Review Article

Imaging of Acquired Immunodeficiency Syndrome (AIDS)

P Corr,* *MBChB, FRCR, FFRad (SA)*

Abstract

Imaging plays an important role in the detection and characterisation of opportunistic infections and malignancies in patients with the acquired immunodeficiency syndrome (AIDS). The imaging features of opportunistic infections are often non-specific, but when examined in the context of CD4 levels will often allow a correct diagnosis to be made. It is important to be aware of specific syndromes such as lymphoproliferative disease and AIDS nephropathy. The radiologist is often the first clinician to suspect the possibility of human immunodeficiency virus (HIV) or AIDS in a patient's diagnostic work-up and it is, therefore, important that radiologists are familiar with the imaging features of this disease and its complications.

***Ann Acad Med Singapore* 2003; 32:477-82**

***Key words**: Acquired immunodeficiency syndrome, Human immunodeficiency virus, Imaging, Opportunistic infections*

Introduction

The pandemic of human immunodeficiency virus (HIV)/ acquired immunodeficiency syndrome (AIDS) is a global healthcare problem and HIV infection is the most common cause of death worldwide.[1] There are now 60 million deaths recorded from the infection worldwide by the United Nations AIDS (UNAIDS) organisation, most of them in sub-Saharan Africa and Asia. Over the next 20 years, 68 million people are estimated to die from HIV/AIDS. Forty million people are currently living with the disease; 28 million live in sub-Saharan Africa, 6 million in Southeast Asia, 1.5 million in Latin America, 1 million in East Asia and 1 million in central Europe and Asia.[2] According to the latest UNAIDS report released last year, infection is increasing rapidly in countries in South Asia and Southeast Asia.[1] Unfortunately, there are less than 1 million people on antiretroviral drugs worldwide due to their expense, mostly in the developing world. This means that clinicians will increasingly come into contact with patients suffering from HIV/AIDS even in countries that currently have a low incidence.

HIV Virus

HIV is a ribonucleic acid (RNA) containing retrovirus from the Lentivirus family. It was first isolated by Gallo and Levy in 1984. There are 2 subtypes: HIV-1 and HIV-2. It is a particle of 100 nm in diameter containing a core of 2 strands of RNA with the enzyme reverse transcriptase and a surrounding protein capsule. This is surrounded by a viral envelope of lipids and glycoprotein receptors called gp 41 and gp 120 inserted into the envelope. The virus replicates 120 times faster than similar deoxyribonucleic acid (DNA) viruses once inside the host cell. It rapidly changes its antigenicity, therefore making it difficult to produce a vaccine against the virus. Outside the host cell, the virus is extremely fragile and rapidly dies in minutes. Transmission of infection is through contaminated body fluids, especially via sexual contact, contaminated blood transfusions and intravenous drug abuse.

Pathogenesis

The virus rapidly infects host cells within 1 hour of exposure. It attaches via 2 surface receptors: a glycoprotein receptor called gp 120, and a chemokine receptor to macrophages and CD4 lymphocytes. Once inside the cell, the viral RNA rapidly integrates into the host's DNA and starts to produce new viral RNA. The new viral RNA and enzymes are assembled in the host cytoplasm and bud out from the cell surface as new viral particles. In the acute phase, the virus infects the lymphoreticular system in the first 12 weeks of infection. There is a rapid increase in viral load and a decrease in the CD4 count in blood. Clinically, the patient may be asymptomatic or have an infectious mononucleosis like prodromal illness. In the chronic phase,

* *Professor and Head of Radiology*
Nelson Mandela School of Medicine
University of Natal, South Africa
Address for Reprints: Professor Peter Corr, Department of Radiology, University of Natal, Private Bag 7, Congella, Durban 4013, South Africa.
Email: corr@nu.ac.za

which may last from 1 to 10 years, viral replication is kept under control by recovered CD4 cells until the cellular immune system is eventually overwhelmed by the infection. The CD4 count then falls below 400 cells/mm^3 resulting in immunodeficiency and the clinical syndrome of AIDS. With the loss of macrophages, cellular immunity and some B cell immune functions, opportunistic infections and malignancies can occur. Specific infections occur at different CD4 levels; hence, it is important to correlate the patient's clinical and imaging findings with the CD4 count.

Role of Imaging

The role of imaging is to detect opportunistic infection in HIV-positive patients and to characterise the infection or disorder. Imaging is also used to assess the response to treatment of infections and to direct biopsies of focal lesions in solid organs.

Pulmonary Disease

Eighty per cent of AIDS patients will have pulmonary disease during some period of their illness. Tuberculosis (TB) is the most common pulmonary infection. HIV and TB are synergistic infections. There is evidence that gamma interferon production by TB-infected lymphocytes is reduced, and that viral replication is accelerated leading to progressive HIV infection.[3] The imaging features of TB are dependent on the degree of immunosuppression as detected by CD4 lymphocyte levels. Above a CD4 count of 200 cells/mm^3, pulmonary TB is identical to that detected in patients with normal cellular immunity. There are upper lobe cavities, pulmonary infiltrates and pleural effusions on the chest radiograph. In patients who are more immunosuppressed with CD4 counts below 200 cells/mm^3, the features resemble primary TB detected in children with unilateral hilar lymphadenopathy, lower lobe opacification from pulmonary infection. Cavitation is uncommon in these immunosuppressed patients as this requires normal macrophage and T cell lymphocyte function to occur. Multiorgan involvement is common with other foci of infection in the abdomen, lymph nodes and bone. Atypical forms of mycobacterial infection are also common in AIDS patients.

Pneumocystis carinii is an obligate intracellular protozoan that causes pulmonary infection in patients with a CD4 count below 100 cells/mm^3. Patients present with non-productive cough, fever and dyspnoea. Radiographs classically demonstrate a perihilar "ground glass" opacification (Fig. 1a). Atypical features, such as pulmonary cysts, nodules, cavitating masses, military infiltrates and pleural effusions, can occur. However, mediastinal and hilar lymphadenopathy are rare in this infection. High-resolution computed tomography (HRCT) imaging of the lungs demonstrates the "ground glass" appearance of this infection extremely well (Fig. 1b). Diagnosis can only be made by pulmonary or bronchial biopsy; therefore, most patients are treated with antibiotics, such as co-trimoxazole based on the imaging diagnosis alone. Patients usually respond rapidly to this treatment.

Bacterial infection is common, especially from bacteria with capsules such as *Haemophilius influenzae* and *Pseudomonas*. Imaging findings are pulmonary opacification, cavitation and rapidly progressive, destructive pulmonary disease. Fungal infections are less common. Aspergillus infection occurs when the CD4 count is below 50 cells/mm^3. This infection spreads through the pulmonary vessels to cause pulmonary infarcts, pulmonary cavities and nodules. Cryptococcal infection is from a "yeast like" organism *Cryptococcus neoformans*. This is usually a disseminated infection involving the central nervous system, lungs and bones when the CD4 count is below 100 cells/mm^3. The imaging features resemble adult-type TB or pulmonary masses in the upper lobes.

Cytomegalovirus (CMV) infection of the lungs is very common when the CD4 count is below 100 cells/mm^3. It is identical to pneumocystis pneumonia or pneumonitis with a "ground glass" appearance on the radiograph, and often co-exists with *Pneumocystis carinii* infection. Herpes simplex pneumonitis presents with an identical "ground glass" appearance.

AIDS-related pulmonary neoplasms include Kaposi's sarcoma and non-Hodgkin's lymphoma (NHL). Kaposi's sarcoma is an angiocentric sarcoma associated with herpes virus type 8 that occurs in up to 25% of AIDS patients with cutaneous, pulmonary and bowel involvement.[4] In the lung, the sarcoma spreads along the submucosa of the bronchial tree, resulting in bronchovascular wall thickening and the development of pulmonary nodules (Fig. 2a). The appearance of these lesions on HRCT of the lungs is characteristic with "tongue-like" masses extending from the hilar along the bronchovascular bundles (Fig. 2b). Pleural effusions and hilar lymphadenopathy occur in 15% of patients. NHL is usually extranodal in AIDS patients involving the lung parenchyma as pulmonary nodules, while hilar lymphadenopathy is uncommon.[5]

Lymphoproliferative infiltrates are a benign hyperplastic response of pulmonary lymphatic tissue to the HIV virus seen especially in children. There is usually a diffuse pulmonary infiltrate with peribronchial nodules that mimics miliary TB. Pulmonary vasculitis from HIV infection with associated pulmonary hypertension can occur, resulting in large central pulmonary arteries and peripheral vessel pruning.

Cardiovascular Disease

HIV causes a small vessel vasculopathy, aneurysms of

medium-sized arteries, cardiomyopathy and arterial and venous thrombosis.[6] The HIV virus is cardio-myopathic; it causes cardiac failure with dilated ventricles. HIV causes vasculopathy, especially of the small arteries. There are perivascular infiltrates from macrophages and lymphocytes, as well as hyaline thickening of small vessel walls. Aneurysms involving the aorta and carotid arteries of the medium and large arteries are not uncommon (Fig. 3). The cause is probably an endarteritis obliterans secondary to vasculitis, rather than mycotic aneurysms. Both arterial and deep venous thromboses of the lower limb are common presentations in AIDS patients, probably related to generalised cytokine release due to inflammatory response to the virus and polycythaemia.

Gastrointestinal Diseases

Oesophageal disease is common. Candidiasis is very common, involving both the mouth as a stomatitis and oesophagitis. In the oesophagus, there is mucosal fold thickening and longitudinal mucosal ulcers. HIV can cause deep, punched out ulcers that may perforate (Fig. 4)[7] CMV and herpes simplex viruses cause large, shallow ulcers. In the stomach, generalised mucosal fold thickening is detected in cryptosporidium infection and AIDS-related lymphoma.

Small and large bowel involvement from mycobacterial infection is common. There is generalised bowel wall and mucosal thickening with deep, irregular ulcers (Fig. 5). There are enlarged mesenteric and retroperitoneal lymph nodes. The lymph nodes appear hypoechoic on ultrasound and of a low density on computed tomography (CT) with rim enhancement (Fig. 6).[8]

Kaposi's sarcoma commonly involves both the small bowel and colon as submucosal polyps and masses. Patients often present with an intussussception from the tumour. Associated retroperitoneal lymphadenopathy is common. The lymph nodes enhance prominently after contrast injection due to the tumour's vascularity.

NHL is the most common tumour associated with AIDS involving the abdomen. Large bowel wall-related masses, which may cavitate, and extensive retroperitoneal lymphadenopathy are detected. Cryptosporidiosis involves the intrahepatic biliary tree causing obstructive jaundice. The bile ducts appear focally stenosed from focal cholangitis.[9]

Genitourinary Disease

HIV nephropathy is common, but is often asymptomatic with proteinuria being the only manifestation.[10] Patients may develop a nephrotic syndrome. This is thought to be due to immune complex deposition on the basement membrane of the glomeruli resulting in a segmental glomerulonephritis. On imaging, patients have bilaterally enlarged, smooth diffusely echogenic kidneys on ultrasound examination. On CT examination the kidneys appear diffusely swollen and hypodense.

Renal NHL can cause focally and diffusely enlarged kidneys. There are often hypoechoic focal masses which are hypodense on CT with a striated appearance to the parenchyma from infiltration. Renal tuberculosis and bacterial renal infections are more common in patients with AIDS than in patients with normal immune status. Erosions of the renal papilla are detected on both intravenous urogram and contrast enhanced CT studies of the kidneys in patients with renal TB. Pelvic infections, such as salpingitis and endometritis, are common in female patients often associated with other sexually transmitted diseases. Prostatitis in males and cystitis from chronic infections, such as TB, are not uncommon.

Musculoskeletal Disease

Soft tissue musculoskeletal involvement is very common.[11] Symptoms of myalgia and arthralgia are extremely common. A generalised arthritis identical to rheumatoid arthritis commonly involves the hands and feet.[12] Radiologically, there is soft tissue swelling, juxta-articular osteopaenia with articular erosions and joint space effusions. Large joint monoarthritis, especially involving the knee, is also common. This, however, is often transient with only soft tissue swelling detected on radiographs. A non-specific spondyloarthropathy, involving the thoracic and lumbar spine, is a common manifestation. This resembles Reiter's disease radiologically.[12]

Bone, joint and soft tissue infections are common presenting signs in patients from developing countries.[13] The appearance of multifocal infection, such as multiple myositic abscesses, or multifocal osteomyelitis due to unusual organisms, such as salmonella, should suggest immune compromise from AIDS.[13] Multifocal osteomyelitis from TB is a common manifestation in our practice. Patients often have multiorgan involvement as well. Multifocal spinal TB is especially common in AIDS patients in our practice in Africa.

Nervous System Disease

Fifty per cent of patients will develop neurological symptoms during their illness. The spectrum of nervous system involvement is broad. HIV causes infection of the microglial cells and macrophages, but not the neurons. In early, acute HIV infection, there may be a "glandular fever"-type prodrome with headache from a sterile meningitis. Imaging is normal at this stage. Rarely is there acute, disseminated encephalomyelitis due to immune complex deposition in the venules at the gray white matter junction.[14] These patients are often very ill. CT and magnetic resonance (MR) imaging will demonstrate focal white

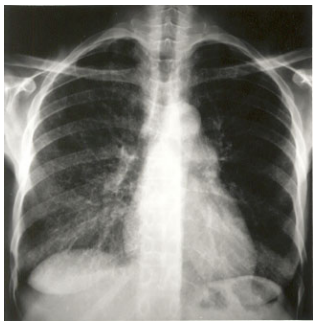

Fig. 1A.

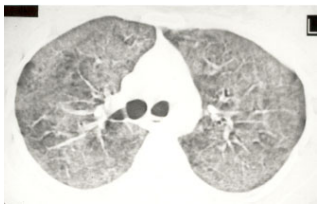

Fig. 1B.

Fig. 1A. Chest radiograph of a patient with Pneumocystis carinii *pneumonia.*

Fig. 1B. HRCT scan of the same patient shows "ground glass" opacification of the lungs.

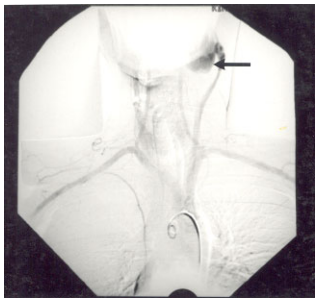

Fig. 3.

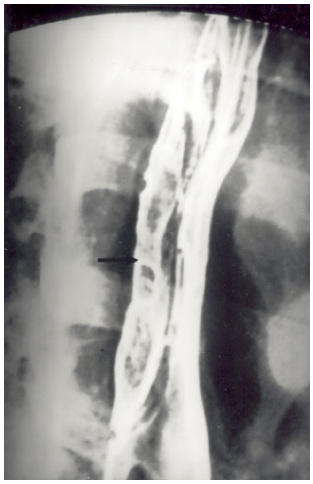

Fig. 4.

Fig. 3. Arch aortogram shows a large left carotid artery aneurysm (arrow) in an HIV-positive patient.

Fig. 4. Barium swallow of a patient with dysphagia shows a giant ulcer crater (arrow) in the thoracic oesophagus from human immunodeficiency virus infection.

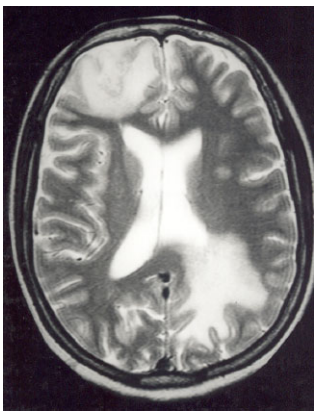

Fig. 7.

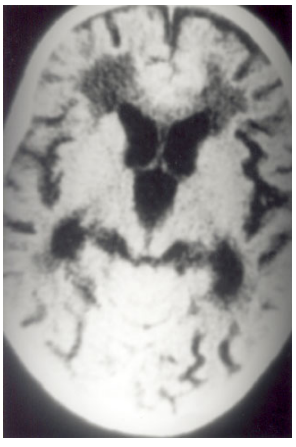

Fig. 8.

Fig. 7. Axial T2-W MR image shows subcortical white matter lesions in the right frontal and left occipital lobes from human immunodeficiency virus-associated acute demyelinating encephalomyelitis. The lesions are low intensity on T1- and high intensity on T2-W MR images.

Fig. 8. Axial CT scan of the brain of a 6-year-old child with acquired immunodeficiency syndrome associated encephalopathy. Note the marked cerebral atrophy and low-density peri-ventricular lesions.

Fig. 2A.

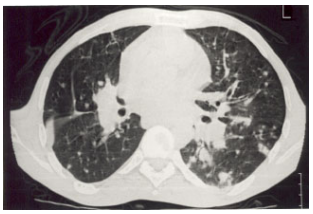

Fig. 2B.

Fig. 2A. Patient with proven pulmonary Kaposi's sarcoma. Chest radiograph shows bilateral bronchovascular wall thickening extending from the hilar regions.

Fig. 2B. HRCT scan of the lungs shows nodular thickening of the bronchovascular bundles like "tongues" extending into the lungs.

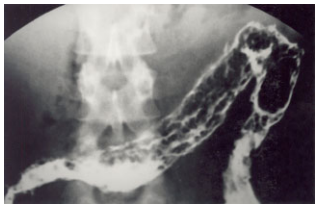

Fig. 5.

Fig. 6.

Fig. 5. Barium enema of a patient with acquired immunodeficiency syndrome presenting with bloody diarrhoea. Extensive deep ulcers are present in the colon. Histology confirmed mycobacterial tuberculosis infection.

Fig. 6. Enhanced axial CT scan of the upper abdomen in a HIV positive patient shows extensive paraortic and preaortic lymphadenopathy with rim enhancement (arrow) from atypical tuberculosis, mycobacterium intracellulare.

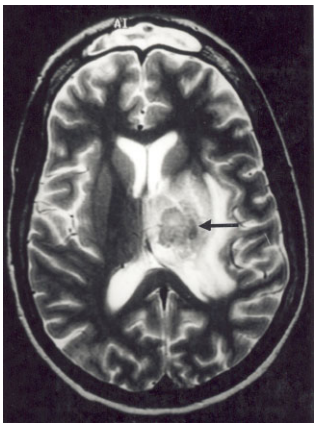

Fig. 9A.

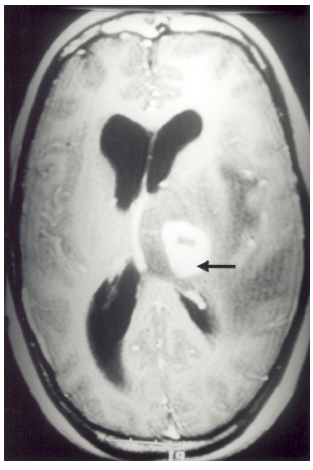

Fig. 9B.

Fig. 9A. Axial T2-W MR image of a patient with a toxoplasmosis abscess (arrow) in the left basal ganglia region. There is a low intensity centre typical of an abscess.

Fig. 9B. Enhanced T1-W MR image shows ring enhancement of the abscess and an eccentric nodule (arrow).

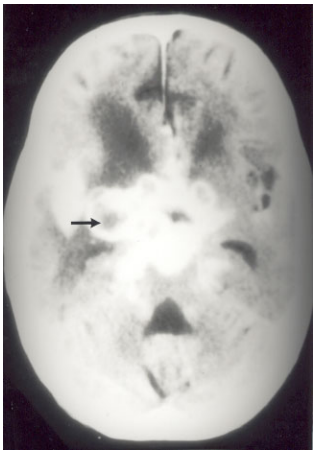

Fig. 10.

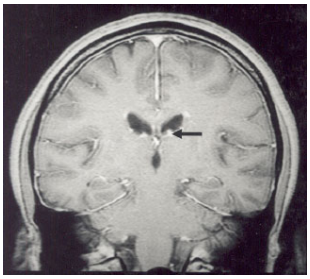

Fig. 11.

Fig. 10. Axial CT scan of the brain of a patient with cryptococcal meningitis shows basal enhancement with dilated perivascular spaces (arrow).

Fig. 11. Enhanced coronal T1-W MR image of a patient with cytomegalovirus ependymitis shows nodular thickening of the ependyma (arrow) of the lateral ventricles.

matter lesions that are hyperintense on T2 typical of focal demyelination (Fig. 7).

HIV encephalopathy occurs in one-third of patients when the CD4 count is below 100 cells/mm^3. Clinically, patients become demented with loss of cognitive functions. This is a progressive leucoencephalopathy, with the development of microglial nodules. These nodules are collections of injured microglial cells, macrophages and lymphocytes. CT and MR imaging are initially normal in the early stages of leucoencephalopathy, however, generalised cerebral atrophy eventually develops (Fig. 8). On MR imaging focal hyperintense periventricular lesions are detected, which characteristically do not enhance after contrast injection. The main imaging differential is progressive multifocal leucoencephalopathy, which is usually located in the white matter of the occipital lobes. It is due to a slow virus called Jacob Creutzveld virus. These patients develop blindness, but do not suffer from dementia.

The most common focal infection in the brain is toxoplasmosis.[15,16] This is an obligate protozoal infection which is important to detect, as it responds well to treatment. The toxoplasma forms an abscess or granuloma, usually in the basal ganglia or deep white matter of the brain. The lesions are ring-enhancing with an eccentric nodule after contrast injection on both CT and MR imaging (Figs. 9a & 9b). Proton spectroscopy will demonstrate an elevated lactate peak.

TB commonly involves the brain and spinal cord, and especially meninges in AIDS patients. Both tuberculous meningitis and tuberculous abscesses are common. Cryptoccocal infection is extremely common. *Cryptococcus neoformans* is an ubiquitous yeast that causes a granulomatous meningitis identical to tuberculous meningitis, as well as focal granulomas in the brain.[16] The infection spreads along the perivascular spaces of the deep, penetrating arteries to enlarge the spaces, thereby causing characteristic cystic lesions in the region of the basal ganglia (Fig. 10). Diagnosis is usually made by examining the cerebrospinal fluid for the gelatinous yeasts on an Indian ink stain.

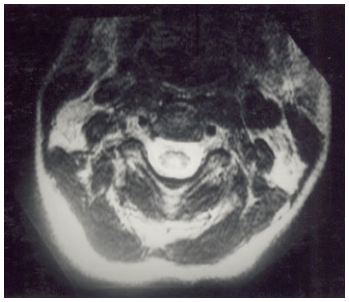

Fig. 12. Axial T2-W MR image of the cervical spinal cord (arrow) of a patient with vacuolar myelopathy from HIV infection.

CMV commonly involves the spinal cord, cauda equina and ependymal surface of the ventricles.[16] It reactivates once the CD4 count is below 100 cells/mm^3. It causes both chorioretinitis and encephalitis as well as a very painful radiculomyelitis. Imaging is often normal. However, careful analysis of contrast-enhanced MR imaging will demonstrate ependymal thickening and nerve root enhancement (Fig. 11).

The only neoplasm that commonly involves the brain is NHL.[17] This tumour commonly involves the corpus callosum and basal ganglia. It has a high density on the unenhanced CT and enhances heterogeneously. Unlike primary gliomas, NHL is often multicentric. On proton spectroscopy, there is an elevated choline peak.[18] The main differential diagnosis is toxoplasmosis.

Spinal cord and nerve root involvement are common in AIDS patients.[19] Forty per cent of patients suffering from AIDS have cord involvement at autopsy. HIV causes a vacuolar myelopathy that targets the posterior columns which resembles subacute combined degeneration of the cord. On MR imaging there is posterior column or central cord hypertensity on the T2-weighted sequences (Fig. 12). A diffuse myelitis can be caused by HIV, CMV, herpes simplex and varicella viruses. Focal cord lesions are due to toxoplasmosis, TB, syphilis and varicella infections.[19]

Conclusion

The multisystem involvement by HIV infection and opportunistic infections needs to be recognised as patients

may present initially with any of the above diseases. An understanding of where imaging can play a positive role in diagnosis and monitoring response to treatment is important for both clinicians and radiologists. Correlation of imaging findings with CD4 counts is especially useful in reaching a working diagnosis.

REFERENCES

1. Hogg R, Cahn P, Katabira E T, Lange J, Samuel N M, O'Shaughnessy M, et al. Time to act: Global apathy towards HIV/AIDS is a crime against humanity. Lancet 2002; 360:1710-11.
2. Accessed 1 December 2002, at http://www.unaids.org/worldaidsday/2002/press/Epiupdate.html.
3. Havlir D V, Barnes P. Tuberculosis in patients with human immunodeficiency virus. N Engl J Med 1999; 340:367-73.
4. Washenik K, Clark-Loeser L, Friedmann-Kien A. Kaposi's sarcoma. N Engl J Med 2000; 343:581-4.
5. Bazot M, Cadranel J, Benayoun S, Tassart M, Bigot J M, Carette M F. Primary pulmonary AIDS-related lymphoma: radiographic and CT findings. Chest 1999; 116:1282-6.
6. Nair R, Robbs J V, Naidoo N G, Woolgar J. Clinical profile of HIV related aneurysms. Eur J Vasc Endovasc Surg 2000; 20:235-40.
7. Levine M S, Loercher G, Katzka D A, Herlinger H, Rubesin S E, Laufer I. Giant, human immunodeficiency related ulcers in the esophagus. Radiology 1991; 180:323-6.
8. Andronikou S, Welman C J, Kader E. The CT features of abdominal tuberculosis in children. Pediatr Radiol 2002; 32:75-81.
9. Chen X M, Keithly J S, Paya C V, LaRusso N F. Cryptosporidiosis. N Engl J Med 2002; 346:1723-31.
10. Zilleruelo G, Strauss J. HIV nephropathy in children. Pediatr Clin North Am 1995; 42:1469-85.
11. Biviji A A, Paiement G D, Steinbach L S. Musculoskeletal manifestations of human immunodeficiency virus infections. J Am Acad Orthop Surg 2002; 10:312-20.
12. Reveille J D. The changing spectrum of rheumatic disease in human immunodeficiency virus infection. Semin Arthritis Rheum 2000; 30:147-66.
13. Bureau N J, Cardinal E. Imaging of musculoskeletal and spinal infections in AIDS. Radiol Clin North Am 2001; 39:343-55.
14. Bhigjee A I, Patel V B, Bhagwan B, Moodley A A, Bill P L. HIV and acute disseminated encephalomyelitis. S Afr Med J 1999; 89:283-4.
15. Israelski D M, Remington J S. Toxoplasmic encephalitis in patients with AIDS. Infect Dis Clin North Am 1988; 2:429-45.
16. Mamidi A, DeSimone J A, Pomerantz R J. Central nervous system infections in individuals with HIV-1 infection. J Neurovirol 2002; 8:158-8.
17. Khoo V S, Liew K H. Acquired immunodeficiency syndrome-related primary cerebral lymphoma. Clin Oncol (R Coll Radiol) 1999; 11:6-14.
18. Miller R F, Hall Craggs M A, Costa D C, Brink N S, Scaravilli F, Lucas S B, et al. Magnetic resonance imaging, thallium-201 SPECT scanning, and laboratory analyses for discrimination of cerebral lymphoma and toxoplasmosis in AIDS. Sex Transm Infect 1998; 74:258-64.
19. Berger J R, Sabet A. Infectious myelopathies. Semin Neurol 2002; 22:133-42.
20. Bhigjee A I, Madurai S, Bill P L, Patel V, Corr P, Naido M N, et al Spectrum of myelopathies in HIV seropositive South African patients. Neurology 2001; 57:348-51.