Anti-Fungal Management in Haem-Onc

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Anti-Fungal Management in Haem-Onc

- The Patient at the Centre of IFI Management: Putting Theory Into Practice
Anti-Fungal Management in Haem-Onc

Optimising management
Anti-Fungal Management in Haem-Onc

- **Integrated Care Pathways (ICP)**
- **Barts Algorithm**
- **Diagnostics**
What is an integrated care pathway (ICP)?

- A *multidisciplinary* outline of patient care within an *appropriate timeline*

- Variations from the ICP may occur to meet needs of individual patients

- Reduce unnecessary variations in care/outcomes
- ‘Care partnerships’
- Empower patients and carers

Bandolier www.medicine.ox.ac.uk
What is an integrated care pathway?

- ICPs can support clinical governance/reduce risk

- Incorporate ICP into *organisational strategy*
Who should be involved?

- Patients
- Managers
- Healthcare professionals:
  - nurses
  - clinical team
  - Microbiologists
  - ID phycisions
  - radiologists
  - pharmacists
  - respiratory physicians etc.
Formulating an ICP
For YOUR Centre

Agrawal S, et al. Optimizing management of invasive mould diseases
J Antimicrob Chemother 2011, 66, Suppl. 1: i45 - 53
Anti-Fungal Management in Haem-Onc - ICP

**Prophylaxis**

Population (High risk)

Preventative measures

None

HEPA

Prophylaxis

None

Mould inactive

Mould active

TDM

Organisational Strategy
Business managers
Significant capital cost
Time-scale
Anti-Fungal Management in Haem-Onc - ICP

Diagnostic-driven

Fever → Clinical features → Biomarker screening

Investigation

Which tests
How often
Internal vs external testing
Cost
Reporting times

Treatment

Follow-up

Discontinuation of treatment

Follow-up
**Diagnostic-driven**

Anti-Fungal Management in Haem-Onc - ICP

1. **Fever** → **Clinical features** → **Biomarker screening**
2. **Investigation**
3. **Treatment**
4. **Follow-up**

**Which tests**
- Radiology dept
- Reporting times
- BAL? Respiratory opinion?
- Cost

**Discontinuation of treatment** → **Follow-up**
Empirical Anti-Fungal Management in Haem-Onc - ICP

- **Refractory fever (3-7 days)**
- **Clinical features**
- **Treatment**
- **Investigation**
- **Follow-up**
- **Discontinuation of treatment**
- **Follow-up**
Empirical

- No diagnostic facilities available
- Use only to buy time

Refactory fever (3–7 days) → Clinical features →

Treatment → Diagnosis

Continue/change treatment → IMD

IMD not confirmed → Review treatment*

Response at day 7

- Yes
  - Duration of therapy ‘Step down’
  - Out-patient follow up

- No
Anti-Fungal Management in Haem-Onc - ICP

Diagnostic-Driven

Diagnostic driven
- Screening tests implemented
- Results same/next day
- CT scan accessible
- Bronchoscopy available

CT abnormal Screen pos
- Probable IFD

CT suggestive Screen neg
- IFD? Other causes?

CT non-specific Screen neg
- Any case possible

CT normal Screen pos
- False-positive test or extrapulmonary IFD

CT normal Screen neg
- Rules out IFD

Further diagnosis*
- IMD
- IMD not confirmed

Treatment

Response at D7

Review treatment!
Antifungal Strategies And ICPs

Little schoolboy enjoys picking his nose
What Is Your IFD Strategy In Haem-Onc?

① Empirical

② Diagnostic-Driven

③ Pre-Emptive / Screening

④ No Strategy
What Tests Do You *Routinely* Use?

1. 1-3-β-D-glucan
2. Galactomannan
3. PCR (for aspergillus)
4. CT chest
5. 4 + any others
Anti-Fungal Management in Haem-Onc

- Integrated Care Pathways (ICP)
- Illustrative case – for some fun!
- Barts Algorithm
- Diagnostics
Invasive Fungal Infections: Challenges in clinical practice

The disappearing nose!
Invasive Fungal Infections: Challenges in clinical practice

- 2001: 16yo man: Pre – B ALL
- Dec 07: Relapse
- Jan 08: CR 2
- Feb 08: Neutropenic sepsis
  - D7 – afebrile + neuts
  - Saddle nose / “boxer’s nose”
  - IFD clinically
  - L. Amphi 3mg / Kg
    (Flucon. Prophylaxis)
Invasive Fungal Infections: Challenges in clinical practice

- Cy / TBI allograft planned in 3 weeks

Ix :

- MRI + ENT review
T1 pre and post gadolinium

High T2

Low T1
Invasive Fungal Infections: How would you manage the patient?

1. Stop anti-fungals
2. Surgical intervention
3. Request a CT chest...
4. Blood tests - GM, PCR...
5. Cancel the allograft

(Well; afebrile; normal neutrophils/renal/liver function)
Invasive Fungal Infections: If fungal, which organism?

1. Aspergillosis
2. Mucormycosis
3. Candidosis
4. Other fungal
5. Not fungal
6. The patient is a boxer!
Invasive Fungal Infections: Would you change treatment?

1. Continue L. Ampho 3mg/kg
2. High-dose L. Ampho
3. IV voriconazole
4. Caspofungin
5. Posaconazole
6. Combination
Invasive Fungal Infections: Challenges in clinical practice

What happened...

1. Biopsied
2. ‘Aspergillus sp.’
Invasive Fungal Infections: Challenges in clinical practice

Does this alter your management?

YES!
Empirical therapy: clinical practice

No Diagnosis

No Organism

I’m Just Guessing
IFD Strategies At Barts 2000 - 2012
Patients at high risk of IFD

Prophylaxis: fluconazole

Clinical suspicion of IFD

CT chest

L-AmB 3 mg/kg

Fever

If fever alone in a ‘well’ patient: Stop L-AmB?

Negative

Positive

L-AmB 3 mg/kg

BAL – GM
EBC – GM, PCR
IFD: strategy at Barts 2008 - 2011

Patients at high risk of IFD

Prophylaxis: fluconazole

Clinical suspicion of IFD

L-AmB 3 mg/kg

CT chest

Positive

EBC – GM, PCR

Negative

L-AmB 3 mg/kg

If fever alone in a ‘well’ patient: Stop L-AmB?

GM Twice Weekly

72 h

Fever Imaging
Barts anti-fungal algorithm 2012
Positive investigations for IFI on BAL

**Response at day 7**
- Clinical resolution of fever / clinical signs symptoms and
- Serum GM negative (if previously positive) and
- Patient able to take oral medication,
- **Change to oral Voriconazole**
  (Overlap for 48 hours with IV AmBisome)

**Continue until:**
- Neutrophils are greater than $1 \times 10^9/L$ and
- Completion of chemotherapy
- Repeat imaging is NOT routine – discuss with consultant

**If evidence of aspergillus:**
- change to IV Voriconazole

**Consultant decision is essential:**
- For out of hours initiation
- If fever is main / only clinical sign
- If change of antifungal within 7 days
- If initiation when other pathogens have been identified

**Alternatives to AmBisome:**
- Voriconazole
- Micafungin
- Posaconazole

If alternative agents are used investigations should still be as outlined above.

**No Response at day 7**
(don’t change prescription before 7 days of treatment)
- Continued persistent fever/other signs/symptoms
- GM positive

MDT review
Repeat GM / infective screen
Repeat CT chest/other imaging

**Options for unwell patients:**
1. Change anti-fungal
2. Combination antifungals - confirm with Dr Agrawal
Barts anti-fungal algorithm 2012: impact

- Tighter control on starting/stopping
- Switch from caspofungin to micafungin
- 50mg daily AmBisome prophylaxis for ALL induction (from 7mg/kg/week)
- IV voriconazole if evidence of IA
- Outpatient prescription pro-forma

Antifungal cost savings: £200k in first year
Empirical therapy: clinical practice

No Diagnosis
No Organism
I’m Just Guessing
Future Anti-Fungal Management

- Diagnostic Driven + TEAM
- Look in the right place! Early BAL

- GM, glucan, PCR + LFD?
- CT scan

- PLA – “immuno-PCR”
- Siderophore bioassays/imaging reagents
Further diagnostics…

1) PCR
   - Pan – Aspergillus
   - 100% efficiency
   - 1 genome


2) ‘Lateral Flow Device’
   - Antigen secreted by growing hyphae of *Aspergillus*
   - 15 min assay
   - Superior to GM

At risk

Primary Prophylaxis
- AML/ALL
- Auto/Allograft
- R-CODOX-M/IVAC
  - Fluconazole 400mg PO OD
- UKALL 14 induction I only
  - Ambisome 50mg IV OD
  - 2nd choice - micasfungin 50mg IV OD

72 h

Clinical suspicion of IFI;
- Persistent >72 hrs or relapsing fever
  +/- clinical signs AND
- No other positive cultures

Order CT Chest
- Other imaging, e.g. sinus/head/abdomen, if clinically indicated
- Order Serum Galactomannan (GM) for 2 consecutive days

Triple Test Strategy
- GM
- PCR
- LFD

Awaiting results

GM negative and CT normal or non specific changes
- Continue Fluconazole

GM positive (x2) and CT normal
- Do not start treatment unless patient unwell.
- Continue Fluconazole

GM negative and CT findings suggestive of IFI
- Do not start treatment unless patient unwell.
- Continue Fluconazole

GM positive (x2) CT non specific changes / findings suggestive of IFI
- Stop fluconazole
- Start Ambisome 3mg/kg

Non pulmonary IFI?
- Imaging - sinus/head/abdomen

Pulmonary IFD?
- Bronchoscopy
- BAL
Triple Test Study in Haem-Onc at Barts

- BAL PCR +ve - 100% GM and LFD positive
- 25 BALs - 5 triple positive
- Blood/serum - GM and LFD negative
- No correlation with EORTC/MSG score

Validation samples (Austria)
- 11 BALs proven IA - all triple positive
- 21 BALs ‘no’ IA - 3 triple positive!

All PCR +ve cases are GM and LFD positive
SAVE THE DATE: Friday 18 October 2013

9th Annual Fungal Update Meeting
Great Hall, St Bartholomew’s Hospital, London
10.00 am – 4.00pm

Programme:
➢ commissioning challenges for anti-fungals within the new NHS

➢ optimising anti-fungal management: stewardship and algorithms in different Trusts

➢ highlights from TIMM 2013

➢ update on novel diagnostic tests

➢ clinical data: GM/LFD/PCR – Cardiff vs Barts vs Austrian
All comments welcome