

8. FUNGAL OPPORTUNISTIC INFECTIONS

8.1 Introduction

Fungal infections are quite common in HIV infected patients ranging from mild skin infections to debilitating disorders such as oesophageal candidiasis and lethal infections such as cryptococcal meningitis. Management of some of the milder fungal infections, such as body ringworm, is well documented in EDLIZ. Through the Diflucan Pfizer Program (DPP), fluconazole is available as a donation in the public sector. **It is free for use only for two conditions: oesophageal candidiasis and cryptococcal meningitis.** (See also Chapter 21- Skin Conditions)

8.2 Oesophageal candidiasis

Oesophageal candidiasis occurs commonly in persons with HIV infection, occurring in up to one third of HIV infected individuals. This condition is most likely to occur in persons who have peripheral blood CD4 lymphocyte counts of less than 200/mm³.

8.2.1 Diagnosis

Patients with oesophageal candidiasis usually present with odynophagia (pain on swallowing) and dysphagia (difficulty with swallowing). If odynophagia (not dysphagia) is the most prominent symptom, the patient is most likely to have ulcerative oesophagitis which could be due to candidiasis or herpes simplex virus infection. Heartburn can also occur. The clinical diagnosis is usually made after a history is taken and a clinical examination is carried out. However the diagnosis can only be confirmed after an upper GI endoscopy is carried out and the oesophageal mucosa visualized directly. Endoscopy should be carried out only after empiric treatment for oesophageal thrush has failed in HIV positive patients with dysphagia and/or odynophagia. Upper GI barium studies should not be used to diagnose oesophageal candidiasis.

8.2.2 Management

Non-drug related treatment

A soft diet may reduce the symptoms of dysphagia. Avoid drinks that are either too hot or too cold when there is odynophagia.

Drug related treatment

Preferred therapy - Fluconazole 200mg daily for two to three weeks.

Alternative therapy – Ketoconazole 200mg twice a day for two weeks.

Consider endoscopy if there is no response after 4 weeks from starting Fluconazole therapy.

TREATMENT OF OESOPHAGEAL CANDIDIASIS						
Drug	Codes		Adult dose	Route	Frequency	Duration
Fluconazole	C	V	200mg	PO	OD	2-3 weeks (Max 4 weeks)
OR						
Ketoconazole	C	V	200mg	PO	BID	2 weeks

1. There is no role for maintenance fluconazole therapy
2. There is no role for topical anti-fungal therapy
3. Consider referral for endoscopy if there is no response in 4 weeks after starting treatment

Nursing Care Requirements

Encourage adequate nutrition by emphasizing eating of small soft but frequent meals. Counsel regarding treatment compliance and adherence to therapy. Regular cleaning of the mouth / brushing of the teeth should be advised. Educate the patient to recognise the symptoms suggesting recurrence of the infection so that they can promptly return for further treatment.

Note that there are potential drug interactions between fluconazole and rifampicin, warfarin and antiepileptic drugs such as phenytoin.

Counseling Requirements

Note that oesophageal candidiasis is an AIDS defining illness and hence, refer the patient for VCT if they have not undergone HIV testing before.

Post Admission care / Discharge plan

There is no place for maintenance fluconazole therapy here, but long-term cotrimoxazole prophylaxis should be commenced.

Social Services Support

Consider referral to the local National/District Aids Council for material assistance. If the patient cannot afford the hospital/ medication fees, refer to the Social Services Department for possible “free” treatment cover note.

8.3 Cryptococcal meningitis

This is a fungal CNS infection which is quite common in our wards and, in some instances, will be the first AIDS defining illness that the patient will present with. There may, occasionally, be skin involvement with lesions resembling molluscum contagiosum. CNS involvement may also occur in the form of single or multiple intracranial masses (cryptococcomas). The prognosis without specific treatment is poor with survival being less than six months following diagnosis in most instances. Management of raised intracranial pressure is necessary for optimal care.

8.3.1 Diagnosis

Symptoms- Patients presents with headaches of varying severity -usually of a fairly chronic duration. There is a fever and perhaps altered mental status. This disease has to be suspected in HIV positive patients who present with unexplained neurological signs. Meningeal symptoms causing neck stiffness are usually present. Do a lumbar puncture and send the CSF for India ink staining for the cryptococcus organism. A serum cryptococcal antigen test can also be carried out where possible if the CSF results are negative. The cryptococcal antigen is positive in > 99 percent of cases of cryptococcal meningitis.

8.3.2 Management**Non-drug related treatment**

Daily lumbar puncture taps have been shown to relieve the headache and improve the survival of these patients by relieving raised intracranial pressure. This will involve taking off at least 10 – 20ml of CSF initially and

may need to be repeated on a daily basis. The aim is to keep the CSF pressure at less than 20cm.

Drug related treatment:

First Line - Ideally Flucystosine (100mg/kg/day in 4 divided doses) and Amphotericin B (0.7mg- 1mg/kg/day daily) are the best combination in the first two weeks of treatment.

Thereafter, Fluconazole 400 - 800mg daily for 8 weeks and then reduce to maintenance Fluconazole at 200mg /day indefinitely. Maintenance Fluconazole should be continued for life.

Alternative therapy – Amphotericin B 0.7mg- 1mg/kg/day daily for 2 weeks and then Fluconazole 400 – 800mg daily for 6 – 8 weeks followed by maintenance therapy. Maintenance Amphotericin B weekly or biweekly is a poor alternative.

TREATMENT OF CRYPTOCOCCAL MENINGITIS – INDUCTION PHASE						
Drug	Codes		Adult dose	Route	Frequency	Duration
Amphotericin B	B	V	0.7mg/kg to 1mg/kg	IV	OD	14 days
PLUS						
Flucytosine	A	V	25mg/kg	PO	QID	14 days
OR						
Fluconazole	B	V	400-800mg	PO	OD	6-8 weeks

TREATMENT OF CRYPTOCOCCAL MENINGITIS – MAINTENANCE						
Drug	Codes		Adult dose	Frequency	Duration	
Fluconazole	B	V	200mg	Once daily	Long term	

Adjunctive therapy:

1. Mild or Moderately strong analgesia eg. Paracetamol or Codeine Phosphate or Morphine 5mg every four hours may be required if codeine is not relieving the headache
2. There is need to make sure that the patient's headache is controlled using adequate analgesia. Watch out for the development of further symptoms such as the side effects of Amphotericin B such as nausea, vomiting, fever, chills and rigors as well as hypokalaemia and renal dysfunction

Nursing Care Requirements

Maintain hydration and nutritional status. Fluconazole can cause hepatotoxicity.

Counseling Requirements

Cryptococcal meningitis may be the first AIDS defining illness that the patient presents with. They may not be aware of their HIV status. Hence they will need to undergo pre-counseling for HIV testing as well as the post-counseling if the test is carried out. The patient needs to be aware of the lifelong nature of the maintenance therapy. Use of HAART is expected to favourably alter the course of the disease.

Post Admission care / Discharge plan

Refer to the National Discharge plan section as well as the Community Home Based Care section.

Social Services Support

Consider referral to the local District Aids Council for material assistance. If the patient cannot afford the hospital/ medication fees, refer to the Social Services Department for possible "free" treatment cover note.

8.4 Disseminated histoplasmosis

Cases of histoplasmosis are increasingly being seen. It is assumed that these represent disseminated histoplasmosis as the patients tend to be quite debilitated with fever and weight loss. The patients have also been HIV positive. Hepatomegaly and splenomegaly also suggest disseminated disease.

8.4.1 Diagnosis

The usual clinical scenario is that of a patient who appears to have nodular skin lesions which look like molluscum contagiosum. The lesions tend to be bigger and are more disseminated. Perforating gum and palatal lesions have also been described. A skin biopsy and microbiological investigation for fungi is the definitive test. Buccal mucosal lesions should be referred to the dentists for biopsy. Further investigations such as full blood count and liver function tests may help in assessing the patient. A chest x-ray should be performed to assess for pulmonary disease.

8.4.2 Management

Non-drug related treatment

Keep the lesions clean to prevent superadded bacterial infection

Drug related treatment

Patients with histoplasmosis need induction treatment and long-term suppressive therapy:

TREATMENT OF HISTOPLASMOSIS-INDUCTION THERAPY						
Drug	Codes		Dose	Route	Frequency	Duration
Amphotericin B	A	B	0.7-1.0 mg/kg	IV	OD	12 weeks
OR						
Ketoconazole	B	E	600 – 800mg	PO	OD	12 weeks
OR						
Itraconazole	A	N	200mg	PO	BID	12 weeks

TREATMENT OF HISTOPLASMOSIS-MAINTENANCE THERAPY						
Drug	Codes		Dose	Route	Frequency	Duration
Amphotericin B	A	B	50 mg	IV	Once a week	Long-term
OR						
Itraconazole	B	V	200mg	PO	BID	Long-term

OR						
Fluconazole	B	V	200mg	PO	BID	Long-term

NOTE:

In the presence of meningitis or septicaemia amphotericin should be used

Nursing Care Requirements

A holistic approach to the patient's problem requires that other issues such as nutrition be addressed.

Counseling Requirements

Consider sending for VCT. If the patient is HIV positive, they will need to be considered for prophylaxis against other opportunistic infections. Counsel the patient about the importance of adherence to therapy and the need to report any problems such as vomiting, abdominal pain and yellowing of eyes which may be indicative of hepatic drug side effects.

Post Admission care / Discharge plan

Make sure that the patient's discharge note is clear about the duration of therapy. The patient will need to be reviewed in the Outpatient department after two weeks of starting the antifungal therapy to assess the response as well as to assess for side effects of the drugs.

Social Services Support

For those who cannot afford their drug treatment, refer them to their nearest Social Welfare Department/local NAC offices for appropriate assistance. A letter of introduction will be required.

8.5 Pneumocystis pneumonia

Pneumocystis pneumonia (PCP) is caused by the fungus *Pneumocystis jiroveci*. The infection is seen mainly in those people whose CD4 count is less than 200/mm³. It is an important cause of pneumonia in immunocompromised people and has a high mortality. It is an AIDS defining condition.

8.5.1 Diagnosis

PCP should be suspected in an HIV positive person who presents complaining of dry cough, tachypnoea, increasing shortness of breath and a fever. The patient may appear to be fine at rest but easily get breathless

after slight exertion such as dressing. Examination of the chest shows minimal findings or is normal.

The CXR may be normal or classically shows a ground glass appearance. Arterial blood gases that show a low PO₂ in the setting of the above history and a clear CXR is suggestive of PCP. The organism is not easily isolated from the sputum. Where possible, a bronchoscopy with transbronchial biopsy and bronchoalveolar lavage should be performed. The microscopy of the fluid may show the cysts of *Pneumocystis*.

8.5.2 Management

Non-drug related treatment

High dose oxygen therapy is mandatory

Drug related treatment:

High dose cotrimoxazole 4 tablets of 480mg each (i.e., 1920mg) orally three times a day, and

Prednisolone 60mg PO OD for 14-21 days

Alternative therapy – Clindamycin 600mg four times a day with Primaquine 15mg orally daily.

All patients who have been treated for PCP should receive life long cotrimoxazole prophylaxis if they are not allergic to sulphonamides

TREATMENT OF PNEUMOCYSTIS PNEUMONIA

Drugs	Codes	Dose	Route	Frequency	Duration
Cotrimoxazole	C V	1920mg	PO	TID	21 days
OR					
Clindamycin	B V	600mg	PO	QID	21 days
AND					
Primaquine	B N	15mg	PO	OD	21 days

Plus steroids as follows:

STEROID THERAPY

Drugs	Codes	Dose	Route	Frequency	Duration
Prednisolone	B V	60mg	PO	OD	21 days

Long-term prophylaxis therapy:

COTRIMOXAZOLE PROPHYLAXIS						
Drugs	Codes		Dose	Route	Frequency	Duration
Cotrimoxazole	C	V	960mg	PO	OD	For life or until CD4+ count is consistently >200/mm ³

Nursing Care Requirements

If there has been a reaction to cotrimoxazole in the past, consider referral for rapid desensitization (see Annexe 2). Ensure that the patient is receiving their oxygen at high doses.

Counseling Requirements

Referral for VCT should be done where appropriate. Emphasise the importance of adherence to therapy and compliance.

Post Admission care / Discharge plan

Make sure that the patient is aware of their review date in the outpatients department. Also ensure that the need for prophylactic cotrimoxazole is clearly documented in the patient's discharge card and that the patient knows where to get their supplies from.

Social Services Support

Arrange for the patient to get financial assistance where appropriate.