ASIA FUNGAL WORKING GROUP
an ISHAM working group

ISHAM
INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

MMTN
MEDICAL MYCOLOGY TRAINING NETWORK

Pulmonary aspergillosis in a patient with hyper-IgE syndrome

Prof Malcolm Richardson, PhD, FRCPath, FRSB, FECMM
Guangzhou Centre for Fungal Diagnostics and Research, China, and
University of Manchester, UK

http://www.richardsonbio.cn

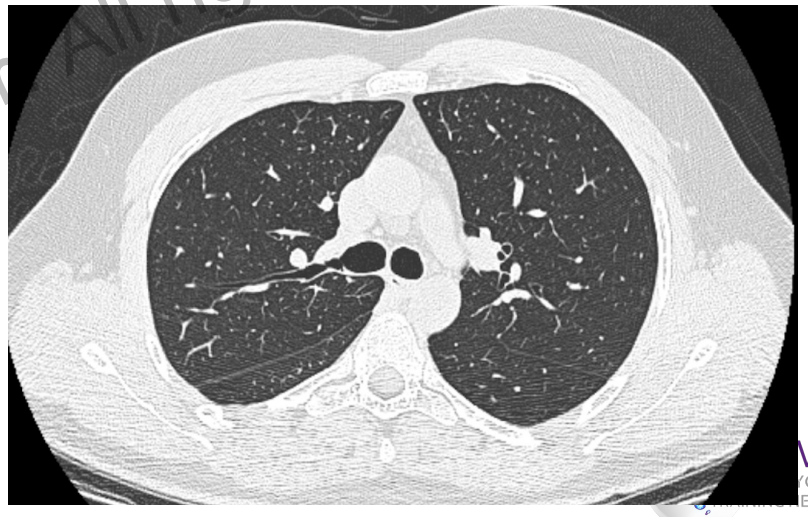
Disclosures

- The speaker declares no conflict of interest.

MMTN
MEDICAL MYCOLOGY
TRAINING NETWORK

Past medical history

- 45-year-old male
- Hyper-IgE syndrome (STAT3 mutation): Autosomal dominant primary immunodeficiency, recurrent eczema, skin abscesses, lung infections (leading to large cavity formation), sinusitis eosinophilia and high serum levels of IgE



CT with contrast 14 years ago

Past medical history

- Right-sided thoracotomy for staphylococcal lung abscess (37 years ago)
- Chronic pulmonary aspergillosis (13 years ago) with pan azole-resistant *Aspergillus fumigatus* (5+ years ago)
- Other previous medical history:
  - Chronic rhinosinusitis, ongoing problem (FESS – functional endoscopic sinus surgery – 11 years ago)
  - Ulcerative colitis
  - Chronic kidney disease
  - Prostatitis due to ESBL-producing *Escherichia coli*

Mycology

	Aspergillus DNA	Ct value
Aspergillus PCR test	Positive	28.8

Pyrosequencing confirmed L98H/TR34 polymorphism.
Expected Susceptibilities: ITR R, VOR I/R, POS S/I/R.
and G54R polymorphism: ITR/POS R, VOR S.
See also M,18.01711
Aspergillus DNA DETECTED
Strong signal, aspergillosis likely

5.3 years ago

Susceptibility results for Aspergillus fumigatus complex

	All values in mg/L		
	MEC	MIC	MFC	RESULT
Itraconazole		>8	>8	R
Amphotericin		0.5		S
Voriconazole		2	2	I
Posaconazole		0.5		R
Isavuconazole		8	8	R
Micafungin		<0.008		

3.5 years ago

Pyrosequencing to determine triazole resistance in
Asp. fumigatus cyp51A target.

Pyrosequencing confirmed TR34/L98H polymorphism.
Expected Susceptibilities: ITR R, VOR I/R, POS S/I/R.

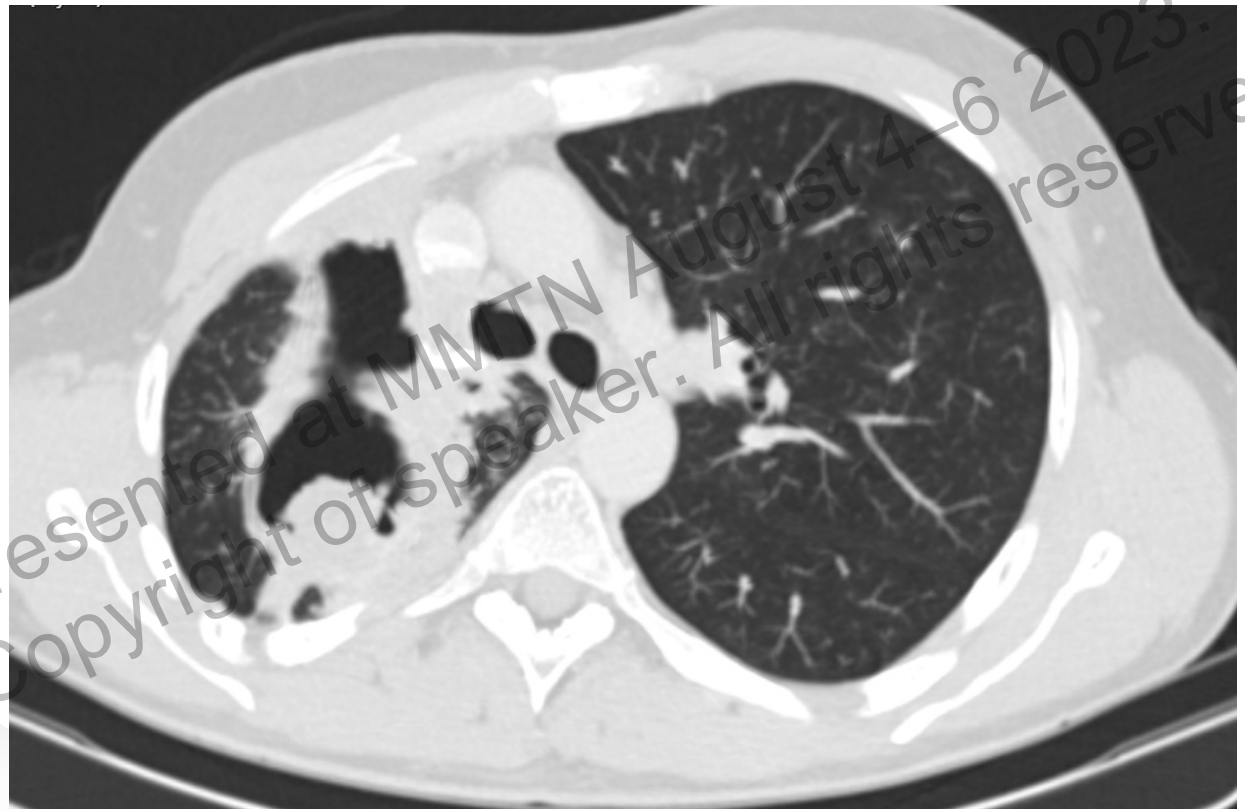
3.3 years ago

MMTN
MEDICAL MYCOLOGY TRAINING NETWORK

Antifungal history

- Itraconazole until 5 years ago, stopped due to treatment failure with pan-azole resistance
- Nebulised amphotericin B trialled but unable to tolerate due to bronchospasm
- Two 3-week pulses of micafungin with poor control of chronic pulmonary aspergillosis
- Swapped to IV Ambisome but stopped due to acute kidney injury
- 3-month course of micafungin pre- and post-lobectomy
- Posaconazole until 2 years ago, stopped due to re-emergence of pan-azole resistance.
- Back to micafungin pulses

CT Thorax 2.4 years ago

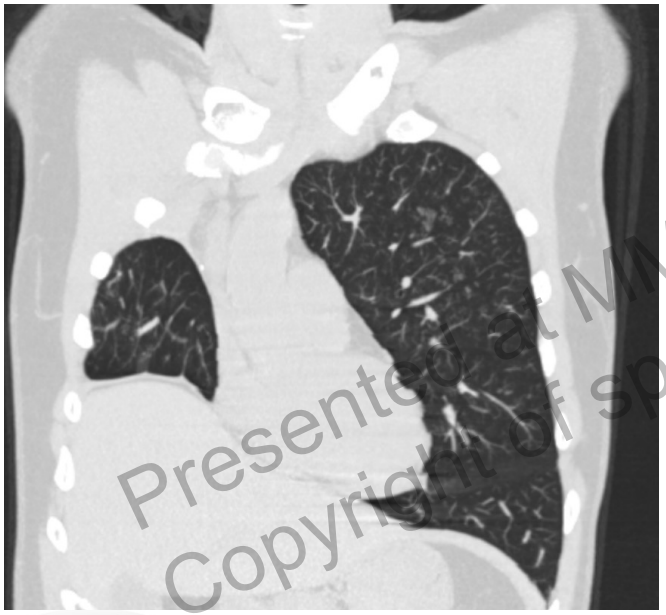


MMTN
MEDICAL MYCOLOGY
TRAINING NETWORK

Past medical history

- Semi-invasive slowly-progressive pulmonary aspergillosis with recurrent isolation of pan-azole *Aspergillus fumigatus*
- Right upper lobe and middle lobe lobectomy (1.7 years ago) followed by right lower lobe lobectomy (1.5 years ago)

CT Thorax after right upper lobe and middle lobe lobectomy 1.7 years ago



CT Thorax 1.3 years ago after completion right-sided pneumonectomy

Past medical history

- 1 year ago, reduced intensity conditioning sibling donor stem cell transplant 14/04/2022 FluMelCampath 100mg, CMV -/+, ABO B+/O+, sex mismatched
- Ciclosporin for GVHD prophylaxis, prednisolone 5 mg OD, acyclovir 800 mg BD, trimethoprim/sulfamethoxazole 480 mg OD, mesalazine, ursodeoxycholic acid, lansoprazole, midodrine, folic acid, carbocisteine, fluticasone inhaler
- Micafungin and IV Ambisome peri-BMT
- Back to micafungin pulses but severe side effects

Mycology

- Until 2 years ago:
  - Sputum GM 5.4–8.4
  - Asp IgE 38–49 (0–0.35) kAU/L
  - Asp IgG 100–295 (0–40) mg/L
- Now Asp IgE <0.1, Asp IgG 13, sputum GM 0.1
- Not productive, no recent cultures or Asp PCR results

Current status

- Off all antifungal therapy for 6 months
- CPA seems to be in remission following right sided pneumonectomy and subsequent stem cell transplant to correct primary immune deficiency (hyper IgE syndrome)
- Exercise tolerance still limited, referred to pulmonary rehabilitation
- Skin GvHD but managing

FBC	
WBC	09/05/23 6.3
RBC	09/05/23 3.75 ↓
Hb	09/05/23 120.0 ↓
Hct	09/05/23 0.354 ↓
MCV	09/05/23 94.4
MCH	09/05/23 32.0
MCHC	09/05/23 339
RDW	09/05/23 13
Plts	09/05/23 244
Neutrophils	09/05/23 4.56
Lymphocytes	09/05/23 0.55 ↓
Monocytes	09/05/23 0.63
Eosinophils	09/05/23 0.48 ↑
Basophils	09/05/23 0.05
Reticulocytes	10/09/22 47
Reticulocyte Hb	10/09/22 37.8 ↑
RET %	10/09/22 1.57 ↑
Immature Granulocytes	09/05/23 0.02
NRBC	09/05/23 0.00

CT Angiogram now

- Findings:
  1. Satisfactory opacification of the normal calibre pulmonary trunk (502 HU). No pulmonary emboli. Normal cardiac size. No size significant intrathoracic lymphadenopathy

  2. Median sternotomy. The bony sternotomy has yet to heal with slight AP displacement of the inferior sternal fragments. **Previous right pneumonectomy with appropriate mediastinal shift to the right. There has been a reduction in fluid within the right pneumonectomy space since January 2022 and resolution of a moderate sized pericardial effusion. The left lung is clear. Tiny right paratracheal air cyst.**

  3. Rather patulous oesophagus. The visualised upper abdominal viscera are unremarkable. No destructive bony lesion

Questions

- Interpretation of antibody levels post BMT?
- Duration of treatment?
- With what? How?
- How do we monitor?

CASE REPORT

Respirology Case Reports | WILEY

Chronic pulmonary aspergillosis in a patient with hyper-IgE syndrome

Keisuke Kasuga | Keitaro Nakamoto | Kazuyuki Doi | Nozomi Kurokawa | Takeshi Saraya | Haruyuki Ishii

2021

- Hyper IgE syndrome in chronic pulmonary patient
- 19-year-old male: History of bacterial pneumonia and skin infection
- Elevated eosinophil count and high serum IgE
- CT: pneumatocele and bronchiectasis
- Genetic mutation: *STAT3 GENE* – Hyper IgE syndrome
- 14-months later: Blood-tinged sputum and hemoptysis
- Chest CT: pneumatocele wall thickening/fungus ball/consolidation
- Sputum culture: *Aspergillus fumigatus*
- *Aspergillus* precipitins: Positive
- Galactomannan: Positive
- CPA diagnosed
- Treatment: Voriconazole/right bronchial embolization
- Symptoms improved
- Patient discharged

MMTN
MEDICAL MYCOLOGY TRAINING NETWORK

Thank you