Morphological Manifestations of the Atypical Mycobacteriosis Caused by Nontuberculous Mycobacteria in the HIV Infected Patients

Marina U. Mayskaya1, Tatiana F. Otten2, Boris M. Ariel3, Elena P. Fedotova4, Robert L. Hunter5, and Ruslan A. Nasyrov4

1Department of Pathology, Kalinin district of St. Petersburg City Mortem Bureau, 2Department of Laboratory diagnosis, St. Petersburg Research Institute of Phthisiopulmonology Health Ministry, 3Department of Pathology, St. Petersburg Research Institute of the Health Ministry Phthisiopneumology, 4Department of Anatomic Pathology, St. Petersburg State Pediatric Medical University, Russia, and 5Department of Pathology and Laboratory Medicine, University of Texas Health Science Center, Houston, TX, USA

Abstract. Infection with atypical mycobacteria (MAC) is a well-known complication of AIDS that typically occurs only in people with advanced immunodeficiency. We studied tissues from 13 patients with HIV and atypical mycobacterial infection who died in St Petersburg Russia from 2009-2012. Three patterns of disease were identified that suggest effects of host resistance. The first pattern was in people paucibacillary disease. They had positive blood cultures and histologic changes consistent with mycobacterial infection, but no stainable acid fast bacilli (AFB). The second group had disseminated infection in many organs including the lungs with extensive necrosis with many AFB. Finally, the third group had massive infection of many organs, but not the lungs, and only minimal necrosis. These observations suggest significant heterogeneity in atypical mycobacterial infections.

Introduction

Non tuberculous mycobacteria are clinically significant in the North-West Russian Federation [1,2,3]. The most common types of potentially pathogenic organisms are M.avium and M.intracellulare, which are integrated in a complex called M. avium-intracellulare complex (MAC) [4,5]. MAC are especially dangerous as an etiologic factor of secondary infection in patients with AIDS, where clinical infections occur with a frequency of 10-53%. Disseminated forms of MAC infection are one of the main causes of mortality in patients with AIDS [1,2,3,6]. This incidence of MAC infection has increased in western Russia. In 2004-2006, only 4 patients developed confirmed MAC cultures in St. Petersburg clinics. In 2007-2009 and 2010-2012 the numbers of positive cultures had risen to 17 and 30 patients respectively. Positive blood cultures were obtained in 6 patients, indicating severe disseminated process that resulted in 4 deaths. Total number of cultures positive in 2004-2012 years was 58.

The aim of our study was to analyze the pathologic changes in the organs and tissues with localized and disseminated forms of MAC infection in HIV-infected AIDS patients on the archival material of St. Petersburg hospitals in the period 2009-2012 years.

Materials and Methods

Autopsy material of 13 patients (10 men and 3 women), with average age was 33.2 years were retrieved and analyzed, including clinical history and autopsy protocols. All patients had an HIV infection in the stage of AIDS. In all cases premortem mycobacteriosis was confirmed by bacteriological culture (blood culture positive in 12 patients). With immunohistochemical confirmation using monoclonal antibodies to common antigen of Mycobacterium-PAB, clone 1.1/3/1 (Vector, USA) and Ziehl-Neelson staining for acid fast organisms (AFB).

Results

The 13 cases were found to consist of three groups. The first group consisted of 3 cases of mycobacteriosis with isolated lesions of the lungs. The second group included 5 cases with multifocal lesions of the lungs, lymph nodes and other organs. The third group contained 5 cases with generalized lesions in kidney, liver, lymph nodes (thoracic, abdominal, retroperitoneal, peripheral), and gastrointestinal tract, without involvement of the lungs.

Group 1. Systemic MAC infection with negative AFB stains. One case revealed a polysegmental bronchopneumonia with serous-neutrophil exudates without destructuve changes in the lung (Figure 1A). Cause of death in this case was HIV-encephalitis. In two other cases intractumeral dissemination with multiple pneumatic foci was found in all lobes of both lungs (Figure 1B). Foci...
Figure 1. Sections of lung of patients with positive blood cultures and characteristic histopathologic lesions, but negative AFB stains. (H&E 100x).

Figure 2. Sections from cases with necrotic lesions of the lungs, lymph nodes and other organs. A. Lymph node (H&E, stain 200x), B. Lymph node, Ziehl-Neelsen acid stain, 400x), C. spleen (100x H&E), D. kidney (100x AFB), E. liver (200x AFB), F. brain (400x AFB).

caseous necrosis with perifocal neutrophil infiltration was found in the centers of pneumonic lesions (Figure 1C). No acid fast bacilli were identified by Ziehl-Neelsen stain in this group even though they all had positive blood cultures for the organism and some had caseous necrosis.

**Group 2. Disseminated MAC infection with necrosis and moderate numbers of AFB.** These cases demonstrated necrotizing bronchopneumonia in combination with caseous adenitis of pulmonary hilar lymph nodes and positive Ziehl-Neelsen acid fast staining. The lymph node architecture was altered, with effacement of corticomedullary junction and loss of lymphoid follicles (Figure 2A). Stroma and sinusoids contained few lymphocytes, scattered polymorphonuclear leukocytes, macrophages and histiocytes. Large foamy macrophages and a few giant multinucleated cells were present showed abundant infection by Ziehl-Neelsen acid fast staining (Figure 2B).

As a consequence of lymphatic and hematologic dissemination multiple foci of MAC were found in all cases not only in the lungs, but also in the spleen (Figure 2C), kidney (Figure 2D), liver (Figure 2E), brain (Figure 2F). These foci all demonstrated central caseous necrosis surrounded by thin layer of leukocytes and lymphocytes. Occasional relatively large foci of caseous necrosis foci were encapsulated by fibrotic shell containing a thick-walled vessels with narrow lumens. This, according to some researchers, may be contribute to resistance of atypical mycobacteria to therapy.

**Group 3. Disseminated MAC infection without necrosis and massive numbers of AFB.** All of these cases demonstrated massive infection by AFB staining, but little inflammation or necrosis. The infection involved the thoracic, abdominal, retroperitoneal, mesenteric lymph nodes, spleen, small intestine and brain without prominent involvement of the lung. Changes in lymph nodes were heterogeneous, from subtotal destruction of the cortical and medullar layers (Figures 3A and B), to predominance of infiltration with atypical histiocytes and macrophages, packed with MAC (Figure 3C). Liver, kidney, small bowel mucosa showed minimal destruction, whereas Ziehl-Neelsen staining revealed innumerable acid fast bacteria, confirmed by immunohistochemical staining (Figures 3D, E, and F).
Pathology of atypical mycobacterial infection in AIDS

Discussion

While it is well known that persons infected with HIV have increased susceptibility to atypical mycobacterial infections, the spectrum of infections in these people is less well studied. Pathological process can be present in localized forms, involving the skin, mucous membranes, respiratory tract and gastrointestinal tract, or in disseminated versions with multiple lesions in the internal organs with non-specific symptoms of generalized infection [8] and often fatal outcome. Along with tuberculosis, atypical mycobacteriosis are among the most common infections in HIV-infected patients, and are included in the group of AIDS-indicating diseases [7,8].

MAC are less virulent than *M. tuberculosis* so that clinical infection typically occurs in people with a greater degree of immunosuppression than does *M. tuberculosis*. The infection is usually diagnosed in AIDS patients only after the exclusion of other opportunistic infections. Nevertheless, our observations demonstrate a spectrum of histologic changes with varying degrees of exudative and granulomas inflammation that suggest differences in competency of immune responses do play a role.

The cellular composition of the granulomas in some cases included lymphocytes and epithelioid cells around areas of coagulative necrosis resembling caseation with no detectable AFB that occurs in immunocompetent people with tuberculosis. In other people, the typical lesions were massive necrosis, slight proliferative processes and accumulation of numerous MAC in macrophages. The abundance of pathogens in macrophages is one of the most striking features of the common morphological patterns of the disease. In still other cases, many tissues contained massive numbers of MAC with little evidence of inflammation or necrosis. This feature is easily observed with Ziehl-Neelsen acid fast stains even at low magnification. Immunohistochemical staining for identification of MAC is indispensable in cases of negative results of Ziehl-Neelsen staining, especially in paraffin-embedded histological slides. The difference of morphological changes MAC may be related to the variation degrees of suppression immunity of ill persons and different degrees of virulence strains MAC.

References