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Exfoliative and Aspiration Cytologies in Patients with Human Immunodeficiency Virus (HIV)

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Summary

Exfoliative and aspiration cytologies play a major role in the management of patients with human immunodeficiency virus infection. Common cytology samples include cervicovaginal and anal Papanicolaou tests, fine needle aspirations, respiratory specimens, body fluids, Tzanck preparations, and touch preparations from brain specimens. While the cytopathologists need to be aware of specific infections and neoplasms likely to be encountered in this setting, they should be aware of the current shift in the pattern of human immunodeficiency virus-related diseases, as human immunodeficiency virus patients are living longer with highly active antiretroviral therapy and suffering fewer opportunistic infections with better antimicrobial prophylaxis. There is a rise in nonhuman immunodeficiency virus-defining cancers (e.g., anal cancer, Hodgkin's lymphoma) and entities (e.g., gynecomastia) from drug-related side effects.

Introduction

The current human immunodeficiency virus (HIV) pandemic has changed considerably, as infected people are now living longer with chronic HIV infection due to highly active antiretroviral therapy (HAART). With HAART therapy, the major cause of death in the later stage of acquired immune deficiency syndrome (AIDS) is malignancy, rather than infection. Moreover, the spectrum of malignancies encountered in HIV-positive patients has expanded to include both AIDS-defining cancers, such as cervical cancer, Kaposi sarcoma (KS), and non-Hodgkin's lymphoma (NHL), as well as non-AIDS-defining cancers (NADC), such as Hodgkin's lymphoma, anal cancer, lung carcinoma, and nonmelanotic skin cancer [1]. However, individuals unlikely to be on HAART therapy are still presented with opportunistic infections, such as tuberculosis, fungi, and parasites. HIV-infected patients have disproportionately high rates of infection with oncogenic viruses, such as human papillomavirus (HPV), Kaposi sarcoma human virus/human herpesvirus-8 (KSHV/HHV-8), and Epstein-Barr virus (EBV). HPV is closely linked to anogenital cancer [2] and HHV-8 associated malignancies include KS [3], primary effusion lymphoma (PEL), and multicentric Castleman's disease. Finally, EBV infection has been linked to Hodgkin's lymphoma, plasmablastic lymphoma (PBL), and leiomyosarcoma [4].

Both exfoliative and aspiration cytologies play a major role in the management of patients with HIV. Fine needle aspiration (FNA) using needles of variable sizes can be used for diagnostic purposes as well as a therapeutic modality, as in draining cystic lesions or effusions. FNA has gained much popularity in evaluating mass lesions in HIV-positive patients because it is noninvasive, well-tolerated, inexpensive, and avoids the necessity of subjecting patients to invasive and costly surgical excision [5]. In addition, an adequate FNA can usually provide sufficient material for ancillary studies, such as microbiology culture, flow cytometry, and/or a cell block for immunocytochemical stains. Anal Pap tests have now been employed at several centers to screen both men and women for possible anal cancer.

HIV Cytopathic Effect

HIV may induce a viral cytopathic effect on host cells. This cytopathic effect was initially observed in vitro by investigators studying HIV-infected lymphocyte cultures. Soon thereafter, researchers identified such viral particles in vivo, while studying HIV-infected human brain and follicular dendritic cells in the lymphoid tissue. HIV causes two types of cytopathic effects: (i) single cell undergoing irreversible cell membrane ballooning, rupture, and lysis, and (ii) multinucleated giant cells formation via cell fusion involving the uninfected CD4 molecule [6]. The ability to lyse CD4 T cells contributes to the clinical condition AIDS. In cytology samples, multinucleated giant cells in lymphoid tissue resembling Warthin-Finkeldey cells are often evident in FNA of HIV-associated benign lymphoepithelial cyst-like lesions of the parotid gland. The giant cells die soon after they are formed, further contributing to the depletion of CD4 T cells.

Cervical Neoplasia

Women infected with HIV have a high prevalence of HPV infection and, therefore, are at increase risk of developing uterine cervical cancer. This can be explained by persistent HPV infection in HIV-seropositive women with multiple HPV subtypes, particularly high-risk HPV types. Depending upon the population studied, squamous intraepithelial lesion (SIL) is up to 40-fold higher in HIV-infected women, and up to 20% of these infected women are likely to develop cervical SIL within 3 years of their HIV diagnosis [7].

Skin and Soft Tissue Pathology

As many as 90% of HIV-positive patients may develop one or more skin diseases during the course of their illness. The spectrum of skin diseases encompasses non-infective and infective dermatoses, adverse drug reactions, and dermatologic neoplasms. Kaposi sarcoma (KS) is the most common AIDS-defining cancer, which may involve both cutaneous and extracutaneous body sites. While most clinicians today perform biopsies for KS, FNA has previously been shown to be useful in the diagnosis of KS.

Key cytologic features of KS include cohesive clusters of spindle cells, a bloody background, and positive immunostaining of lesional cells with vascular (CD34) and lymphatic (D2-40) endothelium markers and/or the HHV-8 antibody latent nuclear antigen-1 (LNA-1). Although the demonstration of HHV-8 DNA by molecular techniques proves to be a useful adjunct in the diagnosis of aspirated KS [3], contamination of samples by mononuclear hematopoietic cells that harbor HHV-8 is possible and can be a misleading finding. The incidence of skin cancers other than KS is increasing in HIV-positive patients. Dermatologic HPV infection in the HIV population can manifest as both anogenital lesions and nongenital skin diseases.

Hematolymphoid Pathology

A large proportion of HIV-infected patients present with lymphadenopathy that is readily amenable to FNA. The etiologies differ by geographic region. In Western countries, such as the USA and England, reactive follicular hyperplasia is more common than infection or lymphoma [8] whereas infections, such as

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tuberculosis, prevail in developing countries. The cytomorphologic findings in reactive lymph node ranging from prominent follicular hyperplasia to aspirates derived from advanced-stage lymphadenopathy with involuted follicles (specimens are lymphoid depleted and rich in plasma cells). With the latter findings, Castleman's disease should be included in the differential diagnosis, and the invariably increasing branching hyaline capillary fragments should at least raise this diagnostic possibility. Although atypical follicular dendritic cells are thought to be diagnostic of Castleman's disease, they are not consistently found on FNA of lymph node. Therefore, FNA is not recommended for the diagnosis of Castleman's disease, and a definite diagnosis will require biopsy, tissue examination, and immunophenotyping. Mycobacterial infection is a common infectious cause of lymphadenopathy in the HIV patient [8].

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