Opportunistic infections: two related cases

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Aim

• To present two related clinical cases with regards to:
  - clinical features
  - diagnostic work up
  - management challenges (present and future)
Case 1: 61 year old Polish man

Background: Type 2 DM

February 2011
- Poor vision and floaters in right eye
- Valganciclovir 900mg bd for 3 weeks

August 2011
- Vitrectomy and topical steroids

October 2011
- Recurrent CMV retinitis,
  Valganciclovir 900mg bd for 3 weeks then 900mg od for prophylaxis

October 2012
- Valganciclovir 900mg od
Case 1: continued

January 2016
Retinal detachment
Valganciclovir 900mg bd for 3 weeks, then od lifelong

April 2016
PCP

May 2016
Oral candida
EBV viraemia (log 4.42)
Bronchiectasis on CT
Case 2: 58 year old Polish man

Background of Asthma

June 2013
- H. Influenzae LRTI
- Bronchiectasis on CT

July 2013
- Infective exacerbation of bronchiectasis

July 2014
- PCP

December 2014
- LRTI, RSV

June 2015
- Recurrent PCP
Immunology Investigations

Both brothers

- Normal Igs (raised polyclonal IgA)
- Normal IgE
- Normal Hib/tetanus/pneumococcal Ab
- Normal CD4 count
- Normal T-cell subsets
- Lymphocyte proliferation (PHA, OKT3) Normal
- CMV Specific CD8+ T cells Normal
- TCR beta repertoire Normal
- Complement functional studies Normal
- TLR assay Normal
- Neutrophil Function Normal
An immunodeficiency?

Antibody mediated
(sino-pulmonary infections with encapsulated bacteria)

Check Immunoglobin, specific Ab to Tetanus/pneumococcus

Normal immunity. Consider complement deficiency

Phagocytic disorder
Recurrent severe bacterial or fungal infections

Check WCC and differential count (neutropenia, leukocytosis)

Normal
Consider chronic granulomatous disease

Primary T cell
PCP, chronic candidiasis and/or diarrhoea, lymphopenia

T cell count >200
Yes
Assess T cell function with mitogens and antigens

Family Tree

? X-linked recessive pattern
Summary of infections

Case 1
- CMV retinitis R eye
- PCP
- Bronchiectasis
- Recurrent oral candida
- EBV viraemia
- Fungal skin infection
- Type 2 diabetes mellitus

Case 2
- Recurrent PCP
- Bronchiectasis
- Recurrent shingles
- EBV viraemia
- Warts on hands and feet
- Abdominal pain and diarrhoea
100000 Genome - BRIDGE Project
WGS method

X-Linked DKC-1 mutation
DKC1 mutation

Causes dyskeratosis congenita (DC) in children

‘Classic triad’ of:
- abnormal skin pigmentation
- nail dystrophy
- oral leukoplakia

Hoyeraal-Hreidarsson syndrome
- Severe form
- X-linked

DC also associated with:
- bone marrow failure
- pulmonary fibrosis
- epiphora/excessive tears, exudative retinopathy
- developmental delay
- oesophageal strictures
- liver disease
- cancers
Telomere length by Flowfish (total lymphocytes)
Management

- PCP prophylaxis
- CMV prophylaxis – not for both
- MAI prophylaxis
- Immunoglobin therapy
- EBV reactivation – will this need treating? (Rituximab ?)
- Bone marrow Transplant
- Monitoring for bone marrow failure, malignancy
Summary

• Consider primary immunodeficiency in unusual presentations of infection

• Diagnosis can be difficult

• Management commonly involves a multidisciplinary team approach
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