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Title	Aspergillus: Allergic Bronchopulmonary Aspergillosis & Aspergillus Bronchitis
Version	3.0

1. Introduction

Aspergillus fumigatus is an environmental fungus found in soil and decaying vegetable matter. It is a common airway coloniser in Cystic Fibrosis, often without causing harm. But it can be pathogenic, presenting as:

- Allergic Bronchopulmonary Aspergillosis (ABPA) - lung disease due to hypersensitivity to Aspergillus fumigatus (rarely sometimes due to other Aspergillus strains or other fungi).
- Aspergillus bronchitis, an emerging aspergillus problem
- Aspergillus invasive infection complicating lung transplantation and immunosuppression
- Aspergilloma, a rare presentation in advanced CF lung disease

2. Allergic Bronchopulmonary Aspergillosis (ABPA)

2.1. Presentation

Increased respiratory symptoms, including wheeze, worsened lung function tests. Suspect in acute clinical exacerbation when response to antibiotic treatment is poor or atypical. Screening as part of CF annual review will help to identify allergic sensitisation and progression to disease.

2.2. Diagnosis

There is no international consensus regarding diagnostic criteria. There is substantial overlap of features between CF and ABPA which complicates the "major / minor criteria" approach. The following diagnostic criteria are modified from the Consensus Conference of the Cystic Fibrosis Foundation[1] for the diagnosis of ABPA in patients with CF:

1. Acute or subacute clinical deterioration (cough, wheeze, exercise intolerance, exercise - induced asthma, decline in lung function or increased sputum production) not attributable to other aetiology.
2. New or recent changes on chest radiograph or CT scan (viz. infiltrates, mucus plugging or central bronchiectasis) that have not cleared with antibiotics and physiotherapy.
3. Immediate cutaneous reactivity to A. fumigatus (skin prick test 3mm > control) OR elevated Aspergillus specific IgE.
4. Precipitating IgG antibodies to A. fumigatus.
5. Total serum IgE > 1000 IU/ml OR four-fold increase in IgE titres.

Note: positive respiratory culture for Aspergillus is not essential for the diagnosis of ABPA.

2.3. Treatment Concept

Treatment concept is with corticosteroids to address allergic inflammation, plus antifungal therapy to reduce antigen burden and act as a "steroid-sparing agent".

2.4 Steroid Therapy

Preferred corticosteroid is oral prednisolone. A three-month tapering course is recommended as first line treatment. Dexamethasone and pulsed methylprednisolone may be considered in individual cases at consultant discretion.

2.5. Itraconazole

May allow lower steroid doses in the treatment of ABPA but is poorly absorbed when given orally to persons with CF.

Adverse Reactions & Cautions:

- Itraconazole absorption may be impaired in patients on ranitidine or omeprazole and these should be stopped if possible.
- Inhaled corticosteroids should be discontinued when starting itraconazole as it may increase their systemic bioavailability
- Caution when co-existing liver dysfunction

Monitoring:

- Levels should be measured after at least 14 days of therapy. Dose adjustment and/or liquid formulation may be required if levels are low.
- Liver function tests pre-treatment, then 1- and 3-months post treatment should be measured. Additional monitoring may be required if there is a history of liver dysfunction.

2.6. Voriconazole has greater bioavailability than itraconazole but is more expensive and has a significant number of interactions with other drugs. Alternative antifungal agents such as posaconazole and amphotericin may be considered at consultant discretion in individual cases.

2.7. Treatment response should be judged by symptom resolution. Improvement in spirometry, resolution in radiographic changes and a fall in IgE by >35% in 2 months are also supportive of remission.

2.8. Drug Doses

Drug	Route	Dose	Frequency	Duration
Prednisolone *...followed by...* *...taper off...*	Oral	1 mg/kg *0.5 mg/kg* *0.5 mg/kg*	once daily *once daily* *alternate days*	4 weeks *4 weeks* *4 weeks*
Itraconazole	Oral	< 12 years 5 mg/kg (max 200 mg) * > 12 years 200 mg *	twice daily twice daily	3 months 3 months
Voriconazole	Oral	2-12 years 9 mg/kg (max 350mg) 12-18 years and weight < 40kg 200 mg then 100 mg (increase to 150 mg if necessary) 12-18 years and weight > 40kg 400 mg	twice daily twice daily twice daily twice daily twice daily	Maintenance Two doses Maintenance (review 3/12) Two doses Maintenance

		then 200 mg (increase to 300 mg if necessary)		(review 3/12)

** Itraconazole dose may need review with itraconazole levels*

3. Aspergillus Bronchitis

3.1. Diagnosis: consider this newly recognised disease entity in patients with respiratory deterioration not responding to appropriate antibiotic treatment. Patients may not meet the diagnostic criteria for ABPA but may have Aspergillus isolation in sputum samples and elevated Aspergillus-specific IgG antibody levels. IgE levels are typically not elevated.

3.2. Treatment: optimal treatment strategies are unknown. An initial three-month course of antifungal therapy (itraconazole as per ABPA recommendations above) without corticosteroids is recommended.

4. References

1. Cystic Fibrosis Foundation Consensus Conference. Clin Infect Dis. 2003 Oct; 37 (Suppl 3), S225-64.PMID: 12975753