Acute Presentations after Kidney Transplantation

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Overview

* Overview of the transplant process
* Surgical complications
* Drugs and the common side effects
* Infections
The renal transplant journey

- Patient approaching or having reached ESKD
- Assessed and approved for living or deceased donor transplant
- Called in for operation; induction therapy
- Post-op recovery (average length of stay 4 - 6 days)
- Discharged to care of clinic:
  - 1-2x weekly first month
  - Weekly/fortnightly for further 1 – 2 months
  - Monthly to six months
Operation
Case 1

* 56 year old male. ESKD 2nd to IgA nephropathy
* Haemodialysis for 6 years, no residual renal function
* Living donor kidney transplant 8 days ago (1-0-0 HLA MM)
* Failed TWOC on ward; sent home with LTC 2 days ago, Cr 105 µmol/L
* Since emptying leg bag this morning, no urine in bag (8 hours)
* O/E:
  
  BP 105/70, P 97, apyrexial. JVP down, no oedema. Abdomen soft

Your thoughts?
Surgical Complications: Oliguria / Anuria
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Surgical Complications:
Oliguria / Anuria

- Oliguria or anuria
- ? Blocked urinary catheter
- Is a catheter required?
- Flush catheter
Surgical Complications: Oliguria / Anuria

- **Oliguria or anuria**
  - ? Blocked urinary catheter
    - Flush catheter
    - Is a catheter required?
    - **Is a catheter required?**
      - Yes
        - Urine output resolved?
          - No further action
          - Yes
        - No
          - Hypovolaemia
            - Urine output resolved?
              - Yes
              - No further action
              - No
            - Fluid challenge
              - Hydrated
                - Urgent ultrasound with duplex
      - No
        - Hypovolaemia
          - Urine output resolved?
            - Yes
            - No further action
            - No
          - Fluid challenge
            - Hydrated
              - Urgent ultrasound with duplex
            - No
Surgical Complications: Oliguria / Anuria

Oliguria or anuria

? Blocked urinary catheter

Flush catheter

Is a catheter required?

? Hypovolaemia

Urine output resolved?

No further action

Yes

Urine output resolved?

Yes

No

Assess fluid status

Dry

No

Hydrated

Urgent ultrasound with duplex

Vascular thrombosis

Hydronephrosis

Normal

Poor peripheral perfusion

Loss of CMD
Surgical Complications: Oliguria / Anuria
Case 2

* 67 year old female. ESKD 2nd to Anti-GBM disease

* Peritoneal dialysis for 3 years prior to DCD Transplant 9 days ago

* Complicated surgery, with delayed graft function

* Discharged 36 hours ago, Cr falling (360 µmol/L)

* Main issue for patient – diarrhoea for last 7 days
  * Culture negative, thought to be related to mycophenolate

* Presents this morning with sudden pain over the graft

* OE:
  Apyrexial, BP 97/54, P 110 reg. JVP down, no oedema, very tender over graft. Wound healthy

Thoughts?
Findings in theatre
Surgical Complications:
Pain or Swelling over graft
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- Pain and or swelling over transplant
  - Urgent duplex USS
  - Renal vein thrombosis
  - Surgical exploration
Surgical Complications: Pain or Swelling over graft

- Pain and or swelling over transplant
  - Urgent duplex USS
    - Renal vein thrombosis
      - Surgical exploration
    - Haematoma
      - Hb fall? Yes
        - Surgical exploration
      - No
        - Fluid collection
          - Graft oedema
            - Transplant biopsy
              - Rejection
                - Treat
          - Conservative management
    - Fluid collection
Surgical Complications: Pain or Swelling over graft

- Pain and or swelling over transplant
  - Urgent duplex USS
    - Renal vein thrombosis
      - Surgical exploration
    - Haematoma
      - Fluid collection
        - No
        - Conservative management
          - Aspirate sample for biochemistry
            - Lymphocele
              - Asymptomatic
                - Conservative treatment
              - Symptomatic
                - Aspirate
                  - Recurrent
                    - Fenestration
                - Cystogram or Pyelogram
                  - Surgical or radiological drainage
                    - Abscess
                      - Surgical exploration
                        - Hb fall?
                          - Yes
                            - Surgical exploration
                          - No
                            - Conservative management
                              - Urinoma
                                - Cystogram or Pyelogram
                                  - Aspirate sample for biochemistry
                                    - Surgical repair
                                      - Conservative management with JJ stent
Surgical Complications: Pain or Swelling over graft

[Flowchart diagram showing the process for managing pain or swelling over a transplant, including options for haematoma, fluid collection, abscess, urinoma, and lymphocele, with steps for further investigation and treatment such as urgent duplex USS, surgical exploration, and aspirate sample for biochemistry.]
Surgical Complications:

Summary

- Sudden pain/swelling over graft or decreased UO in the first few days/weeks = emergency

- Urgent ultrasound always required (including OOH)

- Early discussion/blue light transfer to local transplant team may be required

- Vascular thrombosis – very high incidence of graft loss
Transplant medication

- **Induction**
  - T cell depletion/inhibition, high dose steroid
  - Effects last weeks to months (depending on agent)

- **Maintenance**
  - Calcineurin inhibitor (tacrolimus, ciclosporin)
  - Anti-proliferative (Mycophenolate, azathioprine)
  - +/- prednisolone
Other drugs to expect

- **Anti-microbials**
  - PJP prophylaxis (co-trimoxazole; 6 - 12m)
  - CMV prophylaxis (valganciclovir / valaciclovir; 0 - 6m)
  - TB prophylaxis (isoniazid, pyridoxine; 12m)
  - HIV – ongoing treatment (HAART)
  - Fungal prophylaxis (nystatin; 1w or until prednisolone <20mg OD)

- **Others**
  - Statin, GI protection, aspirin
31 year old female, ESKD 2nd to T1DM

Living related renal transplant 14 days ago (0-1-0 HLA MM)

Good post-op recovery, Cr 76 µmol/L

Significant issues with postural hypotension since surgery

Presents today with intermittent palpitations and pre-syncope

OE:

Apyrexial, BP 102/70 (89/50 standing), P 42 reg, euvolaemic. Nil else

Thoughts?
Investigations

\[ K^+ 7.2, \ HCO_3^- 17, \ Ur \ 6, \ Cr \ 74 \]
Causes of hyperkalaemia post Tx

* **Renal impairment**
  * Delayed graft function
  * Acidosis

* **Renal Tubular Acidosis type 4**
  * Diabetics; medication induced
    * Calcineurin inhibitors (inhibit collecting duct Na⁺/K⁺ ATPase)
    * Co-trimoxazole (Collecting duct apical Na⁺ channel inhibition)
    * Heparin (inhibit aldosterone synthase)
    * ACEi/ARBs/β-blockers

* **Treatment**
  * Standard initial steps
  * Bicarbonate +/- fludrocortisone
  * Medication review (with specialist input)
Case 5

- 63 year old Afro-carribean male, ESKD 2nd to FSGS
- DBD renal transplant 3 months ago
  - Early wound infection and dehiscence (obesity related) - now healed
  - Maintained on prednisolone, tacrolimus, azathioprine; Cr 135 µmol/L (stable)
- Presents today concerned about increasing urinary frequency and volume
  - Family report he is very fatigued and his concentration is poor
- OE:
  - Apyrexial, BP 134/80, P 90, JVP down, no oedema, nil of note

Thoughts?

- Results:
  - FBC normal, Cr 160µmol/L, glucose 47
New Onset Diabetes After Transplant (NODAT)

* Incidence of 5 – 20% in first year (~30% in LT follow up)

* Risks
  * Age >60
  * BMI >30
  * Ethnicity (high risk: afro-carribean and indo-asian)
  * Family history of T2DM
  * Hepatitis C
  * Immunosuppression
    * Steroids
    * Calcineurin inhibitors (tacrolimus > ciclosporin)

* Treatment
  * Diet/lifestyle
  * Steroid withdrawal (specialist advice)
  * Medication as per T2 DM
* 48 year old female. ESKD 2nd to polycystic kidneys

* Renal transplant 9 months ago, Cr stable (~110 µmol/L)

* Recent LRTI; seen by GP 6 days ago and given clarithromycin (penicillin allergic)

* Increasing confusion last 48 hours, headache, and seizure in ED

* OE:
  
  Apyrexial, BP 191/98, P 70, Euvolaemic, 
  GCS 14/15, bilateral tremor, no meningism, no focal neurology

* Results:
  
  FBC normal, CRP <1, Cr 480 µmol/L. CTB ‘normal’. Lumbar puncture within normal limits

Thoughts?
T2 weighted MRI Brain

Lab ring: trough tacrolimus level 39 ng/mL (target 5 - 10)
Calcineurin Inhibitor (CNI) Toxicity

* **Side effects:**
  * Diabetes (Tac>CyA), dyslipidaemia (CyA>Tac), hypertension, hirsuitism (CyA), gum hypertrophy (CyA), alopecia (Tac)

* **Nephrotoxicity**
  * Dose dependent vasoconstriction
  * Chronic exposure – ischaemia, tubular atrophy, scar
  * Tubular toxicity (RTA 4)
  * Thrombotic microangiopathy
  * Hypertension

* **Neurotoxicity**
  * Tremor, encephalopathy, convulsions, PRES (rare)
  * Responds to dose reduction or withdrawal
### CYP3A4 Inhibitors – risk of CNI toxicity

<table>
<thead>
<tr>
<th>Anti-microbials</th>
<th>Ca(^{2+}) channel antagonists</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin</td>
<td>Diltiazem</td>
<td>Grapefruit juice</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Verapamil</td>
<td>Ritonavir</td>
</tr>
<tr>
<td>Ketoconazole, fluconazole, itraconazole, voriconazole</td>
<td>Dihydropyridines (lercanidipine&gt;amlodopine/others)</td>
<td>Other protease inhibitors?</td>
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### CYP3A4 Inducers – risk of rejection/low CNI levels

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<th>Anti-microbials</th>
<th>Anticonvulsants</th>
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</thead>
<tbody>
<tr>
<td>Rifampicin</td>
<td>Phenobarbitone</td>
<td>St. John’s wort</td>
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<tr>
<td>Rifabutin</td>
<td>Phenytoin</td>
<td></td>
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<tr>
<td>Caspofungin</td>
<td>Carbamazepine</td>
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Case 7

* 52 year old female. ESKD 2nd to lupus nephritis

* HLA incompatible kidney transplant 13 months ago
  * 2 episodes of acute rejection
  * Treated with methylprednisolone and then ATG
  * Current Cr 180 µmol/L (stable)

* Presents with 2 weeks of increasing dyspnoea, dry cough

* OE:
  
  Temp 37.5. Ob’s stable. Sat’s 97% on air.
  Chest clear.
  Bloods: Hb 110, WCC 1.7 (Neut 0.9, Lymph 0.1), CRP 47, Cr 169

Thoughts?
Further investigation

- Sat’s fell to 84% on air with walking
- Bronchoalveolar lavage – pneumocystis jirovicii isolated
Case 8

* 38 year old male. ESKD 2nd to IgA Nephropathy.

* Living un-related renal transplant 8 months ago (0-0-0 HLA MM)
  * On prednisolone, tacrolimus, MMF, co-trimoxazole
  * No change in medicines for >2 months, and that was only cessation of some post-Tx drugs
  * Current Cr 103 µmol/L (stable)

* Presents with 3 weeks of progressive (bloody) diarrhoea, weight loss, abdominal pain

* OE:
  Temp 38.1. P 120. BP 101/56. Sat’s 97% on air.
  Chest clear. Abdomen diffusely tender
  Bloods: Hb 110, WCC 2.3 (Neut 1.7), CRP 78, Cr 154 µmol/L
  Stool culture/CDT negative (sent by GP)

**Thoughts?**
Further investigation

* CMV Donor +ve / Recipient –ve.
* Valganciclovir prophylaxis finished at month 6
* CMV PCR = 8.8 x 10⁵ viral copies/mL
* Lower GI endoscopy – severe colitis, biopsy demonstrated inclusion bodies
* Treatment = IV ganciclovir
Infections post transplant

Conventional

POSTOPERATIVE BACTERIAL INFECTIONS
Wound, Pneumonia, Line-Related Sepsis

URINARY TRACT INFECTIONS
Bacteremia, Pyelonephritis, Relapse

HEPATITIS
Hepatitis B

HEPATITIS
Hepatitis C Onset

SYSTEMIC VIRAL INFECTIONS
Herpes Simplex Virus

Cytomegalovirus Onset

Epstein-Barr Virus, Varicella-Zoster Virus, Papovavirus, Adenovirus

RESPIRATORY INFECTIONS
Fungi, Tuberculosis, Pneumocystis

CENTRAL NERVOUS SYSTEM INFECTIONS
Listeria

Aspergillus, Nocardia, Toxoplasma

Cryptococcus

Unconventional

Months

0  1  2  3  4  5  6
Things to remember

* **Highest risk**
  * Chronic IS exposure (consider primary disease e.g. vasculitis, lupus etc., and previous transplants)
  * Lymphocyte depletion (ATG or alemtuzumab: high risk Tx, SPK/bowel Tx, rejection episodes)
  * Naïve recipients of donor positive grafts (i.e. EBV, CMV)
  * Myelosuppression/neutropenic episodes (normally MMF/azathioprine related)

* Immunosuppressed patients may not mount an inflammatory response and can have poorly localising signs

* **Opportunistic infections difficult to diagnose**
  * CMV, EBV etc – PCR (IgM/IgG unhelpful)
  * Fungi/Mycobacterium/protozoa
    * need to consider to send correct test
    * TB culture, indian ink stain etc
  * Consider cross sectional imaging early
  * Obtain diagnostic tissue/fluid (BAL, aspiration etc)

* **If high clinical suspicion treat empirically pending results**
Summary

1. Early presentations
   * Almost always needs urgent USS and discussion with transplant centre

2. Be aware of the drugs expected of a transplant pt
   * Prescribe accurately
   * Check interactions
   * Consider known side effects and complications

3. High clinical suspicion at all times regarding infection
   * Timeframe of presentation will inform differential