

Fever when immunocompromised



Objectives

In this chapter you will learn:

- The potential sources of immunosuppression
- How the respiratory opportunistic infections are differentiated
- The bedside differences between the oral opportunistic infections
- What investigations should be performed on the CSF of an immunocompromised patient with neurological symptoms
- How the fungal skin rashes can be differentiated.

Patients who are immunocompromised for whatever reason are liable to contract opportunistic infections. The initial part of the history should cover details of the immunocompromised state, as in Figure 12.1.

Immunocompromised patients can have the same infections as immunocompetent people but in addition one needs to consider the infections in Figure 12.2.

RESPIRATORY INFECTIONS

History

Symptoms suggestive of a respiratory cause for feeling unwell would be:

- Dry or productive cough
- Purulent sputum with or without haemoptysis
- Breathlessness on exertion
- Night sweats, malaise and weight loss
- Previous lung disease which could lead to cavitation
- Skin rash prior to the onset of respiratory symptoms.

In HIV, opportunistic infections are more prevalent once the CD4 count is less than $200 \times 10^6/\text{ml}$. Once such an infection has been diagnosed, that is known as AIDS-defining. The full list of AIDS-defining infections is in Chapter 25.



Examination

On inspection of the patient a vesicular pruritic rash with widespread distribution should raise the suspicion of varicella pneumonia. A cachectic patient hints at tuberculosis. On auscultation of the chest there may be no additional sounds to hear or a variable distribution of crepitations. Apical crepitations are suggestive of tuberculosis. A dull percussion note, reduced breath sounds and reduced vocal fremitus may indicate an empyema occurring with nocardia infection. In addition, asking the patient to walk around with a saturation probe on a finger may elicit a decrease in saturations with exertion, as is seen in PCP and CMV pneumonia. The examination should be completed by looking in the sputum pot to check for the purulence of the sputum and for haemoptysis, which is seen with mycobacterial and nocardia infection.

Investigations

- Chest radiograph – may appear normal or show increased shadowing with an alveolar (e.g. PCP), apical (e.g. TB) or diffuse (e.g. VZV) distribution. A round lesion with a crescent of air above it describes an aspergilloma (fungal ball in previously formed lung cavity; Fig. 12.3).
- Sputum microscopy and culture – including for acid-fast bacilli (AFB), fungal hyphae and spores.
- Bronchoalveolar lavage (BAL) washings or lung tissue biopsy – microscopy for fungus of PCP.
- Serology – to identify CMV, VZV and *Aspergillus precipitans*.
- Blood cultures – for identification of MAI.

Fever when immunocompromised

Fig. 12.1 Issues related to immunosuppression

Causes	Details to cover
Immunosuppressive drug regimen	<p>Timetable and drugs involved in regimen</p> <p>Any prophylaxis given to prevent opportunistic infections</p> <p>Can regimen be reduced or stopped temporarily</p> <p>Examples of regimens:</p> <ul style="list-style-type: none"> to prevent rejection of transplanted organ to treat malignancy to prevent flare-ups in inflammatory disease such as rheumatoid arthritis, ulcerative colitis, vasculitis
HIV	<p>Latest CD4 count and viral load</p> <p>Treatment and compliance</p> <p>Previous opportunistic infections and prophylaxis given</p> <p>Date of diagnosis and source of infection</p> <p>If acquired via blood-borne source, other viruses checked (hepatitis B, C)</p> <p>Who knows diagnosis? Who must not find out?</p>
Congenital immunodeficiency	<p>Problems encountered previously</p> <p>Treatment and prophylaxis given</p>

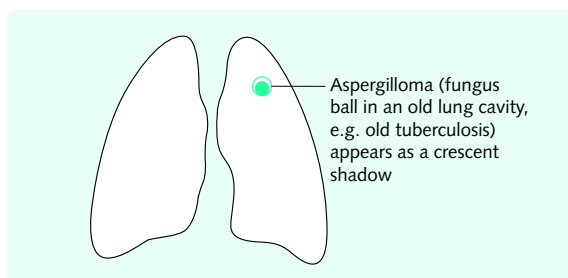


Fig. 12.3 Chest radiograph diagram showing the 'crescent' of an aspergilloma.

A summary algorithm demonstrating how to approach diagnosing respiratory infections in immunocompromised patients is shown in Figure 12.4.

ORAL INFECTIONS

History

The complaints include:

Fig. 12.2 Infections occurring in immunosuppressed patients

Respiratory infections	<p><i>Pneumocystis carinii</i> pneumonia (PCP)</p> <p>Cytomegalovirus (CMV) pneumonitis – rare in HIV</p> <p><i>Mycobacterium tuberculosis</i></p> <p><i>Mycobacterium avium-intracellulare</i> (MAI) – tends to be disseminated</p> <p>Varicella zoster virus (VZV) pneumonia</p> <p>Aspergillosis</p> <p>Nocardia</p>
Oral infections	<p>Candidiasis</p> <p>Epstein–Barr virus (EBV) – glandular fever</p> <p>Herpes simplex virus 1 (HSV-1) stomatitis</p>
Gastrointestinal infections	<p>Oesophageal or disseminated candidiasis</p> <p>CMV colitis</p> <p><i>Cryptosporidium parvum</i></p> <p><i>Isospora belli</i></p> <p>Microsporidia</p> <p><i>Mycobacterium avium</i> complex</p> <p>Giardiasis</p>
CNS infections	<p>Toxoplasmosis</p> <p>Cryptococcal meningitis</p> <p>Tuberculous meningitis</p> <p>Encephalitis (HSV, VZV)</p>
Eye infections	<p>CMV retinitis</p> <p>Toxoplasmosis</p>
Skin infections	<p>Fungal, e.g. tinea, pityriasis versicolor</p> <p>VZV (chickenpox)</p> <p>Herpes zoster (shingles)</p>

- Lesions or plaque in the oral cavity or on the lips
- Sore throat.

Examination

Inspection of the mouth may demonstrate vesicles or ulcers on the lips with HSV or white clumps/plaque on the tongue and buccal mucosa with oral candidiasis.



A differential diagnosis of white plaque on the tongue is oral hairy leukoplakia, which is associated with EBV. This can be distinguished from oral candidiasis as it extends to cover the lateral borders of the tongue which candida does not.

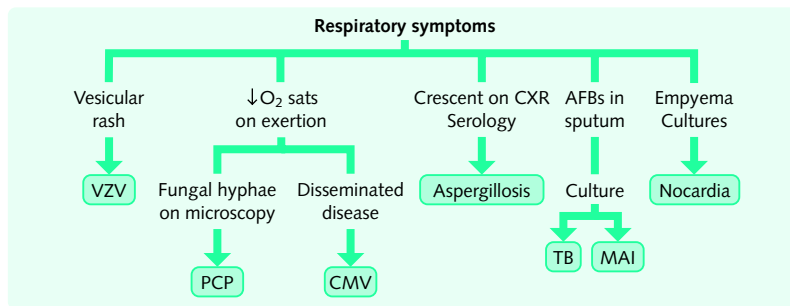


Fig. 12.4 Diagnostic algorithm for respiratory symptoms in an immunocompromised patient.

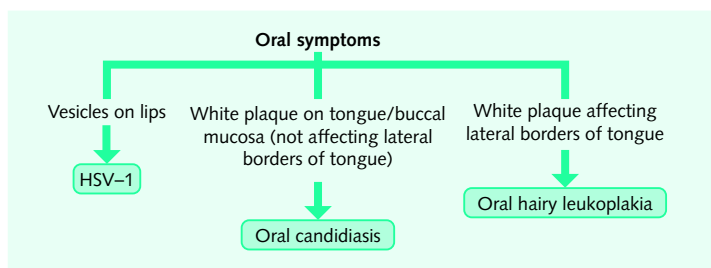


Fig. 12.5 Diagnostic algorithm for oral symptoms in an immunocompromised patient.

Investigations

Diagnosis is mostly clinically but the following may be performed:

- Microscopy and culture of oral plaque material
- Serology from vesicular fluid.

A summary algorithm demonstrating how to approach diagnosing oral symptoms in immunocompromised patients is shown in Figure 12.5.

ABDOMINAL INFECTIONS

History

The symptoms suffered are:

- Dysphagia (difficulty swallowing) and odynophagia (pain on swallowing) indicating oesophageal candidiasis
- Diarrhoea, especially if it has occurred over a prolonged period or is explosive in nature – may be watery or bloody
- Abdominal pain associated with the diarrhoea
- Malabsorptive symptoms, e.g. steatorrhoea, bloating, flatulence and weight loss
- Weight loss associated with night sweats.

Examination

On inspection, look for evidence of recent weight loss and whether the patient appears dehydrated. Check in the mouth for candida. Palpate the abdomen for tenderness and hepatosplenomegaly.

Investigations

- Stool microscopy for bacteria, ova, cysts and spores.
- Stool culture – to identify the causative organism.
- Barium swallow – shows ‘moth-eaten’ appearance to oesophagus with oesophageal candidiasis (Fig. 12.6).
- Abdominal radiograph – loops of dilated bowel are seen in CMV colitis.
- Serology – to check for CMV.
- Blood cultures – to identify MAI.
- Oesophagogastroduodenoscopy (OGD) – shows ulceration and white plaques of oesophageal candidiasis.
- Rectal tissue biopsy – for inclusion bodies indicating CMV colitis.

A summary algorithm demonstrating how to approach diagnosing gastrointestinal infections

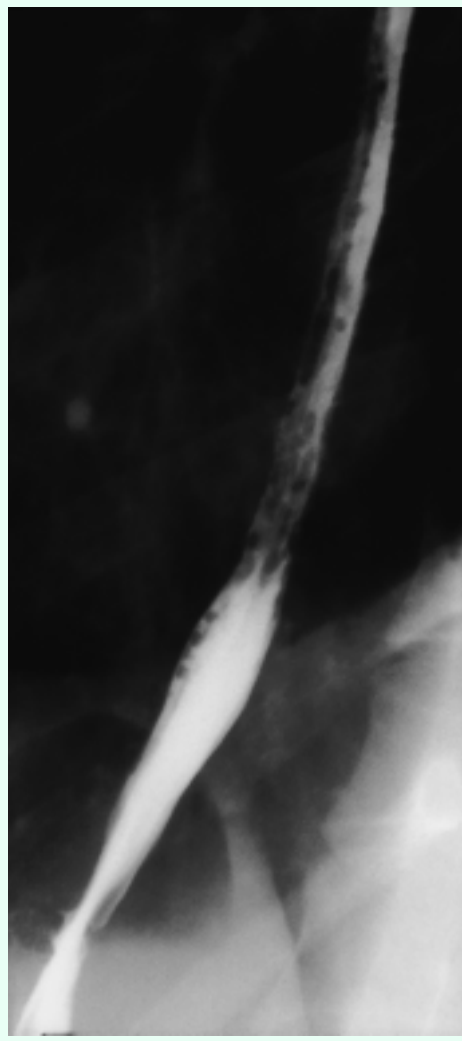


Fig. 12.6 Barium swallow showing ulceration due to candida.

Source: Conlon CP, Snyderman DR. Mosby's Colour Atlas and Text of Infectious Diseases. Edinburgh: Mosby; 2000: Fig. 9.2.

in immunocompromised patients is shown in Figure 12.7.

CENTRAL NERVOUS SYSTEM INFECTIONS

History

A number of the following symptoms may be present:

- Triad of meningitis: headache, photophobia and neck stiffness

- Cognitive impairment
- Seizures
- Focal deficits, e.g. limb weakness, visual impairment.

Examination

The Glasgow Coma Score should be calculated to assess consciousness (see Ch. 2). If possible, a rudimentary evaluation of mental function using the Abbreviated Mental Test is useful (see Ch. 4). Both peripheral and central nervous system examinations are required to elicit any potential focal signs, e.g. hemiparesis or ophthalmoplegia, and note should be taken of whether there is any photophobia. The patient should have the neck checked for stiffness and Kernig's sign tested (see Ch. 2).

Investigations

- CT or MRI of the head (Fig. 12.8) – if there are any focal neurological signs, to evaluate them and to check it is safe to perform a lumbar puncture.
- Lumbar puncture (LP) – to obtain cerebrospinal fluid (CSF) for microscopy and culture.
- Serology – to identify toxoplasmosis, HSV and VZV.
- PCR (polymerase chain reaction) on CSF for HSV.
- Electroencephalogram (EEG) – to show the slow wave changes typical of encephalitis.

A summary algorithm demonstrating how to approach diagnosing CNS infections in immunocompromised patients is shown in Figure 12.9.

EYE INFECTIONS

History

The patient reports visual disturbances either related to decreased acuity or due to 'floaters' across the visual field.

Examination

An ophthalmoscope is required as there is usually nothing abnormal to see externally. On fundoscopy an appearance of 'pizza pie' or 'cheese and ketchup' (i.e. ischaemic areas and haemorrhages) indicates CMV retinitis, whereas in toxoplasmosis there tends to be chorioretinal scarring with ischaemia.

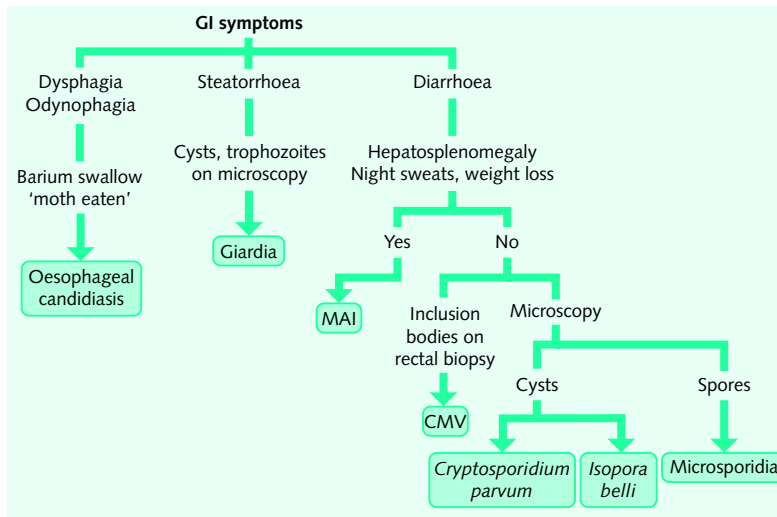


Fig. 12.7 Diagnostic algorithm for gastrointestinal symptoms in an immunocompromised patient.

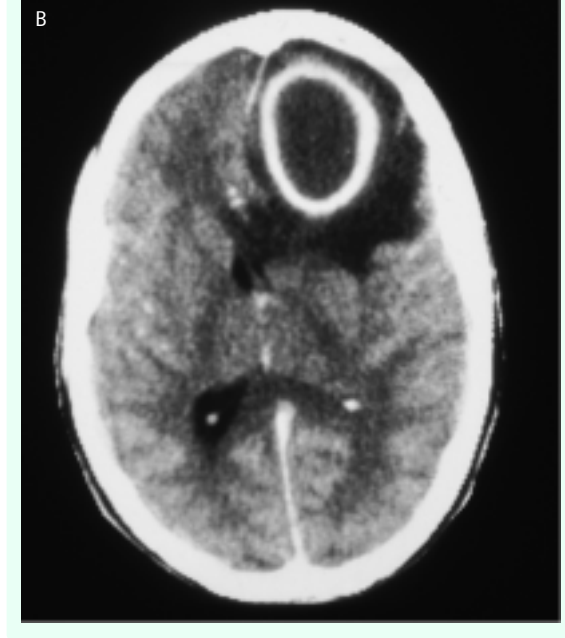
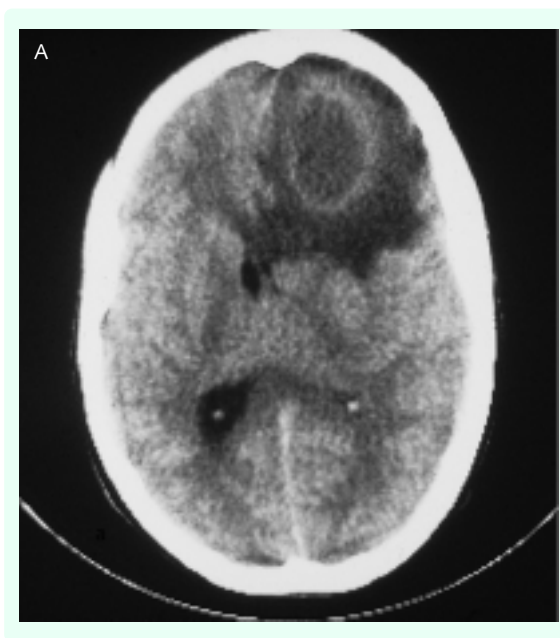


Fig. 12.8 CT scan of the brain with contrast showing brain abscess:

- (A) pre-contrast;
- (B) post-contrast.

Source: Conlon & Snyderman, 2000: Fig. 7.11.

HSV-1 and -2 can cause retinitis in conjunction with encephalitis but the patient is usually so unwell that this aspect is not highlighted and the intravenous aciclovir used, treats all complications.



Investigations

The diagnosis is usually clinical, but serology can be used to confirm the clinical suspicion.

A summary algorithm demonstrating how to approach diagnosing ocular infections in immunocompromised patients is shown in Figure 12.10.

Fever when immunocompromised

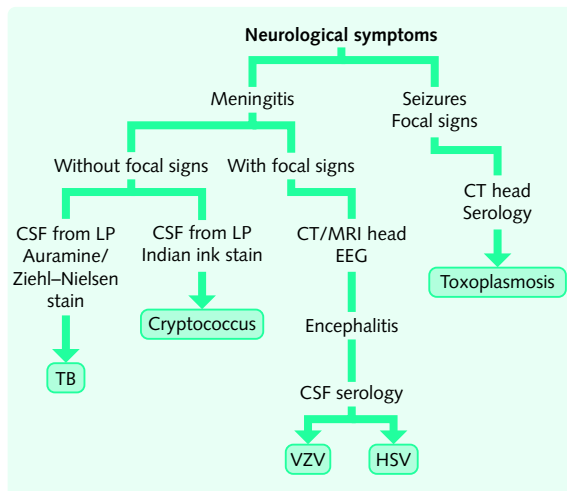


Fig. 12.9 Diagnostic algorithm for neurological symptoms in an immunocompromised patient.

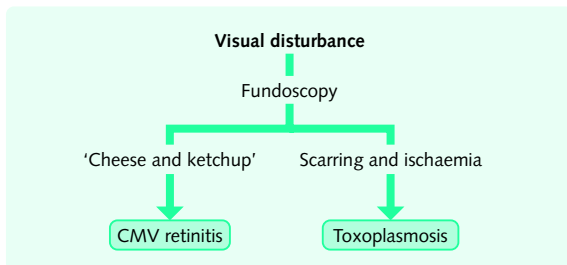


Fig. 12.10 Diagnostic algorithm for eye symptoms in an immunocompromised patient.

SKIN INFECTIONS

History

The patient will be suffering with a rash, the details of which need to be clarified.

- Are there itchy vesicles?
- Is the distribution widespread or only at specific sites?
- Are the lesions large or small?
- Are the lesions 'ring'-shaped?
- Are lesions itchy?
- Are there pigmentation changes to the skin?
- Is there nail involvement?

Examination

Large, slightly itchy ring-shaped lesions with a red scaly outer region and a clear central area occur in

ringworm. The fungus can also infect the scalp leading to patches of hair loss, moist skin folds (erythema and not a ring shape) and nails where it tends to cause discoloration and onycholysis (lifting of nail from nail bed). A brown scaly rash in white-skinned patients or a loss of pigment in tanned or black-skinned patients is indicative of pityrosporum infection. Vesicles in a single or two neighbouring dermatomes with an abrupt stop at the midline define shingles, whereas a widespread distribution occurs in chickenpox. The lesions are painful in shingles but merely itchy in chickenpox.



In immunocompetent patients shingles affects a single dermatome but in immunocompromised patients more than one consecutive dermatome may be involved and it can disseminate to cover the whole body.

Investigations

Often the diagnosis can be made clinically but the following tests may be useful to confirm:

- Skin scrapings for fungus identification on potassium hydroxide examination and fungal culture
- Viral PCR of vesicle fluid
- VZV serology.

A summary algorithm demonstrating how to approach diagnosing skin infections in immunocompromised patients is shown in Figure 12.11.

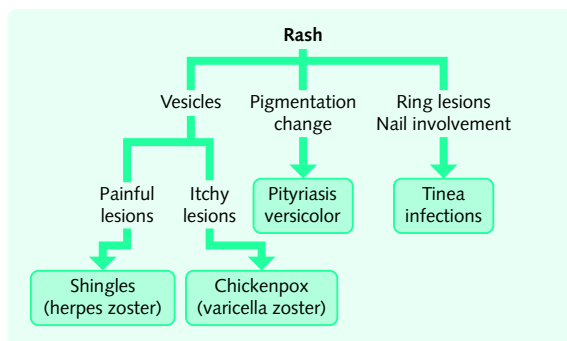


Fig. 12.11 Diagnostic algorithm for a rash in an immunocompromised patient.



Serology tends to be a less helpful investigation in immunocompromised patients as they have an impaired immune response, and tissue samples for culture are much better. A more aggressive approach to acquiring tissue is required, such as using endoscopy and bronchoscopy to obtain biopsies. The effect of being able to make a diagnosis and treat the appropriate infection can be more marked than with immunocompetent patients.