4 The Pathologic Patterns of AIDS

MARIJKE R. CANNINGA-VAN DIJK and JAN G. VAN DEN TWEEL

CONTENTS

4.1 Introduction

Infection with the human immune deficiency virus (HIV) results in a variety of pathologic lesions, leading to multisystem disease (KLATT 1989, 1992; LUCAS 1995; LUCAS et al. 1993, 1996). Although some of the effects are the direct results of HIV infection, the majority of the lesions are due to secondary infections with opportunistic organisms (LYON et al. 1996). In addition, a considerable number of proliferative lesions, both benign and malignant, occur as a direct result of the immunodeficiency status of the patient, and the intense therapy also has its drawbacks (JOHN et al. 1998, PAXTON and JANSSEN 2000).

We shall first discuss the most important opportunistic infections and tumors (Table 4.1, Centers for Disease Control and Prevention 1992) that are associated with HIV infections. In the second half of the chapter we will give an overview of the most important pathologic lesions of the relevant organ systems.

M.R. CANNINGA-VAN DIJK, MD
J.G. VAN DEN TWEEL, MD, PhD
Department of Pathology, H04.312, University Medical Center, PO Box 85500, 3508 GA Utrecht, The Netherlands

4.2 Opportunistic Infections

The main causes of opportunistic infections are bacteria, viruses, protozoa, and fungi. Most of these infections are seen in all kinds of patients with immun-

Table 4.1. The 1987 and 1992 CDC lists for the case definition of AIDS

Viral infections
CMV
Herpes simplex
JC virus
Molluscum contagiosum
Bacterial infections
Recurrent bacterial pneumonia (commonly *Strep. pneumoniae*)
Mycobacterium tuberculosis
Nontuberculosis mycobacteriosis (particularly *M. avium-intracellulare* complex)
Systemic nontyphoid *Salmonella* infections (notably *S. enteritidis* and *S. typhimurium*)
Fungal infections
Severe *Candida* infection
Cryptococcus neoformans
Histoplasma capsulatum
Coccidioides immitis
Protozoal infections
Pneumocystis carinii
Toxoplasma gondii
Cryptosporidium parvum
Isospora belli
Tumors
Kaposi's sarcoma
Primary cerebral lymphoma
High-grade non-Hodgkin B cell lymphoma
Carcinoma (invasive) of the cervix
Other conditions
HIV-wasting syndrome (fever, weight loss, diarrhea)
HIV-associated dementia

J. W. A. J. Reeders et al. (ed.), *Radiology of AIDS*

odeficiency diseases, whatever the reason. However, patients with HIV show these diseases more frequently. The opportunistic infections affect many organ systems, but mainly the respiratory tract, the digestive tract, and the central nervous system (CNS). The pattern of infections in AIDS patients has changed in the last decade (Lyon et al. 1996). The general aspects of these infections are discussed in the first part of this chapter, while the organ-specific aspects will be dealt with under the respective organs.

4.2.1 Bacterial Infections

4.2.1.1 Mycobacterium tuberculosis

Although strictly speaking tuberculosis is not an opportunistic infection, its incidence and the number of AIDS patients dying from tuberculosis have increased (Barnes et al. 1991). Especially the extrapulmonary forms of tuberculosis are occurring with increasing frequency as a complication of HIV infection. Morphologically the granulomas display caseous necrosis with identifiable acid-fast microorganisms, as is also seen in non-HIV-infected patients. The extrapulmonary dissemination of this disease is regarded as diagnostic of AIDS. It is suggested that the disease is probably the result of reactivation of a previous infection rather than being a primary infection (Race et al. 1998). If the disease is disseminated, it involves the respiratory tract (Fig. 4.1), spleen, lymph nodes, liver, and genitourinary tract. The bone marrow, gastrointestinal tract, and kidneys are less commonly involved.

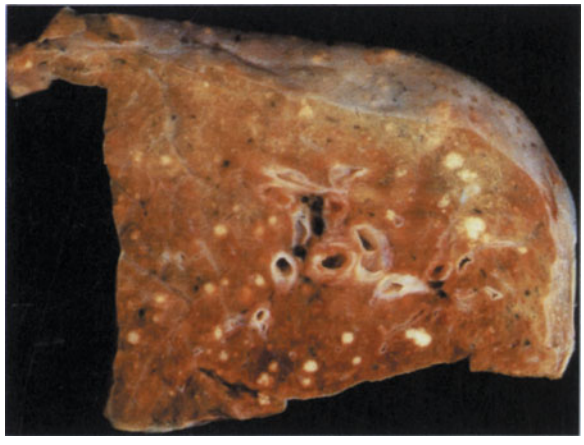

Fig. 4.1. Cut surface of a lung with diffuse small foci of tuberculosis

4.2.1.2 Mycobacterium avium-intracellulare

The most frequent atypical mycobacterial infection is caused by *Mycobacterium avium-intracellulare*. The infection is characterized by single cells, small clusters or large groups of histiocytes that are filled with small rods. In massive infections the lymph node has a homogeneous yellow color, similar to the color of microbiologic culture plates. Although the microorganisms can be seen using hematoxylin and eosin (H&E) staining, they are better visible with special stains such as Ziehl-Neelsen, periodic acid-Schiff, Giemsa, and metaminamine silver. The size of the macrophages/histiocytes can be up to 50 µm. As well as the lymph nodes, the spleen (Fig. 4.2) and liver are frequently affected. Other organs that are affected by this infection include the bone marrow, the gastrointestinal tract, and the respiratory tract (Fig. 4.3). It is rarely found in the CNS, skin, and heart. Even widespread *Mycobacterium avium-intracellulare* infection is infrequently a cause of death.

Fig. 4.2. Cut surface of the spleen, massively infiltrated by *Mycobacterium avium*

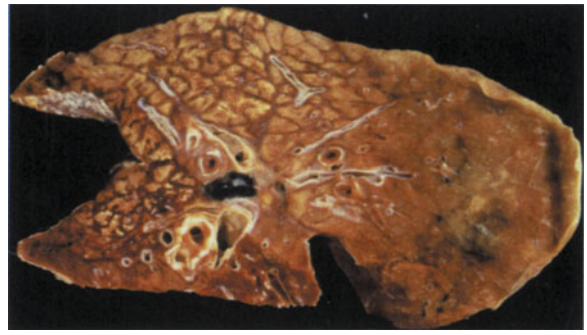

Fig. 4.3. Cut surface of a lung that is distally massively infiltrated by *Mycobacterium avium*

4.2.2 Viral Infections

4.2.2.1 *Cytomegalovirus Infection*

Cytomegalovirus (CMV) is a virus of the herpes family. It is a worldwide ubiquitous pathogenic agent that only gives rise to serious complications in immunodeficient patients, either by primary infection or after reactivation of a latent infection. Approximately 50% of HIV patients develop CMV infections in the course of their disease. The organs most frequently affected are the adrenals, respiratory tract, and gastrointestinal tract, followed by the CNS and the retina. CMV is most often identified within the endothelial cells or histiocytic clusters. The infected cells are enlarged and show large violaceous to dark red, intranuclear inclusions, surrounded by a thin clear halo (Fig. 4.4). Usually CMV infection is not an aggressive disease. Often it is unclear whether such lesions represent a pathologic condition or a symbiotic relationship.

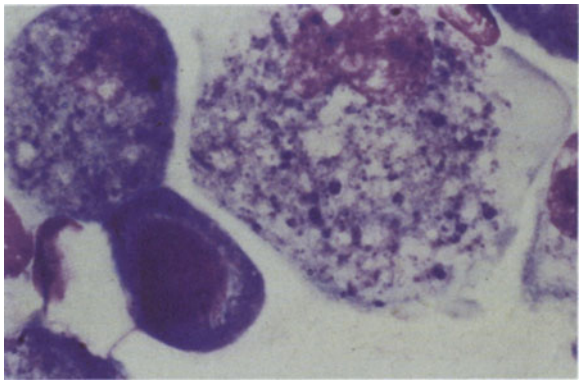

Fig. 4.4. Cytologic preparation of a lung infected by *Pneumocystis carinii* (cloudy areas) and cytomegalovirus (large nuclear inclusion surrounded by a halo (*lower left*)

4.2.2.2 *Herpes Simplex Virus and Herpes Zoster Virus*

Herpes zoster and herpes simplex usually present as a mucocutaneous disease (Fox et al. 1999). Other localizations are very uncommon. Particularly the perianal region is frequently involved. Oropharyngeal and esophageal infections are less common. Macroscopically the lesions manifest as vesicles or ulcers. Under the microscope the infected cells show eosinophilic intranuclear inclusions. Secondary infections of ulcers are commonly seen.

4.2.2.3 *Human Papilloma Virus*

Human papilloma virus, a DNA virus, is found in many proliferative epithelial lesions. In AIDS patients it is seen in association with dysplasia and with carcinomas of the anorectal epithelium and also with condylomata acuminata. It is also seen in hairy leukoplakia, a white lesion that is usually present on the lateral border of the tongue. Currently, however, there is more evidence for Epstein-Barr virus (EBV) involvement in the etiology of this lesion.

4.2.3 Protozoal Infections

Protozoal infections are important sources of significant disease in immunocompromised patients. Among them, the three most important ones are *Pneumocystis carinii*, *Cryptosporidium*, and *Toxoplasma gondii*.

4.2.3.1 *Pneumocystis carinii*

Infection by *Pneumocystis carinii* is often one of the first symptoms of AIDS. The protozoa consist of small cysts that eventually rupture and release up to eight protozoites. After rupturing, they differentiate into trophozoites. These trophozoites form new cysts and repeat the cycle of the microorganism. The microscopic picture is very characteristic. The lungs, the organs that are most often involved, show cloudy alveoli (Fig. 4.4) owing to extensive growth of the protozoa (Gal et al. 1987). Although the H&E sections are rather specific, the microorganisms can be stained by Grocott staining and by methylene blue. These staining methods confirm the expected diagnosis. Extrapulmonary localizations are rare, although this disease can be found in hilar lymph nodes and very occasionally in other organs (Radin et al. 1990).

4.2.3.2 *Cryptosporidium*

Cryptosporidium infection usually presents in the gastrointestinal tract. There are no specific gross pathologic lesions. The microorganisms are small, 2–6 μm in diameter, and are usually found along the mucosal brush border of the stomach and the small

and large intestine. They can be recognized by Ziehl-Neelsen staining since they are acid-fast. Rarely these organisms are seen in other organs, such as the biliary system and the respiratory tract.

4.2.3.3 *Toxoplasma gondii*

Toxoplasmosis is an infectious disease that is quite common in a wide variety of animals, especially mammals and birds. It is a very common parasitic infection in the Western world and many children are infected annually at birth. In adults the disease usually manifests as a lymphadenopathy. *Toxoplasma gondii* infection by itself is not an opportunistic infection. In HIV patients the CNS is often involved (Tschirhart and Klatt 1988). Extracerebral toxoplasmosis is infrequent in AIDS. While the respiratory tract and gastrointestinal tract are sometimes involved, such involvement is usually found only at autopsy. Microscopically, the disease is diagnosed by finding cysts that measure ca. 50 µm and are filled with bradyzoites. Free protozoa are very difficult to find. Only ruptured cysts can induce an inflammatory response.

4.2.3.4 Other Protozoa

Other protozoal infections that should be mentioned here are *Isospora belli* and *Microsporidium* (Schwartz et al. 1996). Their pathology is usually located in the small intestine. Sometimes regional lymph nodes are also involved.

4.2.4 Fungi

4.2.4.1 *Cryptococcus neoformans*

Cryptococcus neoformans organisms are small, sometimes budding, yeasts with a diameter of approximately 4–7 µm. The cells have a prominent capsule that can be easily recognized using routine histologic stains. The organisms form pale, mucoid areas in affected tissues. Sometimes the capsule of the organism is missing and epithelioid granulomas with giant cells are present. In this case the organisms appear small and may be confused with *Candida* and histoplasmosis. The CNS is frequently involved, as is the lung. In disseminated disease, other organs can also be affected, e.g., lymph nodes, spleen, bone marrow, and liver.

4.2.4.2 *Candida albicans*

Candida albicans is a ubiquitous yeast that can be found in the skin and in the oral cavity of healthy individuals. To fulfill the criteria for candidiasis, the fungus must invade the mucosa of the esophagus and the respiratory tract. The gross manifestation of these organisms is by white plaques or patches. The involvement of other organs is very rare.

Histologically, the invading fungi are surrounded by granulocytes. The fungus is characterized by buds and pseudohyphae without branching or true septations. Although *Candida* can be demonstrated in many patients with AIDS, it is a rare cause of death.

4.2.4.3 Other Fungal Infections

Among other fungi, *Aspergillus fumigatus* can cause considerable organ damage (Fig. 4.5). *Histoplasma capsulatum* and *Coccidioides* are also frequently encountered in AIDS patients.

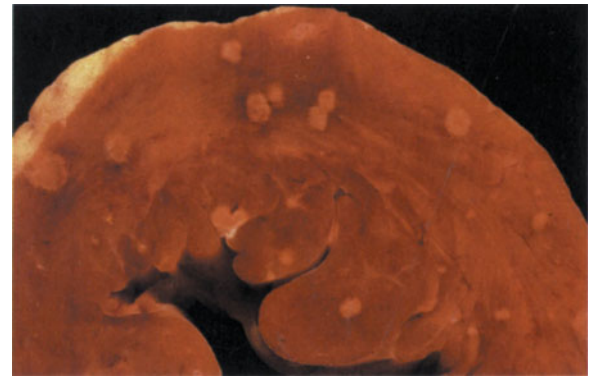

Fig. 4.5. Cut surface of the left ventricular myocardium with many small areas of *Aspergillus* infection

4.3 Neoplasms

Patients with AIDS have a high incidence of malignancies, compared with patients in the same age group without this disorder. Malignant lymphomas, Kaposi's sarcoma, and squamous epithelial tumors deserve special attention here.

4.3.1 Malignant Lymphomas

Approximately 3% of HIV-positive patients present with a non-Hodgkin lymphoma. The risk of developing lymphoma is increased 100-fold 6–8 years after the infection, and the risk approaches 1% per year once the diagnosis of AIDS has been established (Biggar and Rabkin 1992; Levine 1991; Lucas et al. 1993; Luxton et al. 1991). The most common lymphoma in this group of patients is the diffuse large B cell lymphoma in the WHO classification. These tumors tend to be extranodal and involve the lungs, intestines, and CNS (Fig. 4.6). The risk of developing a primary cerebral lymphoma is increased approximately 1,000 times in HIV-positive patients, compared with a normal population. Most of the lymphomas are EBV associated. Since there are various genetic mutations in these lymphomas, the pathogenetic pathways along which the lymphomas develop are probably variable.

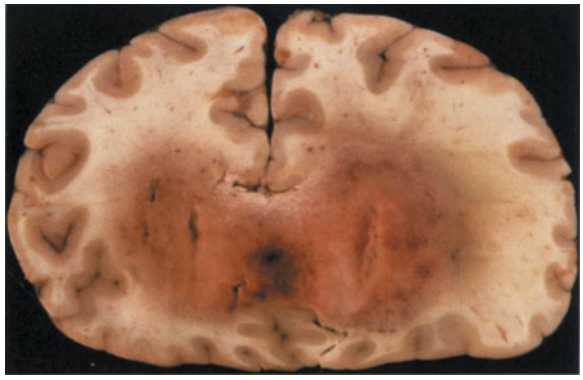

Fig. 4.6. Cross-section of the frontal brain with an extensive localization of a diffuse large B-cell lymphoma

A second B cell lymphoma that is associated with HIV infections is the primary effusion B cell lymphoma (DePond et al. 1997). This tumor develops in the pleura, the pericardium, and the peritoneal cavity and is associated with human herpes virus HHV8 infection.

Hodgkin's disease (Ames et al. 1991; Gold et al. 1991) is also reported to be associated with HIV infection but is not considered a criterion for the diagnosis of AIDS, in contrast to non-Hodgkin lymphomas. Most patients present with advanced disease (82% with stage 3 or 4) and with mixed cellularity histology. In contrast to the normal response to therapy, HIV patients react poorly to conventional therapy and more than two-thirds will die within 1 year of diagnosis. A statistical analysis by Gold and colleagues of a large group of patients revealed that HIV-associated Hodgkin's disease has a strong tendency to occur outside of the normal age range for Hodgkin's disease (Gold et al. 1991).

4.3.2 Lymphoproliferative Disorders

Due to the immunosuppressed state of the patient, lymphoproliferative lesions are seen in this group, and are similar to lesions in patients with organ transplants. The lymphoproliferative disorders may involve nodal and extranodal structures, especially the mucosa of the gut and the brain (Knowles 1999). Some of them transform into a malignant lymphoma. Also Castleman's disease (especially the plasma cell type) is associated with HIV infection and may eventually progress into a non-Hodgkin lymphoma. Now that HIV patients live longer, lymphoproliferative disorders and malignant lymphomas are becoming a bigger problem and present diagnostic and clinical challenges.

4.3.3 Kaposi's Sarcoma

Kaposi's sarcoma is a mesenchymal tumor, probably of vascular origin, that manifests in the skin, the mucous membranes of the bronchial tree, the oropharyngeal and gastrointestinal mucosa (Fig. 4.7), and the lymphatic tissue, with a preference for MALT (Ensoli et al. 1991; Haverkos et al. 1990; Palca 1992; Roth et al. 1992; Tappero et al. 1993). It is a reactive proliferation of endothelial cells and shows a strong relation

Fig. 4.7. Mucosal aspect of the ileum with extensive localizations of a Kaposi's sarcoma. This tumor is also present in the serosal surface

with human herpes virus HHV8 (Cesarman and Knowles 1999; Chang et al. 1994). The presence of HHV8 increases the risk that patients will develop Kaposi's sarcoma. The tumor is also described in HIV-seronegative individuals and in patients receiving immunosuppressive therapy. Since the tumor usually develops simultaneously in different organs, this suggests a multifocal genesis. The early lesions of this disease are small red nodules having a diameter of 1–2 mm. Later in the disease, macular and plaque-like lesions occur. Histologically, the cytonuclear pleomorphism is slight to moderate and mitoses can be found. The tumor cells may show erythrophagocytosis. The lesions show expansile growth along existing vessels in the deeper layers and surrounding support tissues of organs, especially the lung, the liver, the heart, and the kidneys.

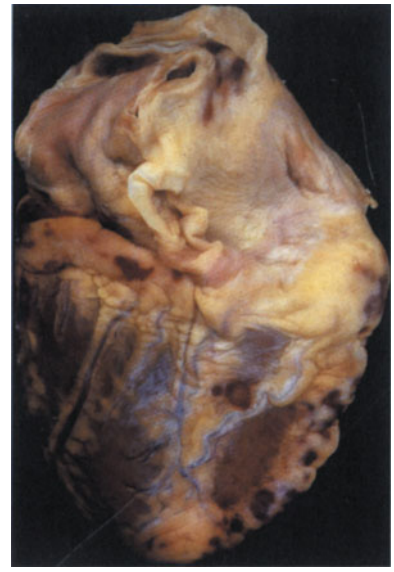

Fig. 4.8. Surface of the heart with many small areas of Kaposi's sarcoma in a patient with generalized Kaposi's sarcoma

4.3.4 Squamous Epithelial Tumors

Squamous cell carcinoma of the cervix was made an AIDS-defining disease in 1992. Strangely enough, although there is a clear increase in cervical intraepithelial neoplasms among HIV-positive women, there is no marked increase in the occurrence of carcinomas. A parallel is seen in HIV-positive gay men. They display more anal interepithelial neoplasms, but this does not lead to more invasive anal carcinomas. In contrast, there is a definite increase in invasive and in situ conjunctival squamous cell carcinomas in HIV patients (Waddell et al. 1996). Bowen's disease, squamous cell carcinoma, and basal cell carcinoma of the skin are also reported to occur with increased frequency.

4.4 Organ System Pathology

4.4.1 Cardiovascular System

All parts of the heart can be involved in HIV disease, although gross abnormalities are rare. If a tumor, is present it is usually a malignant lymphoma. Approximately 20% of patients with malignant lymphoma show cardiac involvement. Kaposi's sarcoma is rare (Fig. 4.8).

Pericarditis is usually of tuberculous origin in countries where that infection is common. Bacterial endocarditis and subsequent myocardial abscesses are usually found in patients who use i.v. drugs. Protozoal and viral infections may occur. HIV itself can also cause myocardial damage (Grody et al. 1990). In the later stages of the disease, dilated cardiomyopathy, predominantly of the left ventricle, is seen and is a cause of congestive heart failure in those patients (Barbaro et al. 1999; Cohen et al. 1986). The etiology of this disorder is drug use and nonspecific damage complicating a septic shock.

Sometimes arterial aneurysms, often multiple, are seen in association with HIV infection (Nair et al. 1999). This is especially true in South Africa, where HIV infections have a high prevalence.

In addition, vascular complications associated with the use of HIV protease inhibitors have been reported (Behrens et al. 1998).

4.4.2 Pulmonary Tract

The respiratory tract is frequently involved in patients with AIDS. Infections of the lung are a major cause of death in AIDS patients. X-rays mostly reveal diffuse bilateral interstitial and alveolar infiltrates (McKenna et al. 1986). The clinical features of the different diseases can be indistinguishable, although infections generally cause more diffuse interstitial patterns and malignancies a more nodular appearance. Among the infections, *Pneumocystis carinii*

(PCP) and CMV are the most prominent. Most AIDS patients will have at least one episode of PCP during their disease. PCP was originally a major cause of death in AIDS patients, but the disease is now under good control. The pathologic features of PCP are those of widespread involvement of the alveolar spaces with a gross appearance of pneumonic consolidation with scattered areas of hemorrhage or congestion. Later in the disease, the surface develops a slimy appearance and finally it turns dry, as a result of fibrosis and organization (Fig. 4.9). Bronchoscopy and bronchiolar lavage are the best diagnostic procedure.

CMV is an important cause of diffuse alveolar damage and adult respiratory distress syndrome (ARDS). Clinically and morphologically, it is very difficult to distinguish infections causing ARDS. Microscopically, viral inclusions can be found in endothelial cells and pneumocytes. There are some case reports of a role of HIV in primary pulmonary hypertension (Pellicelli et al. 1998). Tumors are rare although malignant lymphomas (including the effusion type) and Kaposi's sarcoma occur in the lungs.

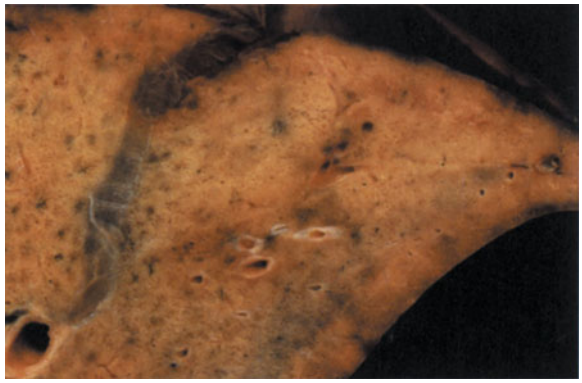

Fig. 4.9. Lung lobe with a consolidated aspect. The dry cut surface is characteristic of *Pneumocystis carinii* infection

4.4.3 Gastrointestinal Tract

A wide range of opportunistic infections can involve the gastrointestinal (GI) tract in HIV-positive patients. In many cases, such infections serve to establish the diagnosis of AIDS according to the official criteria (Table 4.1). The mouth and the esophagus are often involved by invasive candidiasis. The stomach and the upper gastrointestinal tract frequently show the presence of cryptosporidiosis and microsporidiosis. Patients often suffer from diarrhea, weight loss, and malabsorption. The microorganisms live intracellularly in an extracytoplasmic niche of the surface epithelial cells. Microscopically the only morphologic abnormality is atrophy of the microvilli. For the diagnosis of microsporidiosis, electron microscopic examination is very helpful.

CMV infection is also an important cause of gastrointestinal disease. The virus is present in endothelial cells, causing local vascular damage and consequent necrosis of the mucous membrane.

Mycobacterium avium infection results in small yellow plates with a characteristic macroscopic appearance. An inflammatory infiltrate is usually absent microscopically. Often the regional lymph nodes are also infected.

Kaposi's sarcoma occurs frequently in the GI tract and can be present from the mouth to the anus. Malignant lymphoma of the GI tract is also a frequent complication of HIV infection; as already mentioned, the tumor is usually a diffuse large B-cell lymphoma.

The hepatobiliary system is involved by opportunistic infections or neoplasms in approximately 30% of AIDS patients (Cappell 1991; Hinnant et al. 1989). Clinically these are of minor importance since they almost never result in hepatic failure. Among the infections that are found are *Mycobacterium avium*, *Cryptococcus*, and *Histoplasma*. Hepatitis is at present an increasing complication (Brau et al. 1997; Lesens et al. 1999). Kaposi's sarcoma is rare and, when present, is located in the connective tissue surrounding the large portal venous branches and the large biliary tracts (Fig. 4.10). Malignant lymphomas of the liver are rarely seen as primary tumors (Caccamo et al. 1986); they usually occur in association with lymphomas elsewhere.

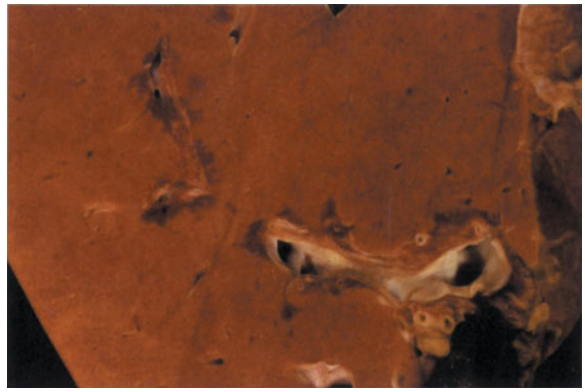

Fig. 4.10. Cut surface of the liver with surrounding vessels and ducts infiltrated by Kaposi's sarcoma

4.4.4 Hematopoietic Organs

Lymphadenopathy is often seen in patients with AIDS. Usually an AIDS-specific reaction to HIV is seen, characterized by extreme follicular hyperplasia with many starry sky macrophages. Later in the disease, an architectural destruction of the lymph node takes place, with fragmentation and disappearance of follicles and finally depletion of lymphoid tissue (Öst et al. 1989).

The mesenteric lymph nodes are often involved in *Mycobacterium avium* infections.

As has been previously stated, malignant lymphomas are an important cause of lymphadenopathy, although extranodal lymphomas are more frequent than nodal ones.

The bone marrow usually shows dysplastic features of the hematopoiesis (Bain 1997; Sun et al. 1989), resulting in peripheral cytopenias. In addition, opportunistic infections can be found, although they are infrequent. EBV infection of HIV patients may result in a hemophagocytic syndrome (Albrecht et al. 1997).

4.4.5 Central Nervous System

The CNS can be affected by HIV infection (Budka 1989; Everall et al. 1999) with the clinical manifestation of an HIV encephalopathy/AIDS dementia complex or of secondary lesions, including infections and localizations of malignant tumors, especially lymphoma.

The morphologic spectrum of HIV encephalopathy is the result of multiple perivascular accumulations of multinucleated giant cells with inflammatory reactions and necrosis or of diffuse white matter damage of cerebral and cerebellar hemispheres.

Among the opportunistic infections, toxoplasmosis is the most frequent, being localized in the cerebral hemispheres, the basal ganglia, and the brainstem (Fig. 4.11). The gross appearance is multiple areas of ill-defined necrosis, microscopically accompanied by a mild inflammatory infiltrate with many macrophages and large numbers of *Toxoplasma gondii* tachyzoites in the periphery of the necrotic areas. In addition, fungal infections may be seen, mainly caused by *Cryptococcus neoformans*, *Candida* species, and *Aspergillus*.

An important viral infection in HIV-positive patients is polyomavirus (JC virus or SV 40), which leads to so-called progressive multifocal leukoencephalopathy. This disease is characterized by multiple confluent areas of demyelination in both hemispheres, the cerebellum, and the brainstem. Viral inclusion bodies are detected both in cells of astrocytic origin and in cells of oligodendroglial origin.

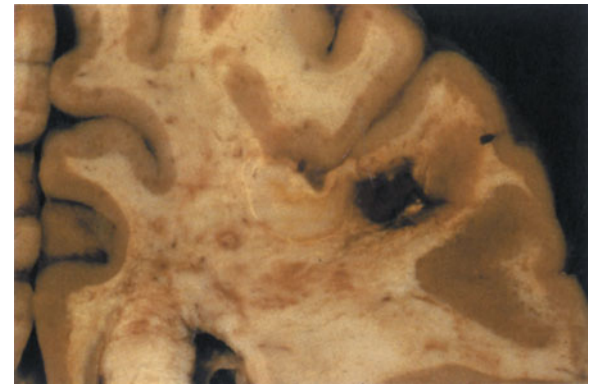

Fig. 4.11. Parietal lobe of the cerebellum with a hemorrhagic area due to infection by toxoplasmosis

In addition, CMV (Fig. 4.12) causes both encephalitis and microglial nodules. Sometimes herpes simplex virus type I is reported. Destruction of retinal cells due to CMV causes "cotton wool" spots in the retina.

Non-Hodgkin lymphomas are the most frequent tumors to be located in the CNS. They show a predominant perivascular involvement of the brain.

4.4.6 The Skin

The first cutaneous manifestation of HIV infection, occurring in approximately 23% of patients, is acute HIV exanthema (Goldman et al. 1995). This macu-

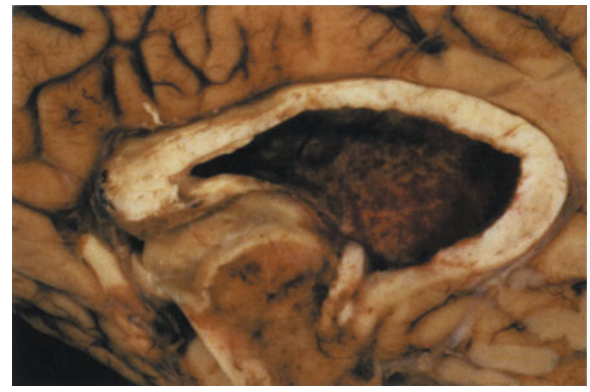

Fig. 4.12. Section of the brain with a hemorrhagic aspect of the third ventricle as the result of a CMV infection

lar, roseoliform dermatosis represents the acute seroconversion reaction. A skin biopsy shows perivascular infiltrates of lymphocytes with usually mild epidermal changes.

Cutaneous diseases occurring at a later stage can be classified into three categories: infections, neoplasms, and noninfectious dermatoses. In addition to the bacterial, viral, protozoal, and fungal infections discussed in the first part of this chapter, arthropod infections (scabies and demodicosis) can be seen in the skin. Scabies is caused by *Sarcoptes scabiei*, a mite penetrating the skin. In HIV-positive patients, scabies usually presents with an extremely heavy infestation with mites, resulting in keratotic and psoriasiform lesions. This severe manifestation is known as Norwegian scabies. *Demodex folliculorum* and *Demodex brevis* are follicle mites, often found in normal human skin. They are found at a higher rate in patients with rosacea, which is usually restricted to the face. In immunocompromised patients, *Demodex* can cause a widespread eruption. Histopathology shows mites in the stratum corneum (scabies) or in the hair follicles (demodicosis).

A bacterial infection that should be mentioned in this chapter is bacillary angiomatosis (LeBoit et al. 1989), a vascular proliferation that most commonly involves the skin but can also affect other organs such as liver, bone and brain. It is caused by *Bartonella henselae* and *Bartonella quintana*. The skin lesions resemble Kaposi's sarcoma. It is very important to recognize bacillary angiomatosis and distinguish it from Kaposi's sarcoma because of the good response of the former to antibiotic therapy. Under the microscope one sees a proliferation of blood vessels in combination with a mixed infiltrate with many neutrophils. A viral infection limited to the skin is molluscum contagiosum: pearly, umbilicated papules caused by a poxvirus. Histopathology shows large eosinophilic intracytoplasmic inclusions in keratinocytes.

Neoplasms of the skin (Kaposi's sarcoma, lymphoma, Bowen's disease, and squamous and basal cell carcinoma) have already been discussed in the first part of this chapter. In a few case reports, HIV positivity has been mentioned as a risk factor for the development of malignant melanoma (Rivers et al. 1989).

The noninfectious dermatoses are mostly "common" dermatoses that present with increased frequency and often increased severity in HIV-positive patients. A frequent skin disease among these patients is seborrheic dermatitis. Scaly, erythematous and sometimes papular lesions develop on the face, scalp, chest, and genitalia. Histologically there is mild parakeratosis with slight spongiosis. HIV-associated eosinophilic folliculitis (Rosenthal et al. 1991) presents with erythematous, follicular papules on the head, neck, and chest (Fig. 4.13). There is a follicular and dermal infiltrate with many lymphocytes and eosinophils. Small eosinophilic pustules may be seen in the hair follicle epithelium. Many photosensitivity reactions like granuloma annulare, (pseudo)porphyria cutanea tarda, and chronic actinic dermatitis can occur in HIV-positive patients. Cutaneous drug eruptions can show a lot of different clinical patterns: exanthematous eruptions, maculopapular lesions, and also the severe blisters of Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN). These drug eruptions most often entail vacuolar changes of the epidermal basal layer with necrotic keratinocytes. The superficial infiltrate consists of lymphocytes, mixed with a variable number of eosinophils. In Stevens-Johnson syndrome, TEN, and their less severe variant, erythema multiforme, there is a subepidermal blister with clusters of necrotic keratinocytes in the overlying epidermis. The infiltrate is lymphocytic and superficial. In TEN the infiltrate is very sparse or even absent. AIDS-relared muscocutaneous disorders will be described in detail in chapter 13.

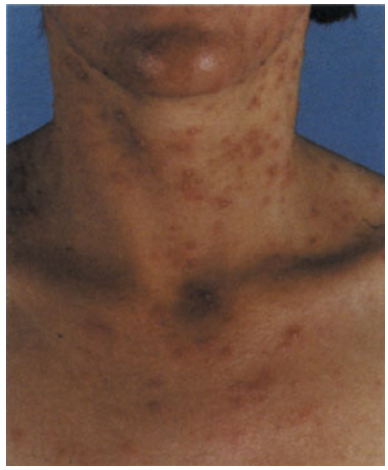

Fig. 4.13. Follicular papules on the face, neck, and chest in a patient with eosinophilic folliculitis

References

Albrecht H, Schafer H, Stellbrink H-J, et al. (1997) Epstein-Barr virus-associated hemophagocytic syndrome. A cause of fever of unknown origin in HIV infection. Arch Pathol Lab Med 121:853–858

Ames ED, Conjalka MS, Goldberg AF, et al. (1991) Hodgkin's disease and AIDS. Hematol Oncol Clin North Am 5:343–356

Bain B (1997) The haematological features of HIV infection. Br J Haematol 99:1–8

Barbaro G, Di Lorenzo G, Grisorio B, Barbarini G (1999) Incidence of dilated cardiomyopathy and detection of HIV in myocardial cells of HIV-infected patients. N Engl J Med 339:1093–1099

Barnes PF, Bloch AB, Davidson PT, et al. (1991) Tuberculosis in patients with human immunodeficiency virus infection. N Engl J Med 324:1644–1650

Behrens G, Schmidt H, Meyer D, et al. (1998) Vascular complications associated with the use of HIV protease inhibitors. Lancet 351:1958–1959

Biggar RJ, Rabkin CS (1992) The epidemiology of acquired immunodeficiency syndrome-related lymphomas. Curr Opin Oncol 4:883–893

Brau N, Leaf HL, Wieczorek RL, et al. (1997) Severe hepatitis in three AIDS patients treated with indinavir. Lancet 349:924–925

Budka H (1989) Human immunodeficiency virus (HIV)-induced disease of the central nervous system: pathology and implications for pathogenesis. Acta Neuropathol (Berl) 77:225–236

Caccamo D, Pervez NK, Marchevsky A (1986) Primary lymphoma of the liver in the acquired immunodeficiency syndrome. Arch Pathol Lab Med 110:553–555

Cappell MS (1991) Hepatobiliary manifestations of the acquired immunodeficiency syndrome. Am J Gastroenterol 86:1–15

Centers for Disease Control and Prevention (1992) 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR Morb Mortal Wkly Rep 41 [RR-17]:1–19

Cesarman E, Knowles DM (1999) The role of Kaposi's sarcoma-associated herpesvirus (KSHV/HHV8) in lymphoproliferative diseases. Semin Canc Biol 9:165–174

Chang Y, Cesarman E, Pessin MS, et al. (1994) Identification of herpes virus like sequences in AIDS-associated Kaposi's sarcomas. Science 266:1865–1869

Cohen IS, Anderson DW, Virmani R, et al. (1986) Congestive cardiomyopathy in association with the acquired immunodeficiency syndrome. N Engl J Med 315:628–630

DePond W, Said JW, Tasaka T, et al. (1997) Kaposi's sarcoma-associated herpesvirus and HHV8 (KSV/HHV8)-associated lymphoma of the bowel. Report of two cases in HIV+ve men with secondary effusion lymphoma. Am J Surg Pathol 21:719–724

Ensoli B, Barillari G, Gallo RC (1991) Pathogenesis of AIDS-associated Kaposi's sarcoma. Hematol Oncol Clin North Am 5:281–295

Everall IP, Heaton RK, Marcotte TD, et al. (1999) Cortical synaptic density is reduced in mild to moderate HIV neurocognitive disorder. Brain Pathol 9:209–217

Fox PA, Barton SE, Francis N, et al. (1999) Chronic erosive herpes simplex virus infection of the penis, a possible immune reconstitution disease. HIV Med 1:10–18

Gal AA, Klatt EC, Koss MN, et al. (1987) The effectiveness of bronchoscopy in the diagnosis of *Pneumocystis carinii* and cytomegalovirus pulmonary infections in acquired immunodeficiency syndrome. Arch Pathol Lab Med 111:238–241

Gold JE, Altarac D, Ree HJ (1991) HIV-associated Hodgkin disease: a clinical study of 18 cases and review. Am J Hematol 39:93–99

Goldman GD, Milstone LM, Shapiro PE (1995) Histologic findings in acute HIV exanthem. J Cutan Pathol 22:371–373

Grody WW, Cheng L, Lewis W (1990) Infection of the heart by the human immunodeficiency virus. Am J Cardiol 66:203–206

Haverkos HW, Freidman-Kien AE, Drotman DP, et al. (1990) The changing incidence of Kaposi's sarcoma among patients with AIDS. J Am Acad Dermatol 22:1250–1253

Hinnant K, Schwartz A, Rotterdam H, et al. (1989) Cytomegalovirus and cryptosporidial cholecystitis in two patients with AIDS. Am Surg Pathol 107:133–137

John M, Mallal S, French M (1998) Emerging toxicity with long-term antiretroviral therapy. J HIV Ther 3:58–61

Klatt EC (1989) Diagnostic findings in patients with acquired immune deficiency syndrome. J Acquir Immune Defic Syndr 5:459–465

Klatt EC (1992) Practical AIDS Pathology. ASCP Press, Chicago

Knowles DM (1999) Immunodeficiency-associated lymphoproliferative disorders. Mod Pathol 12:200–217

LeBoit PE, Berger TG, Egbert BM, et al. Bacillary angiomatosis. The histopathology and differential diagnosis of a pseudoneoplastic infection in patients with human immunodeficiency virus disease. Am J Surg Pathol 1989; 13:909–920

Lesens O, Deschenes M, Steben M, et al. (1999) Hepatitis C virus is related to progressive liver disease in HIV+ve haemophiliacs and should be treated as an opportunistic infection. J Infect Dis 179:1254–1258

Levine AM (1991) Epidemiology, clinical characteristics, and management of AIDS-related lymphoma. Hematol Oncol Clin North Am 5:331–342

Levine AM (1992) AIDS-associated malignant lymphoma. Med Clin North Am 76:253–268

Lucas SB (1995) Tropical pathology of the female genital tract and ovaries. In: Fox H (ed) Haines and Taylor obstetrical and gynaecological pathology. Churchill Livingstone, Edinburgh, pp 1209–1231

Lucas SB, Hounnou A, Paecock CS, et al. (1993) The mortality and pathology of HIV disease in a West African city. AIDS 7:1569–1579

Lucas SB, Peacock CS, Hounnou A, et al. (1996) Disease in children infected with HIV in Abidjan, Côte d'Ivoire. Br Med J 312:335–338

Luxton JC, Thomas JA, Crawford DH (1991) Aetiology and pathogenesis of non-Hodgkin lymphoma in AIDS. Cancer Surv 10:103–109

Lyon R, Haque AK, Asmuth DM, et al. (1996) Changing patterns of infection in patients with AIDS: a study of 279 autopsies of prison inmates and nonincarcerated patients at a University Hospital in Eastern Texas, 1984–1993. Clin Infect Dis 23:241–247

McKenna RJ, Campbell A, McMurtrey MJ, et al. (1986) Diagnosis of interstitial lung disease in patients with acquired immunodeficiency syndrome (AIDS): a prospective comparison of bronchial washing, alveolar lavage, transbronchial lung biopsy and open-lung biopsy. Ann Thorac Surg 41:318–321

Nair R, Abdool-Carrim ACR, Robbs J (1999) Arterial aneurysms in patients with HIV: a distinct clinicopathological entity? J Vasc Surg 29:600–607

Öst A, Baroni CD, Biberfeld P, et al. (1989) Lymphadenopathy in HIV-infection: histological classification and staging. Acta Pathol Microbiol Immunol Scand Suppl 8:7–15

Palca J (1992) Kaposi's sarcoma gives on key fronts. Science 225:1352–1355

Paxton LA, Janssen RS (2000) The epidemiology of HIV infection in the era of HAART. J HIV Ther 5:2–4

Pellicelli AM, Palmieri F, D'Ambrosio C, et al. (1998) Role of HIV in primary pulmonary hypertension – case reports. Angiology 49:1005–1011

Race EM, Adelson-Mitty J, Barlam TF, et al. (1998) Focal mycobacterial lymphadenitis following initiation of protease-inhibitor therapy in patients with advanced HIV-1 disease. Lancet 351:252–255

Radin DR, Baker EL, Klatt EC, et al. (1990) Visceral and nodal calcification in patients with AIDS-related *Pneumocystis carinii* infection. AJR 154:27–31

Rivers JK, Kopf AW, Postell AH (1989) Malignant melanoma in a man seropositive for the human immunodeficiency virus. J Am Acad Dermatol 20:1127–1128

Rosenthal D, LeBoit PE, Klumpp L, Berger TG. Human immunodeficiency virus-associated eosinophilic folliculitis. Arch Dermatol 1991; 127:206–209

Roth WK, Brandsetter H, Sturzl M (1992) Cellular and molecular features of HIV-associated Kaposi's sarcoma. AIDS 6:895–913

Schwartz DA, Sobottka I, Leitch GJ, et al. (1996) Pathology of microsporidiosis. Arch Pathol Lab Med 120:173–188

Sun NCJ, Shapshak P, Lachant NA, et al. (1989) Bone marrow examination in patients with AIDS and AIDS-related complex. Am J Clin Pathol 92:589–594

Tappero JW, Conant MA, Wolfe SF, et al. (1993) Kaposi's sarcoma. Epidemiology, pathogenesis, histology, clinical spectrum, staging criteria and therapy. J Am Acad Dermatol 72:245–261

Tschirhart DL, Klatt EC (1988) Disseminated toxoplasmosis in the acquired immunodeficiency syndrome. Arch Pathol Lab Med 112:1237–1241

Waddell KM, Lewallen S, Lucas SB, et al. (1996) Carcinoma of the conjunctiva and HIV infection in Uganda and Malawi. Br J Opthalmol 80:503–508