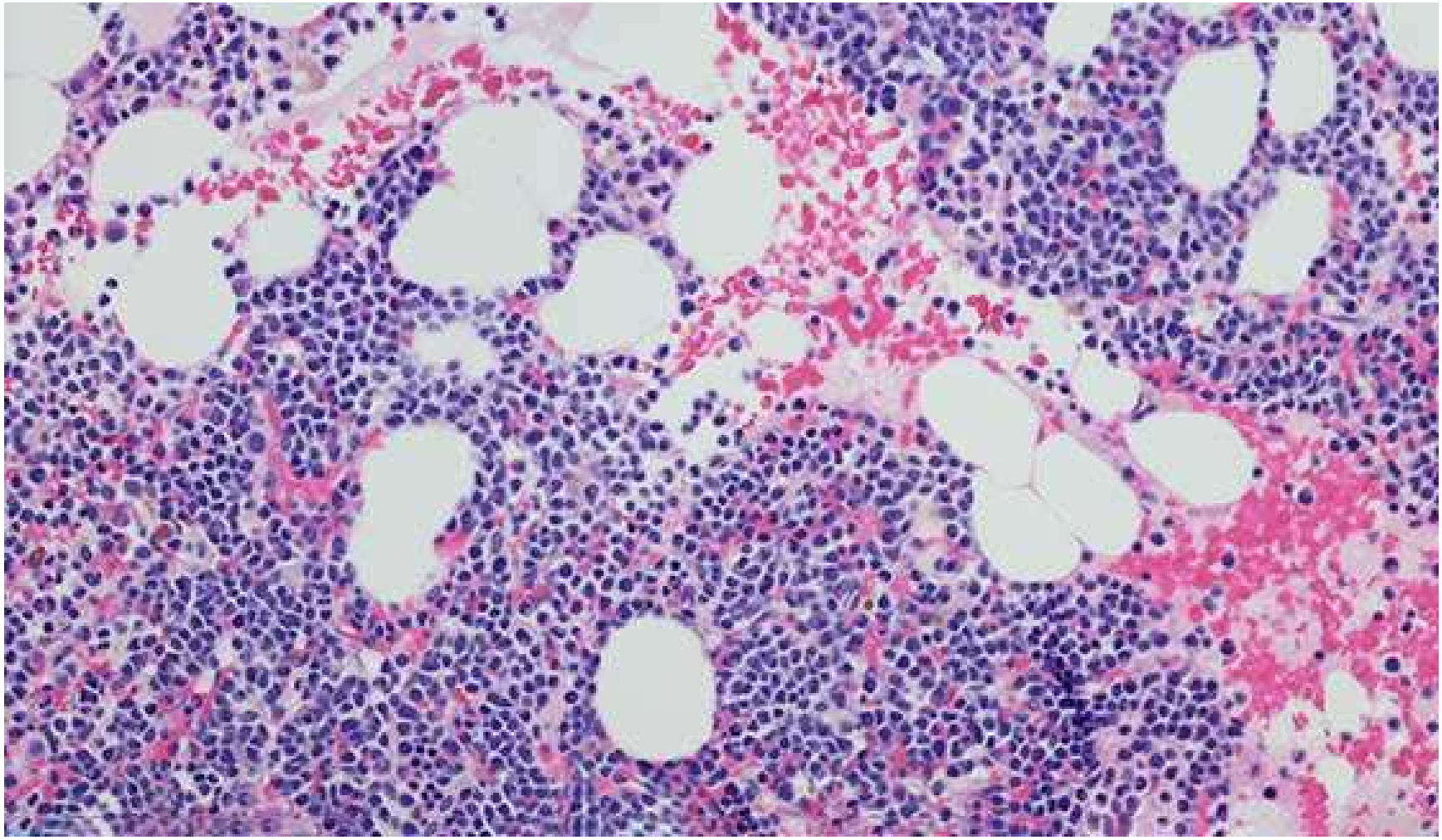
Criteria for the Diagnosis of Multiple Myeloma

- Both of the following criteria must be met:
- Malignant plasma cells in the bone marrow ≥ 10% or presence of bony or extramedullary plasmacytoma, confirmed by biopsy
- Any one or more of the following myeloma-defining events:
  - Evidence of end-organ damage that can be attributed to the disease: (CRAB criteria)
    - **C**alcium elevation—serum calcium > 0.25 mmol/L (> 1mg/dL) higher than the upper limit of normal or > 2.75 mmol/L (> 11 mg/dL)
    - **R**enal dysfunction—creatinine clearance < 40 mL per minute or serum creatinine > 177 µmol/L (> 2 mg/dL)
    - **A**nemia—hemoglobin concentration of > 2 g/dL below the lower limit of normal, or a hemoglobin concentration of < 10 g/dL
    - **B**one lesions—one or more osteolytic lesions found on x-ray, CT or PET-CT scans
  - Clonal plasma cells in the bone marrow ≥ 60% with or without CRAB
  - Ratio of involved/uninvolved serum free light chain ratio ≥ 100 (involved free light chain levels must be ≥ 100 mg/L)
  - One or more focal lesions found on MRI studies (at least 5 mm in size)
- Monoclonal Immunoglobulins (M Protein) and Light Chains (Bence Jones Protein)

Sternal biopsy was performed



Sternal biopsy



Sternal biopsy result

- Bone marrow is moderately cellular, plasma cells - 20%
- By trepanobiopsy of the bone marrow: focal injury of the bone marrow

Serum -Protein –Elektrophorese

TP- 62g/l

Serum -Protein –Elektrophorese

Albumin (elektroph)- 68.6 %

alpha-1 – Globulin -6.90%

- alpha-2 – Globulin - 13.2%
- beta-1 – Globulin - 2.80 %
- beta-2 – Globulin - 3.60 %
- Gamma – Globulin – 4.90%
- Free kappa light chains-11.4 mg/l
- Free lambda light chains-8739 mg/l
- ratio free light chains - < 0.01

- Immunelektrophorese i.Urin

- Free kappa light chains- < 6.3 mg/l
- Free lambda light chains- 827 mg/l

LABs 16.08.2019

Crea – 334 mmol/l
Urea – 21 mmol/l
Abumin- 39.0 g/l
Total Protein - 60 g/l
CRP-5.1 g/l
GOT-15,64 U/L
GGT-16,44 U/L
GPT- 8.47 U/L
UA-5.6 mg/dl
Hb-10.4 g/dl
ESR – 25mm/h
Eosinophiles – 4.8%
WBC - 11.95 10 9/l
PLT- 244 1012/l

LDH – 259 mg/l
Ciclosporin level- 162 ng/ml
Anti HCV (-) neg.
HBsAg (-) neg.
Anti HIV- (-) neg.
Na- 135.9 mmol/l,
K- 4,56 mmol/l
Ca++- 1.21 mmol/l
pH-7,4
Ca- 2.02 mmol/l
P- 1.16 mmol/l
PTH-98.1 pq/ml
25(OH)D3-18.83 ng/ml
Urinanalisis : Protein - (+2), Ery - (+1).

X-ray studies of flat bones - no pathology was detected

Classic radiographic appearance of multiple myeloma

- multiple, small, well-circumscribed, lytic, punched-out, round lesions within the skull, spine, and pelvis.

Risk factors for Myeloma Cast nephropathy :

- Various factors such as:
- dehydration
- hypercalcemia
- use of NSAIDs
- can lead to a decreased glomerular filtration rate (GFR) and promote cast formation in myeloma patients.

Key Factors for Teartment of Cast Nephropathy

Treat underlying disease

- Alkylating-based conventional Chemotherapy
- High-dose therapy with autologes stem cell transplantation
- Bortezomib underling with high dose dexamethasone
- Thalidomide
- Lenalidomide

• Provide supportive care

- Correct dehidratation/ hypercalcemia
- Avoiod contrast dyes. Nephrotoxic drugs
- Discontinue NSAIDS
- Treat infections
- Induce alkaline diuresis (goal of 3 L/d of urine at a pH of 7 if Patient can tolerate fluid volume)
- Early institution of dialisis

Cycle length: 21 days.			
Drug	**Dose and route**	**Administration**	**Given on days**
Bortezomib	1.3 mg/m^2 SC*	Given as a single SC injection.	Days 1, 8, and 15[3,4]
Lenalidomide¶	25 mg$^{\Delta}$ by mouth	Administer with water. Swallow capsule whole; do not break, open, or chew.	Daily, on days 1 through 14
Dexamethasone	40 mg$^{\Delta}$ by mouth	Take with food (after meals or with food or milk) in the morning.	Days 1, 8, and 15[3]

Bortezomib 1.3 mg/m^2 IVP/SC on days 1, 4, 8, and 11 every 3 wk plus dexamethasone 20 mg on the day of and the day after bortezomib.

Laboratory results before and after Treatment

Before

- Creatinine -322 mmol/l, GFR-22 ml/min/1,73m^2 (CKD-EPI 021)
- Free kappa light chains-11.4 mg/l
- Free lambda light chains-8739 mg/l
- ratio free light chains - < 0.01
- Immunelektrophorese i.Urin
- Free kappa light chains- < 6.3 mg/l
- Free lambda light chains- 827 mg/l
- Bone marrow is moderately cellular, plasma cells - 20%
- By trepanobiopsy of the bone marrow: focal injury of the bone marrow

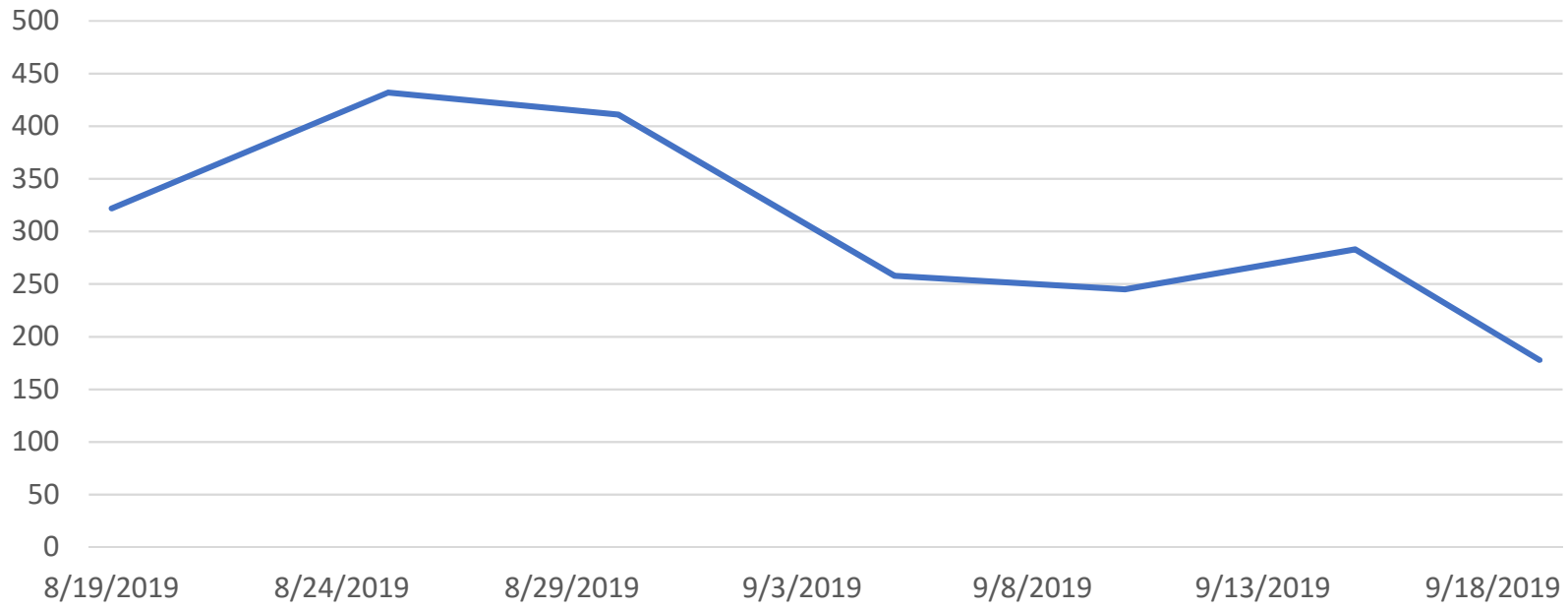
After 3 weeks

- Creatinine -95 mmol/l, GFR-58 ml/min/1,73m^2 (CKD-EPI 021)
- Free kappa light chains-10.2 mg/l
- Free lambda light chains-87 mg/l
- ratio free light chains - < 0.12
- Immunelektrophorese i.Urin
- Free kappa light chains- < 6.3 mg/l
- Free lambda light chains- 82 mg/l

Monitoring - after the end of the chemotherapy courses in the bone marrow punctate, the number of plasma cells was 1%, lambda light chains were normalized by urine immunoelectrophoresis

- The patient was on maintenance therapy for 2 years: lenadomid 10 mg 1-21 days with an interval of one week and dexamethasone 40 mg 1-8-15-22 days.Immunosuppressive therapy: cyclosporine

Creatinine level changes – cont'd



Follow up visits

Date	Brief Description
14 APR 21	No complaints, feels good Crea – 95 umol/l
23 Dec 21	No complaints, feels good Crea – 95 umol/l
25 MAY 22	Creatinine – 105 umol/l No complaints, feels good
06 JUN 23	Creatinine – 98 umol/l No complaints, feels good
22 AUG 23	Creatinine – 98 umol/l No complaints, feels good

Blood Cancer Journal www.nature.com/bcj

CURRENT TREATMENT ALGORITHM OPEN

Check for updates

Multiple myeloma with acute light chain cast nephropathy

Nelson Leung[1,2] and S. Vincent Rajkumar[1]

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Light chain cast nephropathy (LCCN) is a leading cause of acute kidney injury (AKI) in patients with multiple myeloma (MM) and is now defined as a myeloma defining event. While the long-term prognosis has improved with novel agents, short-term mortality remains significantly higher in patients with LCCN especially if the renal failure is not reversed. Recovery of renal function requires a rapid and significant reduction of the involved serum free light chain. Therefore, proper treatment of these patients is of the utmost importance. In this paper, we provide an algorithm for treatment of MM patients who present with biopsy-proven LCCN or in those where other causes of AKI have been ruled out. The algorithm is based on data from randomized trial whenever possible. When trial data is not available, our recommendations is based on non-randomized data and expert opinions on best practices. We recommend that all patients should enroll in a clinical trial if available prior to resorting to the treatment algorithm we outlined.

Blood Cancer Journal (2023)13:46; https://doi.org/10.1038/s41408-023-00806-w

KDIGO Controversies Conference on onco-nephrology: kidney disease in hematological malignancies and the burden of cancer after kidney transplantation

Jolanta Małyszko1 , Aristotelis Bamias2 , Farhad R. Danesh3 , Alicja Debska-Slizien4 , Maurizio Gallieni5 , Morie A. Gertz6 , Jan T. Kielstein7 , Petra Tesarova8 , Germaine Wong9,10, Michael Cheung11, David C. Wheeler12,13, Wolfgang C. Winkelmayer14 and Camillo Porta15; for Conference Participants1

Transplant International 2021; 34: 1789–1800

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Kidney Transplant Outcomes of Patients With Multiple Myeloma

Check for updates

Cihan Heybeli[1], Andrew J. Bentall[2], Mariam Priya Alexander[3], Hatem Amer[2], Francis K. Buadi[4], Angela Dispenzieri[4], David Dingli[4], Morie A. Gertz[4], Naim Issa[2], Prashant Kapoor[4], Aleksandra Kukla[2], Shaji Kumar[4], Elizabeth C. Lorenz[2], S. Vincent Rajkumar[4], Carrie A. Schinstock[2] and Nelson Leung[2,4]

[1]Division of Nephrology, Muş State Hospital, Muş, Turkey; [2]Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA; [3]Department of Anatomic Pathology, Mayo Clinic, Rochester, Minnesota, USA; and [4]Division of Hematology, Mayo Clinic, Rochester, Minnesota, USA

Introduction: Data on kidney transplantation (KTx) outcomes of patients with multiple myeloma (MM) are very limited.

Methods: We investigated the outcomes of patients with MM who underwent KTx between 1994 and 2019.

Results: A total of 12 transplants from 11 patients were included. At the time of KTx, 6 were classified as having stringent complete response (CR), 2 as CR, 2 as very good partial response (VGPR), and 2 as partial response (PR). With a median follow-up of 40 (minimum–maximum, 5–92) months after KTx, hematologic progression occurred in 9 transplants (75%). There were 3 grafts (25%) that failed, and 5 patients (45.5%) experienced death with functioning allografts. Graft survival at 1 and 5 years was 82.5% and 66%, respectively. Progression-free survival (PFS) rates of the cohort at 1, 3, and 5 years were 83.3%, 55.6%, and 44.4%, respectively. The estimated median PFS of patients who received bortezomib at any time (pre-KTx and/or post-KTx) was not reached, whereas it was 24 months for those who never received bortezomib ($P = 0.281$). Overall survival (OS) rates of the cohort at 1, 3, and 5 years were 81.8%, 61.4%, and 61.4%, respectively. OS of patients who received bortezomib at any time was 87.5%, 72.9%, and 72.9%, and that for those who never received bortezomib was 66.7%, 33.3%, and 33.3% ($P = 0.136$). All deaths occurred owing to hematologic progression or treatment-related complications.

Conclusion: Kidney transplant outcomes of patients with myeloma who received bortezomib before or after KTx seem to be more favorable. Nevertheless, relapse after KTx in MM is still common. More studies are needed to better determine who benefits from a KTx.

Kidney Int Rep (2022) **7**, 752–762; https://doi.org/10.1016/j.ekir.2022.01.003

KEYWORDS: chronic kidney failure; graft survival; kidney transplantation; mortality; multiple myeloma; recurrence

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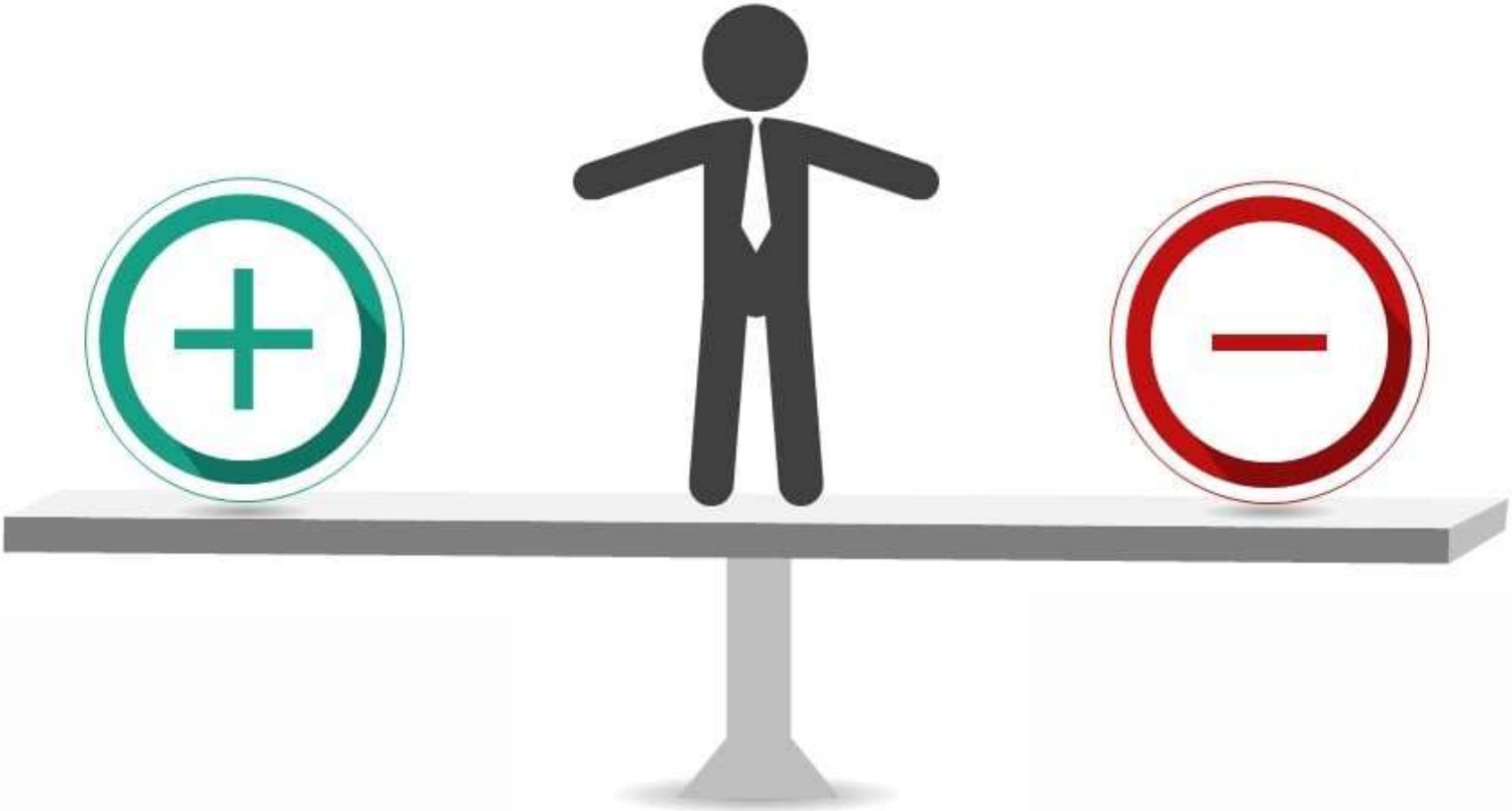
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