10th National Congress of EM & 1st Intercontinental EM Congress

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Renal Transplantation Patient in ER

Mehmet ERGİN; MD, EP, Assist. Prof.

Near East University Medicine School Emerg Dep / Lefkoşa

Turkish Republic of North Cyprus

Principles

- Transplanted organs
  - are devoid of their native innervations.
  - have surgical anastomoses
- Pain ?
- Inflammatory and immunologic response to infection and malignancy?
  - Subtle signs and symptoms…

Principles

- Anatomic relationships
  - To anticipate leakages & blockages of vital anastomoses
- Baseline physiological capacity of allograft
  - …small changes in the baseline functional level ?

Principles

- Transplant organ complications
  - Anatomy
  - Infection
  - Rejection
  - Drug toxicity
- The exact etiology is not determined until admission to hospital!
- Time since transplant!

Transplantation Techniques

Transplantation Techniques

Early Complications

- General
  - Wall Abscesses, Hemorrhage, Hematuria, Incisional Hernia
- Urinary Fistula
- Arterial Thrombosis
- Venous Thrombosis

Late Complications

- Ureteral Stenosis
- Reflux and acute pyelonephritis
- Kidney Stones
- Renal Artery Stenosis
- Arteriovenous Fistula and Pseudo-aneurysms After Renal Biopsy
- Lymphocele

Transplantation Techniques

Early Complications

General: Wall Abscesses, Hemorrhage, Hematuria, Incisional Hernia

Urinary Fistula

Arterial Thrombosis

Venous Thrombosis

- During immediate and early post-operative process

- Management
  - Drainage of abscess or hematoma
  - Ureteral stenting
  - Percutaneous nephrostomy
  - Hernia repair
  - Vesical catheter and/or double J-stent
  - Radiological or surgical thrombectomy
  - Transplantectomy

Transplantation Techniques

Late Complications

① Ureteral Stenosis

- the dilated renal calyces and pelvis
- often an elevated creatinine level
- in 5% (range, 2-7.5%) of transplants
- present late between 1 and 10 years' post transplant.

Transplantation Techniques

Late Complications

Ureteral Stenosis

- Three causes of ureteral dilatation
  - Vesical high pressure in thickened bladder wall or urinary retention
  - Vesicorenal reflux
  - Ureterovesical reflux due to scar formation and/or poor surgical technique
    - 80% of uretral stenosis
    - Most during the first year post transplant

Transplantation Techniques

Late Complications

Ureteral Stenosis

- Management
  - Initial treatment; percutaneous drainage and checking renal function to see if it has improved.
  - Further treatment according to the level of stenosis, degree and delay of occurrence.
    - Endoscopic, either transurethral or percutaneous intervention
    - Open surgery

Transplantation Techniques

Late Complications

② Reflux and acute pyelonephritis

- Acute pyelonephritis is rare
- Reflux in the renal cavity is more common
  - In lower urinary tract infections, the risk of acute pyelonephritis is 80% with reflux and 10% without reflux
- Every reflux complicated by acute pyelonephritis
  - should be treated with an endoscopic injection.
  - If fails, uretero-ureteral anastomosis or an ureterovesical re-implantation…

Transplantation Techniques

Late Complications

③ Kidney Stones

- be transplanted with the kidney or acquired.
- <1% of transplants.
- Hematuria, infection or obstruction.
- Non-contrast CT scan.

Transplantation Techniques

Late Complications

Kidney Stones

- Management
  - Double J catheter or echo-guided percutaneous nephrostomy*
  - Extracorporeal Shock Wave Lithotripsy (ESWL)
  - Percutaneous or open nephrolithotomy.
  - Ureteroscopy

Transplantation Techniques

Late Complications

④ Renal Artery Stenosis

- In 10% (range, 2-38%) of transplants
- should be suspected when
  - existing arterial hypertension becomes refractory to medical treatment ***and/or***
  - an increase in serum creatinine without hydronephrosis.
- Doppler Sonography
  - showing high velocity > 2m/s.

Transplantation Techniques

Late Complications

Renal Artery Stenosis

- Management
  - Medical treatment and renal function follow-up
  - Interventional treatment if the stenosis is > 70%
    - Transluminal dilatations, with or without stenting,
      - the first-line treatment for aligned and distal stenosis.
    - Open surgery
      - in case of plication or anastomotic stenosis, failure of percutaneous dilatation

Transplantation Techniques

Late Complications

⑤ Arteriovenous fistula and pseudo aneurysms after renal biopsy

- in 10% (range, 7-17%) of transplants
- Repeated haematuria.
- Doppler USG & confirmation by MRI or angiography.
- Management
  - Angiography is also the first step in treatment.
    - Selective embolization

- Pseudo aneurysms are often due to mycotic infection and can be fatal.

Transplantation Techniques

Late Complications

⑥ Lymphocele

- 1-20% of complications.
- Generally asymptomatic, but may be pain due to ureter compression or infection.
- Management
  - No treatment for mild lymphocele or if no compression of the iliac vessels or the transplant ureter.
  - Laparoscopic marsupialisation OR open surgery

Immunosuppression

Immunosuppression

- Principle of 'the balance of survival'.
  - a dosage of drug high enough to suppress rejection without endangering the recipient's health.

- Safe modern immunosuppressive agents
  - suppress sensitized lymphocyte activity against a transplant.

Immunosuppression

- Drugs
  - Calcineurin inhibitors
    - Cyclosporine, tacrolimus
  - Antimetabolites
    - Mycophenolate
      - MMF or enteric-coated mycophenolate sodium, EC-MPS
    - Azathioprine
  - Steroids
    - Prednisolone or methylprednisolone
  - With or without induction therapy

Dose-dependent side effects

- Calcineurin inhibitors
  - Nephrotoxic, hypercholesterolemia, hypertension, gum hypertrophy, constipation, hirsutism and acne diabetes, neurological and gastro-intestinal side-effects, polyoma nephritis

- Antimetabolites
  - Inhibition of bone marrow function, gastrointestinal side-effects, polyoma nephritis

Non-specific side-effects of immunosuppression

- A higher risk of
  - Malignancy
  - Infection
    - particularly opportunistic infections

Non-specific side-effects of immunosuppression

Infection

- Primary cause of mortality after transplantation
- Signs - often blunted
- Aggressive management
- Primary sources
  - Pretransplant, community acquired, transmission from organ donor and nasocomial.
- Vaccines with live viral antigens shouldn't be!

Non-specific side-effects of immunosuppression

Infection

- First month post transplant
- Between 1 to 6 month
- More than 6 month

Non-specific side-effects of immunosuppression

Infection

First Month After Transplant

- Related to the transplant procedure, catheters and intubation.
- The typical causes of postoperative fever must be considered!
- Management
  - Similar to that for any immunosuppressed patient

Non-specific side-effects of immunosuppression

Infection

1 to 6 Months After Transplant

- Immunmodulating viral infections
  - Cytomegalovirus (CMV)
  - Hepatitis B and C
  - BK Polymavirus
  - Human Herpes Virus 6
  - Ebstein-Barr Virus (EBV)
- Opportunistic infections
  - Pneumocytis
  - Listeria
  - Fungal

Non-specific side-effects of immunosuppression

Infection

1 to 6 Months After Transplant

- CMV
  - produce multisystem disease
    - Pneumonitis – particularly common
    - Typically, signs at 40 days after transplant
  - Early diagnosis with bronchoscopy
  - Aggressive treatment with gangcyclovir and CMV-specific immunoglobulin
- Active infection trigger or exacerbate organ rejection!

Non-specific side-effects of immunosuppression

Infection

1 to 6 Months After Transplant

- EBV
  - Similar clinical effects as CMV
  - Often coexistence with CMV
- Mononucleosis like syndrome
  - Lymphadenopathy, weakness, low-grade fever
- B cell lymphoproliferative syndrome

Non-specific side-effects of immunosuppression

Infection

6 Months After Transplant

- Healthy Transplant
- Chronic Viral Infection
- Chronic Rejection

Non-specific side-effects of immunosuppression

Infection

6 Months After Transplant

- Healthy Transplant
  - No chronic immunomodulating viral infection
  - Mildly-increased susceptibility to normal community-acquired infections

Non-specific side-effects of immunosuppression

Infection

6 Months After Transplant

- Chronic Viral Infection
  - Progressive liver disease
    - due to recurrent or acquired viral hepatitis
  - B cell lymphoproliferative disorders
    - Associated with EBV
  - Primary Varicella Infection
  - Reactivation of latent VZV infection
  - HSV reactivation

Non-specific side-effects of immunosuppression

Infection

6 Months After Transplant

- Chronic Rejection
  - In need of aggressive immunosuppressive tx
    - High risk of life threatening opportunistic infections with
      - Fungi

        Candida, Cryptococcus, Coccidioides, Blastomyces, Histoplasma
      - Bacteria

        Listeria, Nocardia
      - Parasites

        Pneumocystitis, Toxoplasma, Strongyloides

IMMUNOLOGICAL COMPLICATIONS

Determining factors in rejection episodes and response to treatment

- Degree of sensitization to HLA
- Degree of HLA-mismatch, particularly in sensitized recipients
- History of previous episodes
- Previous transplantations, especially when graft loss has occurred due to acute rejection
- Non-compliance with immunosuppressive treatment
- Some virus infections, e.g. CMV

Immunological Complications

Main types of rejection

- Hyper acute rejection (HAR)
- Acute allograft rejection
  - Acute cellular rejection (ACR)
  - Acute humoral Rejection (AHR)
- Chronic allograft rejection (CAR)

Hyper Acute Rejection (HAR)

- Antibody-mediated rejection is caused by pre-formed anti-HLA or anti-AB (Blood group) antibodies

- Rare due to donor-recipeint ABO matching and routine pre-transplant cross-matching between donor cells and recipient serum

Acute Allograft Rejection

Acute Cellular Rejection (ACR)

- Much more than common than HAR, occurring in 10-40% of transplants
- Usually occurs from 5 days' post transplant
- Most likely within 3 months, though may occur after this time
- Usually responds well to steroid bolus treatment

Acute Humoral Rejection (AHR)

- Much less frequent than HAR, occurring in 5-20% of transplants
- Most likely within 3 months' post transplant
- Presence of certain histological features and/or C4d immunostaining and/or anti-HLA antibodies
- Worse prognosis than ACR since more difficult to treat

Chronic Allograft Rejection

- Rare, slowly progressive, immunological process
- Certain non-specific histological features and/or anti-HLA antibodies
- Requires clear strong evidence for a solely chronic immunological process

Differential diagnosis for rejection

- Transplant biopsy
  - The gold standard for the diagnosis of ACR, AHR and CAR!
  - demonstrate a mixed histological picture in many cases.
    - The Banff criteria
      - uniform criteria applied to biopsy
      - the basis for deciding prognosis and treatment

Take home messages

Clinical Features

- Allograft rejection symptoms are usually unclear and non-specific.
- The signs and symptoms of infectious complications depend on
  - the nature of pathogenic organism
  - location of infection
  - level of immunosuppression
- Careful attention to maintain appropriate level of immunosuppression and watching for the typical transplant-related complications.

Take home messages

Diagnostic Features

- Transplant patient must undergo extensive laboratory and radiographic evaluation
  - To rule out myriad infectious etiologies
  - To assess allograft function
  - To survey for signs of drug toxicity

Take home messages

Laboratory assessment

- Organ-specific measures of function
- Evidence of infection

Radiologic assessment

- Sources of infection
- Relevant anatomy of the patient's allograft

FURTHER READINGS…

- Guidelines on Renal Transplantation 2010. European Association of Urology
- Clinical practice guidelines. Post-operative Care of the Kidney Transplant Recipient. UK Renal Association 5th Edition Final Version (5th February 2011)
- Keadey MT. The Solid Organ Transplant Patient. In Marx JA, Editor. Rosen's Emergency Medicine Concepts and Clinical Practice. 7th ed. Philadelphia: Mosby Elsevier; 2010. pp.2365-74

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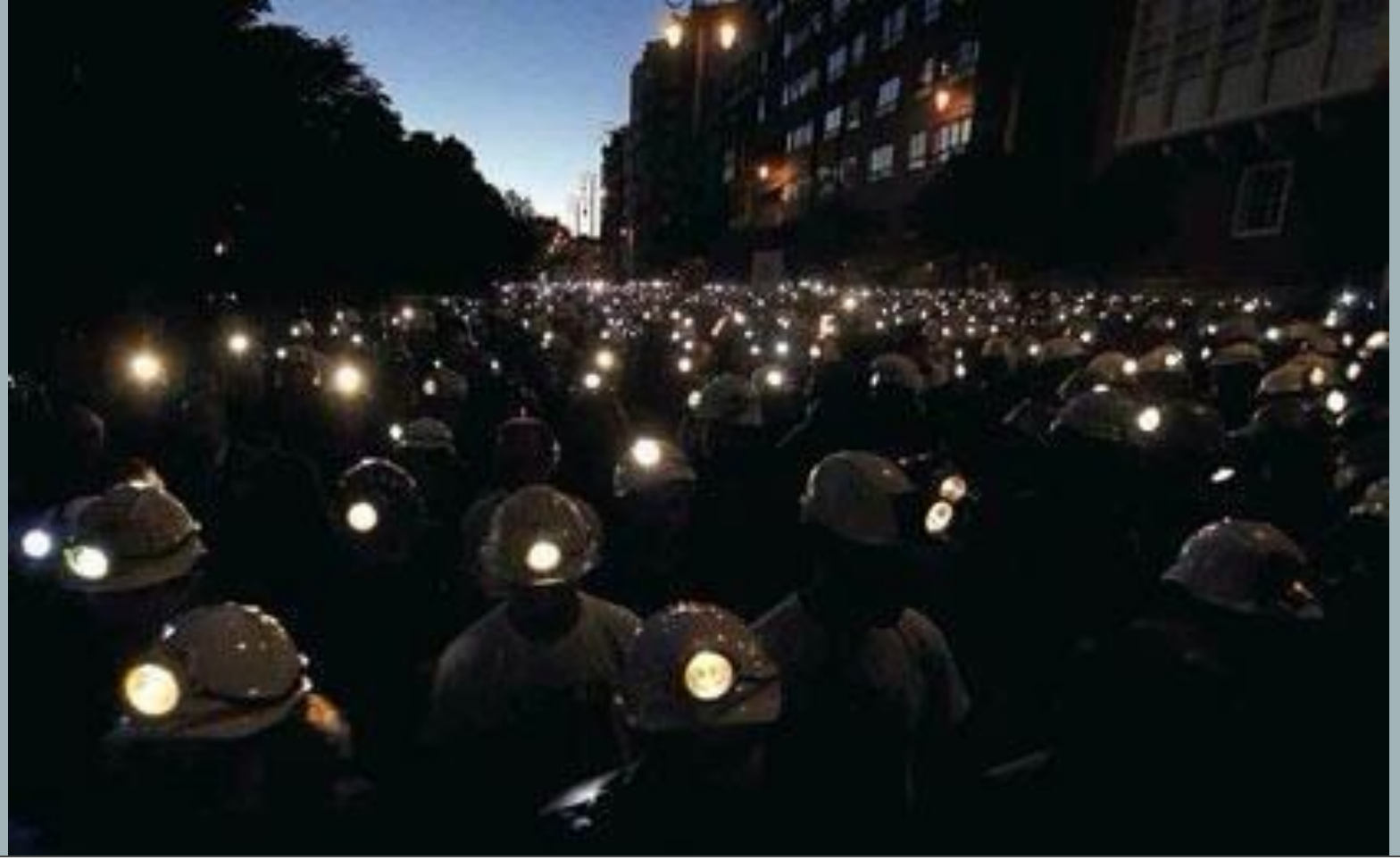

Soma / Manisa…

Thanks for listening

drmehmetergin@gmail.com