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Abstract

Background: HIV/AIDS is a global disease and despite intensive research it is one of the main causes of human death. Postmortem studies have proven accurate in determining the various pathologies in these patients.

Aims & Objectives: Our aim was to analyze the post mortem results of individuals who died after HIV infection in the same geographical region. We evaluated the most frequent opportunistic diseases and their clinical and morphological outcomes.

Methods: We studied case reports and autopsy research data from 32 patients who died after HIV infection in Smolensk, Russian Federation, between 2003 and 2008. All patients had been diagnosed with HIV infection before death, using HIV-specific enzyme linked immunosorbent assay (ELISA) and immunoblotting. Autopsy specimens of various organs were examined histologically and microbiologically.

Findings: The mean survival period from the moment of detection of seropositivity in all the patients was less than five years. Twelve patients had a parenteral mode of contact, six had been infected by sexual contact, and 14 patients had unknown modes of infection. Most patients (69%) had chronic hepatitis C. The main causes of death were various infectious diseases. The most common were generalized miliary tuberculosis and progressive secondary tuberculosis of the lungs. Three (9%) patients had tuberculosis of the meninges and five (16%) had peritoneal infections, but tuberculous peritonitis had not been diagnosed before death. Six patients had pulmonary tuberculosis and bacterial pneumonia simultaneously. Two (6%) patients died from bacterial sepsis as a result of cervical lymphadenitis, and eight (12.5%) from abscess-forming pneumonia. The opportunistic infections revealed were *Pneumocystis carinii* pneumonia (eight patients), cytomegaloviral pneumonia (three), bronchopulmonary aspergillosis (one) and mucosal candidiasis (three). In three patients, the causes of death were advanced neoplastic processes: two cases of leukemia and one case of cervical cancer.

Conclusions: Tuberculosis was the most widespread among the opportunistic infections, which often had affected the entire lung and had a destructive form. In the morphological picture of tuberculous inflammation, alterative and exudative changes dominated. Moreover, HIV infection had a characteristically broad spectrum of causative agents of pneumonia, including bacteria, viruses, fungi, and protozoa.

Keywords: HIV infection, Morphology, Opportunistic infections, Secondary neoplasms

Introduction

HIV infection is a global pandemic, the extent of which is difficult to evaluate. HIV infection at the present includes all the inhabited continents. It has become a huge problem for the World Heath Organization (WHO), overtaking cancers and cardiovascular diseases as a cause of morbidity. In the Russian Federation there were 461,756 HIV-infected patients officially registered on December 31, 2008. In the Smolensk region (the population on January 1, 2007 was 1,059,000) there were approximately 1,226 and specialists are confident that this was only the 'tip of the iceberg' (Doronin, Makeyenkov, & Yu, 2007).

The high-risk groups for the transmission of HIV are people in their 20th and 30th decades. This prevalence is because of a high rate of unprotected sexual activity, together with intravenous drug use (Royce, Seña, Cates, & Cohen, 1997). Moreover, lack of knowledge about safe sex techniques and the use of nonsterile syringes in drug use help spread the virus significantly.

Severe immunodeficiency in humans with HIV infections makes them prone to numerous opportunistic infections of different systems. The most common targets of these infections are the respiratory tract, the gastrointestinal tract, the central nervous system, the genitourinary tract, and the skin. Recent data has shown that mortality in HIV-infected patients is not only from HIV-related causes but also from other causes, such as neoplasia, and liver and heart disease. These increase with immunological impairment (Weber et al., 2005). Opportunistic infections have gradually decreased in recent years in HIV-infected patients, thanks to highly active antiretroviral therapy (HAART), particularly in early diagnosis and treatment regimens. However, in certain developing countries, HAART is not available to the general population, especially in prisons, so opportunistic infections are frequently encountered in these settings. Tuberculosis plays a significant role as one of the commonly found infectious pathologies, and in severely immunocompromised patients, it is typically found in a destructive phase. Moreover, the respiratory tract, being the most vulnerable for such infections, is often affected the most. Therefore, bacterial pneumonia is a frequently found pathology and is often exacerbated by viral, fungal, and protozoal superinfections (Furrer and Fux, 2002).

Our experience for the past six years has shown that opportunistic infections are the most widespread in HIV-infected patients who undergo delayed HAART or who do not receive any treatment. In recent years, we have also found cases with neoplasia.

The aim of this study was to analyze the cases, and reveal the most frequently occurring opportunistic diseases and their clinical and morphological characteristics in patients who died following HIV infection in the Smolensk region.

Materials and Methods

We used case histories and autopsy research protocols of 32 patients (27 males and five females) aged between 24 and 49 years (mean 31.1 years) who died following HIV infection in various hospitals in the Smolensk region between 2003 and 2008. Autopsy specimens of various organs were studied histologically and microbiologically.

Histopathology

Large tissue sections (1.0 × 0.5 × 0.5 cm) were taken during autopsy, fixed in 10–15% formalin and embedded in paraffin wax for sectioning. The standard protocol is shown in Table 1.

Table 1: Autopsy Specimens of Organs Included in this Study

System	Organs	Suspected Specific Pathology
Respiratory system	Larynx, trachea and bronchi	Laryngitis, tracheitis, endo- and panbronchitis of viral and bacterial origin
	Lungs (each lobe, subpleural and deep, pleura)	Tuberculosis, pneumonia, cytomegalovirus (CMV) infection, pneumocystosis, fungal infections
Gastrointestinal system	Tongue (root and lateral surfaces)	Candidiasis
	Esophagus (lower third part)	Candidiasis
	Stomach	Lymphoma
	Small and large intestine, rectum	Tuberculous ulcerations, CMV infection
	Liver, gall bladder and ducts	Miliary tuberculosis
	Pancreas and ducts	CMV infection
	Omentum, peritoneum	Tuberculous peritonitis

Cardiovascular system	Heart	Cardiomyopathy
Genitourinary system	Kidneys (cortex and medulla)	Miliary tuberculosis
	Ectocervix	Papilloma virus infection and associated neoplasia
Central nervous system	Meninges	Meningitis
	Cerebrum and cerebellum:	Viral infections
	Perivascular (subependymal zones)	
	Cortex	
	Thalamus	
Lymphoid organs	Spleen	Miliary tuberculosis, septic abscesses
	Lymph nodes	Lymphadenitis, tuberculosis
	Thymus	Neoplasia
	Bone marrow	Tuberculosis, neoplasia
Skin	Perianal region	Viral infections
Glands		CMV infection
Retina		Retinitis, CMV infection

Microbiology

Microbiological study included cultures of blood, spleen and lungs in cases of suspected sepsis. Bacterioscopy, histopathology of freshly prepared cytology smears and virological investigations were used routinely in diagnosing the infectious agents.

Histology

The standard staining protocol is shown in Table 2.

Table 2: Stains Used for the Differentiation of Infectious Agents

Type of Stain		**Purpose**
Standard stains	Hematoxylin and eosin (H & E)	Routine microscopy revealing tissue morphology
	van Gieson (Picrofuchsin)	
Ziehl–Neelsen		Revealing acid-fast mycobacteria
Periodic acid Schiff (PAS)		Revealing fungi and protozoa
Gram–Veigert		Revealing specific and nonspecific microflora
Gomori methenamine silver (GMS)		Revealing *Pneumocystis carinii* and fungi

Mucicarmine	Differentiation between various fungi
Alcian blue	Differentiation between various fungi
Romanovskii stain	Differentiation between *Candida* and *Aspergillus*

Results and Discussion

Staging of disease was performed following the guidelines of the Russian classification of HIV and AIDS according to Pokrovskiĭ et al. (2001), which can be summarized as: stage 1, incubation period; stage 2, primary manifestations; stage 3, latent period; stage 4, period of secondary disease. Stage 4 is further divided into: substage 4A, prevalence of superficial infections; substage 4B, prevalence of visceral disease; substage 4C, generalized pathologies; and stage 5, terminal. Accordingly, 10 patients (31%) were diagnosed as at stage 4B, while 22 patients (69%) were diagnosed as stage 4C.

The mode of infection was revealed in 18 patients (56%): parenteral (12 patients) and sexual (six patients), while in 14 patients, the mode of infection could not be determined. Sixteen patients (50%) were diagnosed with HIV infection in prison. Most (69%) patients had chronic hepatitis C. All the patients were diagnosed with HIV infection before death, based on HIV-specific enzyme-linked immunosorbent assay (ELISA) and immunoblotting, and no patient survived for more than five years from the time of detecting HIV seropositivity.

Pathology revealed that the cause of death was an infectious process in all cases, and a neoplastic growth was detected in three patients. The most frequently occurring during autopsy was tuberculosis: miliary tuberculosis with affection of various internal organs (72% of cases) and similarly progressive secondary tuberculosis of the lungs (16%). In 9% of cases, miliary tuberculosis was accompanied by affected meninges and 16% of patients had peritoneal infections. In all the patients with tuberculosis, caseous changes had affected many groups of visceral lymph nodes. Six patients suffered simultaneously from pulmonary tuberculosis and pneumonia of bacterial etiology (*Staphylococcus, Pneumococcus* and *Klebsiella spp.*). In 6% of cases, the cause of death was adenogenous sepsis of bacterial etiology as a result of cervical lymphadenitis and 12.5% patients died from abscess-forming pneumonia. Three patients died from AIDS-related neoplasms. It is important to note that a patient can suffer from multiple pathologies. The opportunistic diseases revealed in our study are summarized in Table 3.

Table 3: Opportunistic Diseases Recorded in 32 Patients who Died Following HIV Infection

Type of Pathology	**Number (%)**
1. Tuberculosis	23 (72%)
2. *Pneumocystis carinii* pneumonia	8 (12.5%)
3. CMV infection	2 (6%)
4. Bronchopulmonary aspergillosis	1 (3%)
5. Mucosal candidiasis	3 (9%)
6. AIDS-related neoplasms	3 (9%)

In 12 patients (37.5%), tuberculosis and pneumonia were diagnosed during life (bacteriologically and radiologically). In the remaining 20 cases, the pathologies were revealed during postmortem investigation.

HIV infection is characterized by generalized lymphadenopathy, which in its growth, passes through a sequence: hyperplasia, involution, depletion, and sclerosis (Libman, 1987). Lymphadenopathy is one of the earliest manifestations of HIV infection. In the stage of hyperplasia, the lymph nodes were characterized by disorderly arranged multiple follicles resembling a 'starry sky' picture caused by many macrophages. Formation of multinuclear cells resembling symplasts merged from lymphocytes affected by virus were rarely found. With the progression of disease, lymphoid depletion became extensive and a fibrovascular carcass was more evident. There was increasing vascularity (angiomatosis) and macrophages in the pulp and sinuses.

As the damage to the immune status of an organism continues following HIV infection, secondary diseases begin to appear and manifested forms of infections and tumors become evident. One of the most frequently revealed causes of death in these patients with HIV infection was tuberculosis, with a prevalence of its generalized form, extensive dissemination and acute progression of specific processes. Tuberculosis is the most virulent infection that is manifested in such cases, usually before other opportunistic infections, and HIV-infected patients comprise one of the high-risk groups for infection.

Morphology of Tuberculosis in HIV-Infected Patients

There was a high prevalence of pulmonary and extrapulmonary tuberculosis. The main forms of tuberculosis were generalized (44%), disseminated (6%), fibro-cavernous (12.5%), caseous pneumonia (9%), and others (tuberculosis of the central nervous system, cirrhotic tuberculosis of lungs, and tuberculosis of the intestine, 4%). All forms of tuberculosis seen in the terminal stages were actively progressive. Various organs were affected, most often the lymph nodes, lungs, liver,

kidneys, spleen, intestine, and central nervous system. Tissue reactions in the terminal stage were typical tuberculosis granulomas in only 20% of cases, and in the remaining 80%, there were many foci of nonreactive caseous necrosis.

Pulmonary tuberculosis

Pulmonary tuberculosis was manifested as a bilateral disseminated type or polycavernous variant. In disseminated tuberculosis, foci of specific lesions (granulomas) comprised large central zones of caseous necrosis surrounded by a few inflammatory cells. Giant cells were rarely found. Ziehl–Neelsen staining showed numerous acid-fast bacteria in the foci of caseous necrosis. Thus, tuberculosis was in the progressive phase and highly active.

Macroscopic study of the lungs often revealed miliary bilateral disseminated tuberculosis, but macronodular dissemination and caseous pneumonia were rare. Dissemination occurred in most of the cases of bilateral, with a predominance of micronodular, miliary and submiliary types, although large foci (~1 cm diameter and mixed—macro–micronodular—dissemination) was common (Fig. 1). We found tuberculous foci in all parts of the lungs, evenly spread to the whole organ or localized to one of the lobes. The intrathoracic lymph nodes were also affected, enlarged (3–4 cm in diameter), and aggregated; on sectioning, they were partially or totally replaced by caseous masses.

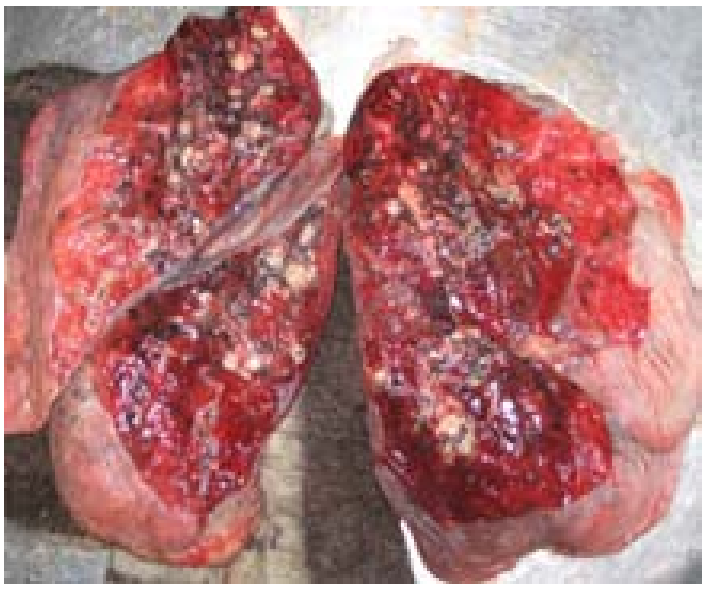


Figure 1: Gross appearance of tuberculous dissemination in the lungs.

(Patient G, male, aged 35 years.)

The characteristic feature was a predominance of alterative and exudative changes with the absence of

a productive component of inflammation or its minimal manifestation (Fig. 2). The latter is marked by the absence of signs of encapsulation and organization of inflammatory foci. Typically, there were few multinuclear giant cells of Langerhans. Granulomas were infrequent and there was little evidence of the wave-like course of disease characterizing the classical variant of tuberculosis. The specific foci of inflammation had monomorphic structures and consisted of a few Langerhans cells surrounded by infiltrates of macrophages and lymphocytes (Fig. 3).

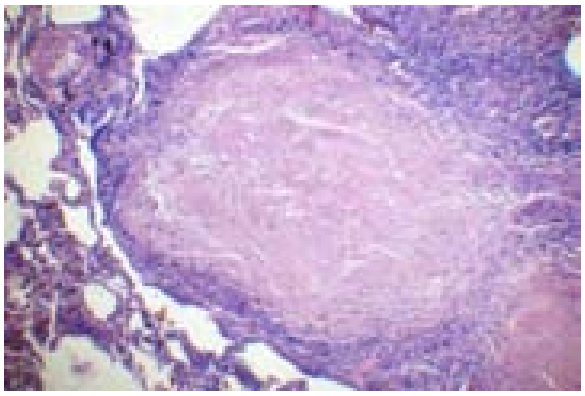


Figure 2: Large focus of caseous necrosis in disseminated tuberculosis. (Patient L, female, aged 30 years.) H & E × 140.

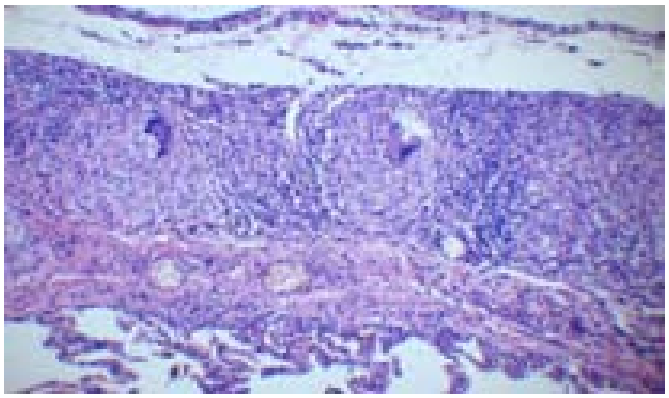


Figure 3: Subpleural localization of tuberculous granulomas containing multinucleated giant cells. (Patient S, male, aged 26 years.) H & E × 200.

Initially, there was formation of colonies of *Mycobacteria* in the pulmonary parenchyma, which was accompanied by cellular infiltration with a significant predominance of polymorphonuclear leucocytes. The cells had phagocytosed the bacteria and this step was marked by karyorrhexis. Later, this process was characterized by massive breakdown of leucocytes and formation of necrosis and microabscesses. Tissue sections stained by Ziehl–Neelsen showed numerous acid-fast bacteria in the foci of caseous necrosis (Fig. 4A–B).

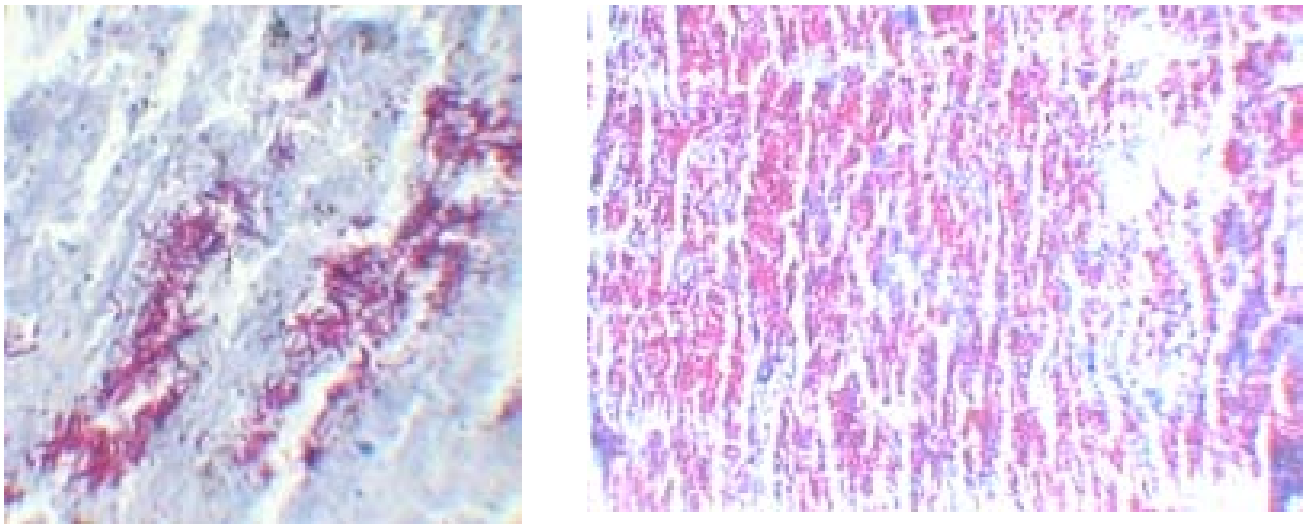


Figure 4: Ziehl–Neelsen stained sections showing colonies of acid-fast *Mycobacteria*. (A) Two microcolonies embedded among masses of caseous necrosis (× 280). (B) Extensive spread of *Mycobacteria* in lung tissue (× 200). (Patient S, male, aged 34 years.)

An extensive exudative reaction in the form of serous-fibrinous pneumonia or fibrinous-purulent pneumonia with predominance of neutrophilic leucocytes was detected at the peripheries of caseous foci. In some fields of view, there were minute foci of accumulations of foamy macrophages that are characteristic for typical tuberculous inflammation.

There was an increase in the thickness of the pleura caused by extensive hyperemia and edema. Cell infiltrates differed according to localization and intensity: perivascular, diffused, diffused-focal and with various stages of intensity. Cells present in nonspecific infiltrates were leucocytes, macrophages and small numbers of lymphocytes or specific granulomatous foci (Fig. 3).

In mediastinal lymph nodes, in many cases there was partial or total caseous lymphadenitis with the spread of inflammatory processes to the surrounding soft tissues. There was fusion of purulent and necrotic masses and absence of productive and granulomatous reactions in the foci. Evident reduction of follicular structures and lymphoid depletion was a characteristic feature of these lymph nodes.

In most cases, macroscopic detection of tuberculous changes in lungs was extremely difficult, but histopathology revealed miliary and submiliary necrotic foci. Typically, these showed alterations with the absence of typical granulomas, monomorphic-type foci and effects on blood vessels in the form of vasculitis. Moreover, morphological changes in lungs were characterized by an acute progression of the disease with absence of a wave-like course of pathology, absence of typical granulomatous tissue reactions, and specificity of inflammatory changes.

Extrapulmonary tuberculosis

Tuberculous meningitis was found in three cases, grossly characterized by typical basilar localization with insignificant gray-white exudates and tubercles in the subarachnoid space. Microscopic examination of the meninges revealed evident hyperemia and edema accompanied by alterative reactions. The latter was manifested as areas of coagulative/caseous necrosis extensively infiltrated by polymorphs, lymphocytes, and macrophages. The endothelium of blood vessels was edematous with pale hypertrophied nuclei and signs of desquamation of endothelial cells in the vascular lumen. Various types of vasculitis such as endovasculitis, panvasculitis, thrombovasculitis, and perivasculitis were evident. Perivasculitis was more often present with edema and excessive mononuclear, neutrophilic, eosinophilic, and plasma cell infiltrates in all layers of the vessel wall (Fig. 5).

Five patients (16%) had tuberculous peritonitis. Unless this localization was included as a component of generalized tuberculosis, specific peritonitis was recorded as the leading cause of death. It is important to note that none of these cases was diagnosed before death, as the clinical picture was confused with chronic pain syndrome, intestinal obstruction, or recurrent intestinal infection. The source of dissemination was assumed hematogenous from the lungs in three cases, lymphogenous from affected mesenteric lymph nodes in one case, and from microperforations of multiple tuberculous ulcers in one patient. At autopsy, peritonitis had an adhesive character and in some cases it had resulted in the formation of fibrous tissue between intestinal loops. Despite the longer course of inflammatory processes in the peritoneum, microscopically there was a typical alterative character with miliary foci and extensive areas of caseous necrosis without expressed productive reaction. Moreover, granulomas were found in the subadventitia of the large intestine in two cases of generalized tuberculosis. However, there were no signs of peritonitis in these two cases on visual inspection. We suppose that in these cases, the process was present at an initial stage, but the death of the patients from other causes interrupted the course of tuberculous peritonitis.

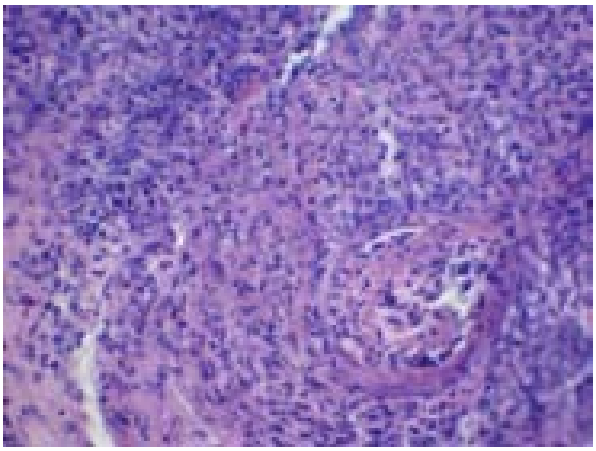


Figure 5: Panvasculitis and thrombovasculitis in the meninges, surrounded by necrotic debris. (Patient

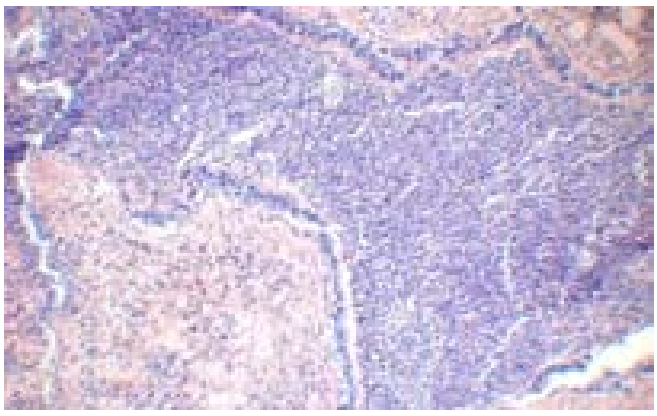
N, male, aged 25 years.) H & E × 240.

Extrapulmonary foci of tuberculous infection were detected in 23 patients (44%) as a component of a generalized type of tuberculosis. Monomorphic miliary foci of caseous necrosis were found in various internal organs, more often in the spleen, kidneys, and liver in descending frequency, and rarely in the meninges, peritoneum, ovaries, pancreas, or adrenal glands. As a whole, in cases of generalized tuberculosis (14 patients), *Mycobacteria* caused alterative and exudative reactions simultaneously in several organs (the mean number of organs involved with *Mycobacterium* was 5.4). All the foci were suspected to be spread hematogenously from lungs. Histopathology of the organs revealed miliary nodules of caseous necrosis with rare giant cells, as in other organs. In many cases, signs of affective reactions were not visible by visual inspection. In the spleen, the foci of caseous necrosis had a tendency to fuse and often covered up to 50% of the cut surface.

Bacterial Pneumonia

Bacterial pneumonia was the second most common cause of death of these patients (25%). There was a broad spectrum of causative agents of pneumonia revealed by microbiology. Besides typical microflora, bacterial pneumonia can be caused by opportunistic agents, which are activated in conditions of general immunodeficiency and extensive decrease in local resistance of respiratory tract and various agents simultaneously. Figure 6A–B shows typical histopathology.

Often, the course of pneumonia in these HIV-infected patients had a tendency to form microabscesses, and in such cases, the microscopic changes resembled microfocal dissemination in pulmonary tuberculosis. In microabscesses, purulent necrotic foci were found with expressed perifocal exudative reaction, which strengthened their resemblance to pulmonary tuberculosis in HIV-infected patients. The causative agents of pneumonia were *Klebsiella pneumoniae, Staphylococcus aureus, Streptococcus pneumoniae* and *E. coli.*



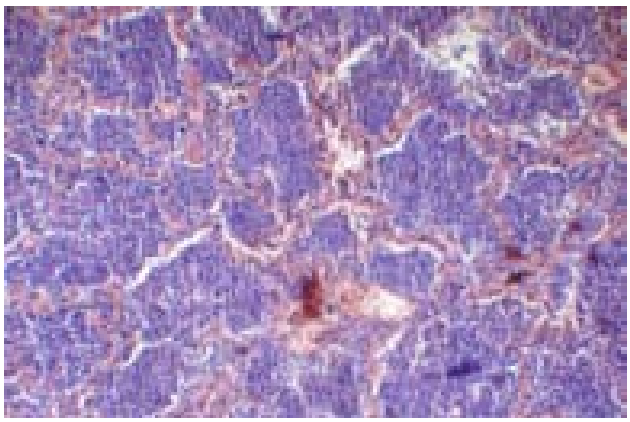


Figure 6: Microscopic appearance of purulent pneumonia. (Patient E, male, aged 30 years.) H & E × 140. (A) Multiple polymorphs in the lumen of a large bronchus. (B) Massive leucocytic exudate in alveoli.

H & E and Gram staining of sections of lungs helped in revealing nonspecific microflora (Fig. 7). At autopsy, staining of smears of lung sections using Romanovskii–Giemsa and by Gram staining also helps in establishing the nonspecific character of microflora in cases of bacterial pneumonia, because at autopsy, Ziehl–Neelsen staining of smears does not reveal causative agents of tuberculosis. Microbiology (bacteriological culture of lung tissue) helps in revealing the nature of the causative agents of pneumonia most accurately.

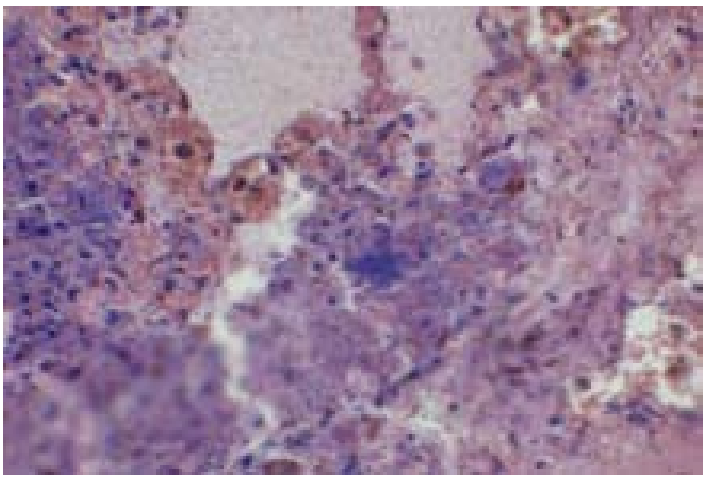


Figure 7: Colony of *Staphylococcus aureus* in the pulmonary parenchyma. (Patient S., male, aged 30 years.) H & E × 300.

Pneumocystis carinii Pneumonia

Pneumocystis carinii typically produces pneumonia that is widespread throughout the lungs with a chronic course of disease and rapid progression. Pulmonary pneumocystosis is a disease caused by intense multiplication of relatively pathogenic single-celled saprophyte *Pneumocystis carinii* in the human respiratory tract (Garcia, 1993). The terminal period of pneumocystosis is pneumonia, manifested in the later stages of HIV infection, and leads to death in most cases. The gross appearance resembled pneumonic consolidation. The cut surface of the lung was pale pink with scattered areas of congestion and, rarely, hemorrhages.

Microscopically, in the edematous stage, a characteristic, homogenous, foamy protein containing eosinophilic exudates in cysts with fistulae was found in the alveolar lumen. This is a pathognomonic sign of pneumocystic pneumonia (Fig. 8). Neutrophils, macrophages, and plasma cells were detected around the collections of *Pneumocystis carinii*. In some fields of view, pink foamy alveolar exudates

were present and the interstitial inflammatory changes were minimal.

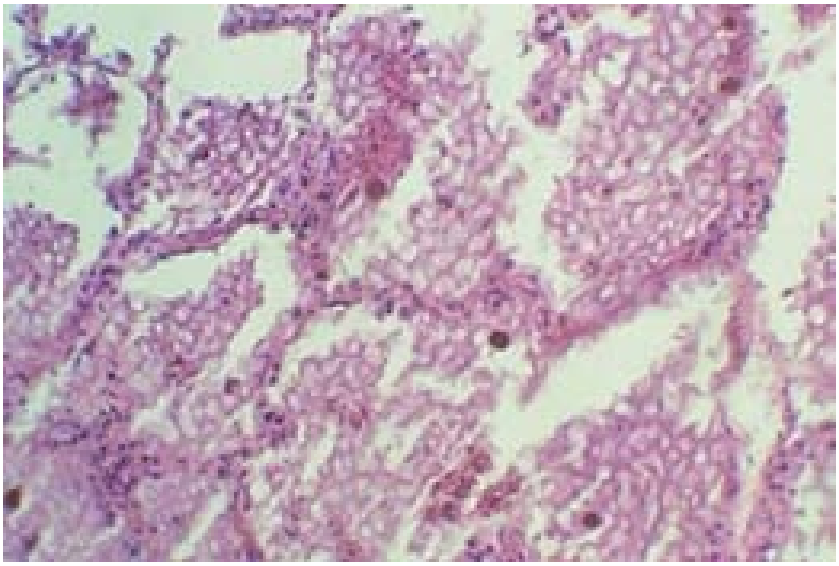


Figure 8: Foamy exudates in the alveolar lumen. (Patient T, male, aged 30 years.) H & E × 200.

Cytomegaloviral Infections

CMV infection is caused by a DNA virus of the herpes virus group. Infection proceeds diversely from latent infection to severe acute generalization in the later stages of HIV infection (Wang, Huong, Chiu, Raab-Traub, & Huang, 2003). Microscopically, CMV infections appear as characteristic metamorphosis of alveolar and bronchial epithelium. They are usually well determined and do not cause difficulties in diagnosis. The persistence of viruses in the epithelial cells leads to cytomegalic giant cell metamorphosis.

Epithelial cells increased in size up to 25–40 μm. About 1–2 nuclear inclusions were detected containing viral particles in the chromatin in each cell and there was a thin perinuclear clear halo. The nucleus of each affected cell was usually eccentrically positioned and the cell border was not prominent. Additionally, the cytoplasm of affected cells contained coarse dark basophilic bodies.

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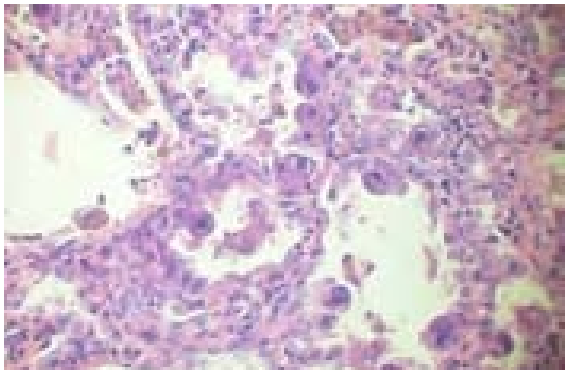

Figure 9: 'Owl-eye' appearance of alveolar cells in CMV infection of lung tissue. (Patient T, male, aged 36 years.) H & E × 200.

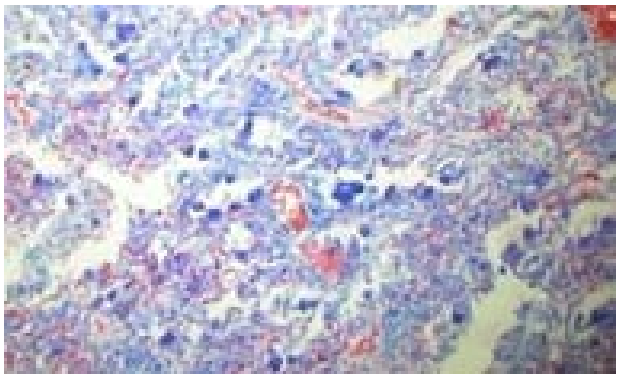

Figure 10: Diffuse pattern of CMV transformation in lung tissue. (Patient T, male, aged 30 years.) Alcian blue × 140.

Characteristic infiltrative changes and cytomegalic transformations were numerous. We found focal accumulations of serous fluid and protein masses in the alveolar cavities with admixtures of macrophages and erythrocytes, moderate cytomegalic transformation of alveolar and bronchial epithelial cells (2–3 typical cells in the form of an 'owl-eye' in the field of view), and weak infiltrations of interstitial tissue (Fig. 9).

If the lung changes consisted of diffuse persisting alveolitis with CMV transformation (up to 20 cells per field of view), then this process was accompanied by extensive fibrosis but uncommonly led to the formation of a 'honeycomb-like' structure (Fig. 10). The outcome of CMV infection of the lungs was peribronchial and widespread interstitial fibrosis with thickening and vast deformation of the interalveolar septa.

Mycoses

Characteristic gross findings of candidiasis were found in the pharynx, larynx, and trachea with invasion into principle bronchi, which included a pseudomembranous form with white, elevated mucosal plaques. Bronchopulmonary aspergillosis and candidiasis were characterized by the collection of fungal mycelium in the lumen of small bronchi and invasion of fungus into the acini. *Candida* microabscesses were common and they had a typical polymorphonuclear leucocytic infiltration. Histologically, *Candida* organisms could be identified by their size, budding property, and pseudohyphae.

The pseudohyphae could be distinguished from *Aspergillus* hyphae by the lack of branching, the smaller size, and frequent absence of true septations in the former (Fig. 11). Results were confirmed using the Romanovskii staining technique, which is used to differentiate between *Candida* and *Aspergillus*. Bronchopulmonary Aspergillosis was characterized by the collection of mycelia of Aspergillus in the bronchial lumen with involvement of the bronchial wall and further invasion of the fungus into the acini (Fig. 12).

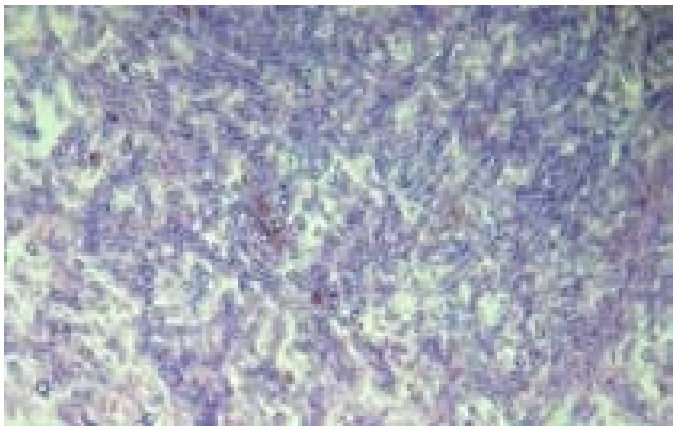

Figure 11: *Aspergillus* accumulation in lung tissue. (Patient T, male, aged 36 years.) H & E × 400.

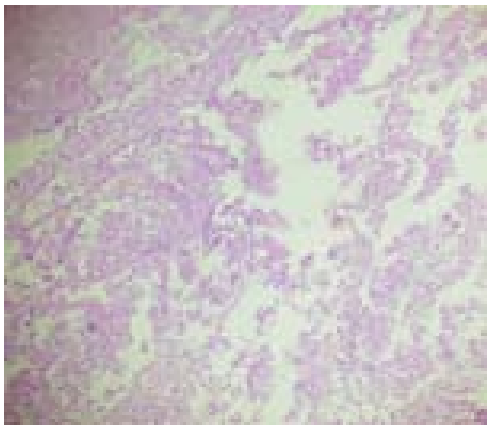

Figure 12: *Aspergillus* hyphae invading the pulmonary parenchyma. (Patient S, male, aged 30 years.) PAS × 200.

Combinations of Opportunistic Infections

The pathological processes found in the respiratory tracts are summarized in Fig. 13.

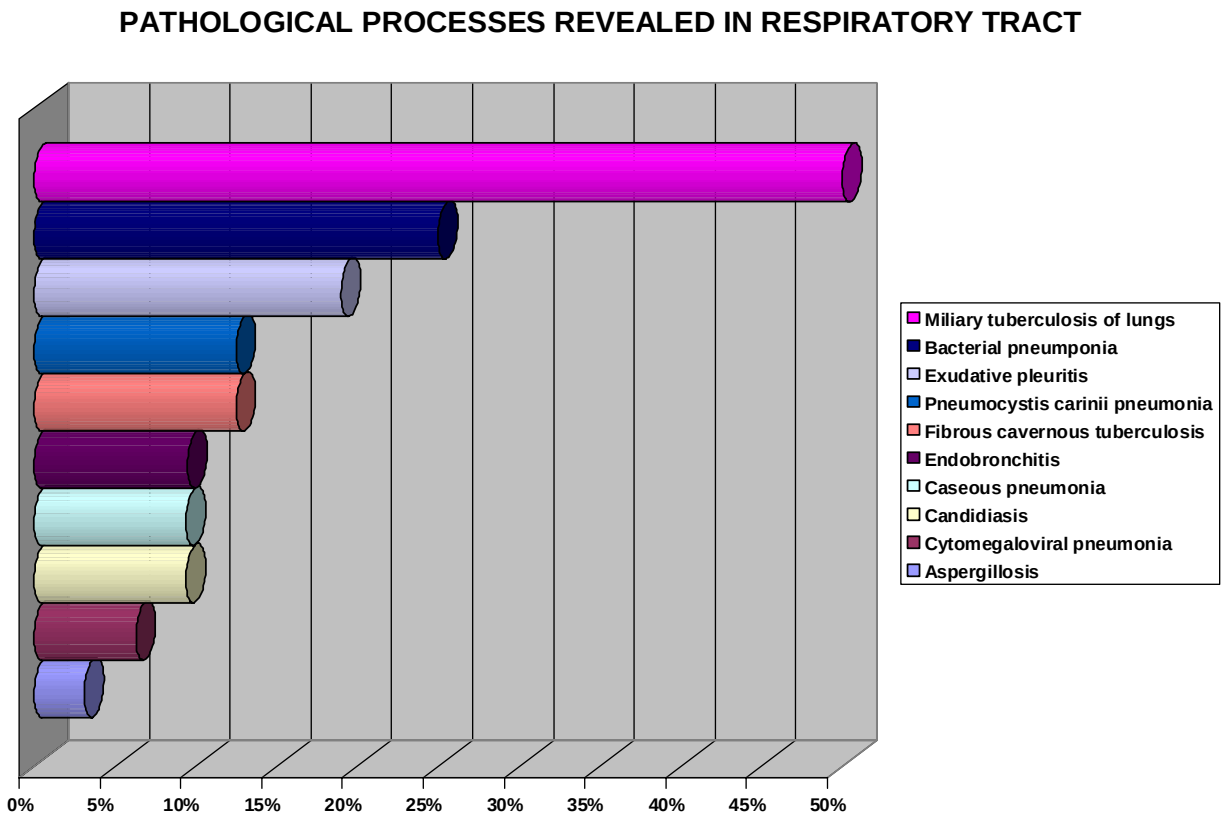

Figure 13: Pathological processes found in the respiratory tract.

One peculiarity of the course of opportunistic pathologies in this series was simultaneous combined infections of the lungs (28% of patients). The most frequent was the combination of tuberculosis with CMV infection (two patients) and *Pneumocystis carinii* pneumonia with CMV infection (one patient). There was a wide spectrum of combined infections of respiratory organs and diverse types of combinations of two or more infections, such as tuberculosis with CMV, *Pneumocystis carinii* pneumonia and purulent bacterial pneumonia, and candidiasis with *Pneumocystis carinii* pneumonia in three cases. Histopathology revealed alternation of some of the various infections, as in focal changes, localized in various lobes or segments of lungs.

HIV-Associated Neoplasia

About 30% to 40% of patients with HIV infection develop a malignancy during their lifetime (Spano, Atlan, Breau, & Farge, 2002). Most cancers affecting HIV-positive patients are those established as

AIDS-defining: Kaposi's sarcoma, non-Hodgkin's lymphoma (NHL), and invasive cervical cancer. Analyses have revealed a two- to threefold increase in the overall risk of developing these cancers (Mbulaiteye, Biggar, Goedert, & Engels, 2003). NHL encompasses several types of lymphoma, including systemic NHL, primary central nervous system NHL (also referred to as primary brain lymphoma or cerebral lymphoma), primary effusion lymphoma (PEL), or body cavity-based lymphoma. We found two cases of high-grade systemic NHL affecting predominantly the spleen, liver, and bone marrow and these were the main causes of death.

Women infected with HIV are more likely to be coinfected with human papilloma virus, possibly because of similar risk profiles and mode of transmission (Palefsky, Holly, Ralston, & Jay, 1998). We detected one case of a well-differentiated cervical squamous cell carcinoma that had invaded the uterus, perforating its wall and leading to peritonitis causing death of the patient. At autopsy, metastases were detected in the liver, lung, and spleen.

Conclusion

The main cause of death of these 32 patients with HIV infection was infectious diseases, in which tuberculosis was the most widespread. Moreover, it had affected multiple organs and had a progressive course of disease with a predominance of miliary tuberculosis. We rarely encountered tuberculous meningitis and peritoneal infection with evident morphological signs of peritonitis. Destructive processes and predominantly alterative and exudative reactions in tuberculous inflammation were typical in all cases. Simultaneous involvement of organs with many infectious processes was a characteristic feature in these patients. Infections such as CMV and *Pneumocystis carinii* pneumonia were revealed at the autopsy, which had not been treated and hence had progressed in their disease course. The respiratory tract was the most affected organ with a prevalence of tuberculosis and pneumonia of various etiologies. The patients that were studied here were mostly young men, which is understandable as they are a high-risk group tending to use unprotected sexual activity and with a high frequency of intravenous drug use. Moreover, most of the patients had been diagnosed with HIV in prison.

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