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Polyomavirus infections and its clinical relevance in cancer patients: A Prospective Study

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Summary BK and JC polyomaviruses (PyV) have been demonstrated to be associated with the pathogenesis of various human cancers. We aimed to investigate the impact of BK and JC polyomavirus infections on several clinical parameters in different human cancers. A total of 150 cancer patients were included in the study (51 patients with solid tumors, 48 patients with lymphomas and 51 patients with leukemias). Amplification of PyV DNA was performed using a semi-nested version of Polymerase chain reaction targeting the T genomic region of PyV. The polyomavirus load was determined using real-time PCR assay. The clinical data were collected. Polyomavirus DNA could be detected in 84 (56%) of 150 of all cancerous patients. The solid tumors had the lowest proportion of JCV (6 (11.8%) of 51), whereas had the highest proportion of JCV (200 copies/μl). JCV was more frequent among NHL patients (30%) and absent in HL patients (0%). During follow-up, PyV positivity decreased significantly ($p = 0.004$) in lymphoma patients ($n = 28$). Although PyV positivity decreased significantly from 39% to 7% in 28 of 48 lymphoma patients after treatment, it significantly persisted in leukemic patients after treatment

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(from 22% to 38%). JC was more frequent among leukemic patients with leukopenia. The presence of JC polyomavirus was more frequent among leukemic patients without any significant impact on their overall survival.

Introduction

The human polyomaviruses (HPyVs) are members of the polyomaviridae family. These viruses are non-enveloped viruses, ranging in size from 45 nm to 55 nm, circular and double-stranded DNA genome. The best-known HPyVs are the BK virus (BKV) and JC virus (JCV), which share 75% of the genomic homology [1]. The human BKV and JCV polyomaviruses are ubiquitous viral agents that infect a large proportion of healthy individuals. Primary infections occur during childhood and are usually latent; however, the viruses establish latent infections in renal tissues and B-lymphocytes, and polyomavirus-related diseases can develop under conditions of severe cellular immunosuppression, such as organ transplantation or hematological malignancies [2]. Adult seroprevalence for BKV and JCV is high: more than 90% of the adult population is seropositive for BKV [3], whereas 50—80% of adults have antibodies to JCV [4].

Reactivation of the BK virus (BKV) infection is related to urinary tract diseases, such as hemorrhagic cystitis, ureteric stenosis, glomerulonephritis, and graft nephropathy, which are most commonly observed in transplant patients receiving immunosuppressive therapy. BKV may contribute to allograft dysfunction in up to 8% of the renal transplant patients, resulting in graft loss in 45% of these cases [5]. Reactivation of JC virus (JCV) is linked to progressive multifocal leukoencephalopathy (PML) in HIV-AIDS, hematological diseases and autoimmune diseases treated with certain lymphocyte-specific antibodies [6].

Recently, JCV was found in non-neural cancers, such as gastric and lung cancers [7]. JCV infection was first reported as a potential risk factor for colorectal cancer (CRC) by Laghi and his team [8], who found that 96% of colorectal colon (CRC) tissues were positive for JCV DNA sequences [7].

Hirsch described five different pathology patterns for PyV infections. One of the described pathology patterns was oncogenic pathology [9]. The different types of polyomavirus pathology are predicted to emerge due to different underlying processes that can cause severe and fatal diseases [9]. Accordingly, increasing or high viral loads must be relevant markers in entities associated with high-level replication, such as polyomavirus-associated nephropathy, PML and hemorrhagic cystitis.

Several studies have shown that polymerase chain reaction is an effective tool for detecting polyomaviruses in a range of clinical samples [10]. However, few records in the literature address the impact of PyV infection on the pathogenesis of cancer diseases.

Therefore, we aimed to investigate the correlation between the presence of BK and JC polyomavirus infections and clinical parameters and its association with the overall survival in patients with various human cancers.

Patients and methods

Study population

This prospective study included 99 patients with hematological malignancies (acute leukemia (acute lymphocytic ALL and acute myeloid AML) and lymphoma (Hodgkin's lymphoma (HL) and Non-Hodgkin's lymphoma (NHL)) and 51 patients with solid tumors who were diagnosed and treated at the Medical Oncology Department, National Cancer Institute (NCI), Cairo University. Additionally, 20 apparently healthy normal individuals served as matched controls. The patients were enrolled in the study between 2010 and 2012. All of the experiments were performed in compliance with relevant laws and institutional guidelines and in accordance with the ethical standards of the Declaration of Helsinki. The Institutional Review Board (IRB) of the NCI approved the protocol, IRB No. IRB00004025, Organization No. IORG0003381. Informed written consent was obtained from all patients and individuals enrolled in the study.

The inclusion criteria for the study were as follows: patients diagnosed with acute leukemia (ALL or AML), lymphoma (NHL or HD), or solid tumors; age $\geq$18 years with no previous treatment nor antiviral treatment. All of the patients were subjected to a pretreatment assessment, including complete history and physical examination, as