WU and KI Polyomaviruses Remain Orphans in Adults

To the Editor—We read with interest the brief report by Barzon et al [1] showing that WU and KI polyomaviruses (WUPyV and KIPyV) reactivate and are frequently detectable in the brains of human immunodeficiency virus (HIV)–positive patients without being associated with progressive multifocal leukoencephalopathy. We also recently disproved such an association between novel polyomaviruses (including lymphotropic polyomavirus [LPyV] and Merkel cell carcinoma polyomavirus [MCPyV]) and progressive multifocal leukoencephalopathy in HIV-negative patients [2].

However, because the prevalence of novel polyomaviruses remains high and because they have been shown to reactivate under conditions of immune deficiency [3], they could still prove to be useful as surrogate markers of functional immunodeficiency, as was recently proposed for another orphan virus, torque tenovirus (TTV) [4]. Therefore, we analyzed the occurrence of WUPyV, KIPyV, LPyV, and MCPyV viremia (by the same methods used previously [3]) at the time of peak TTV viremia after high-dose chemotherapy supported by autologous stem cell transplantation in 17 patients with multiple myeloma, 1 with non-Hodgkin lymphoma, and 1 with systemic sclerosis. All samples tested negative. It remains difficult to identify the body site with the highest prevalence and, hence, the greatest sensitivity for these viruses; it could be feces [5], in contrast to urine for JC and BK polyomaviruses [6].

Given that many polyomaviruses are lymphotropic and retain oncogenic potential, we investigated their occurrence in lymph node biopsy samples from patients with lymphoma or leukemia. We could not find any occurrence of WUPyV, KIPyV, LPyV, and MCPyV in any of 49 lymph node samples tested (from, namely, 11 patients with follicular lymphoma, 14 with diffuse large B cell lymphoma, 10 with B cell chronic lymphocytic leukemia, 7 with Hodgkin lymphoma, 2 with mantle cell lymphoma, 1 with Burkitt lymphoma, 1 with splenic marginal zone lymphoma, and 1 with B cell acute lymphoblastic leukemia).

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Reply to Maggi et al

To the Editor—We wish to reply to the comments of Maggi et al [1] on our recent study [2]. At variance with our findings [2, 3], these investigators did not detect any WU and KI polyomavirus (WUPyV and KIPyV) sequences or Merkel cell carcinoma and lymphotropic polyomavirus sequences in brain biopsy, cerebrospinal fluid, or peripheral blood samples obtained from 7 human immunodeficiency virus (HIV)–negative patients with JC polyomavirus–associated progressive multifocal leukoencephalopathy (Focosi et al [4]). As suggested by Maggi et al [1], the absence of the newly discovered polyomaviruses in the brains of HIV-negative patients seems to support the hypothesis that WUPyV and KIPyV reactivate and are detectable in the brains and other tissues of immunosuppressed subjects, such as HIV-infected patients [2, 5, 6]. However, technical aspects need to be taken into consideration when comparing the results of the 2 studies. In particular, stereotactic brain biopsy samples were analyzed in Focosi et al [4], which were probably smaller than the large samples we could obtain at autopsy from multiple brain areas, thus increasing the sensitivity of our polymerase chain reaction method [2].

To get clues on the tropism and clinical conditions associated with WUPyV and KIPyV infection, Maggi et al [1] investigated other clinical samples from patients potentially at risk for polyomavirus infection (ie, peripheral blood from 18 autologous stem cell transplant recipients and lymph node biopsy samples from 49 patients with lymphoma or leukemia), and all samples tested negative. We also screened transplant recipients and patients with lymphoma or leukemia, in addition to children with acute respiratory syndromes, for the presence of WUPyV and KIPyV genome sequences by means of methods that have been described elsewhere [2, 7]. Our results, summarized in Table 1, show that KIPyV was detectable in the nasopharyngeal aspirate sample from only 1 (1.7%) of 60 investigated children, in agreement with the low prevalence reported in other studies [8, 9]. WUPyV was detected in 2.5% of pediatric hematopoietic stem cell transplant recipi...
patients and in 5% of pediatric kidney transplant recipients, supporting the association between polyomavirus reactivation and immunosuppression. The viruses were not detected in the peripheral blood of 70 adult patients with hematopoietic neoplasia (34 with B cell chronic lymphocytic leukemia, 15 with myelodysplastic syndrome, 4 with chronic myelogenous leukemia, 5 with acute myelogenous leukemia, 7 with non-Hodgkin lymphoma, and 5 with multiple myeloma), confirming the finding of Maggi et al [1].

As mentioned by Maggi et al [1], some recent studies have reported a relatively high rate of WUPyV and KIPyV excretion in the feces of children with acute gastroenteritis [8] and hematopoietic stem cell transplant recipients with gastrointestinal symptoms [10], suggesting oral-fecal transmission of these viruses and replication in the gastrointestinal tract. However, our study of a large series of colorectal samples from patients with normal mucosa, adenomas, and carcinomas did not identify any sample positive for WUPyV and KIPyV genome sequences [7].

In conclusion, we agree with Maggi et al [1] that WUPyV and KIPyV remain orphans in adults (and probably even in children). WUPyV and KIPyV infections seem to occur early during childhood and to be generally asymptomatic. These viruses might establish persistent infection in the host and reactivate during severe immunosuppression, but additional studies are warranted to identify the sites of viral infection and persistence as well as to clarify their pathogenetic roles in both immunocompetent and immunocompromised individuals.

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