Evidence of association of human papillomavirus with prognosis worsening in glioblastoma multiforme.


Abstract

Background Glioblastoma multiforme (GBM) is the most malignant brain tumor in adults, but its etiology still remains unknown. Recently, a role of viruses such as cytomegalovirus and JC virus in gliomagenesis has been suggested. Since human papillomavirus (HPV) is considered the most common oncogenic virus in humans, we evaluated its occurrence in GBM samples.

Material and Methods

Fifty-two formalin-fixed paraffin-embedded primary glioblastoma specimens were retrospectively analyzed. The presence of HPV genome on tumor DNA was assessed by MY/GP nested PCR. Confirmation of HPV detection was obtained by chromogenic in situ hybridization (CISH) and immunohistochemistry (IHC) with an antibody directed against the L1 capsidic protein. Finally, univariate and multivariate proportional-hazards models were used to compare the risk of death among HPV-positive and HPV-negative patients.

Results

Strikingly, viral DNA was detected after PCR in 12 cases (23%). HPV16 genome was present in 25% infected samples, whereas the remaining samples tested positive for HPV6. CISH confirmed positivity in all infected samples for which enough material was available. Moreover, IHC positivity suggested that production of viral proteins from HPV genome is an ongoing process in GBM cancer cells. Finally an association between HPV infection and a worse prognosis was found in patients upon age stratification with a univariate analysis (HR, 2.10; 95% CI, 1.00-4.44; log-rank P = .045).

Conclusions

HPV infection status may be considered an independent prognostic factor in GBM patients and suggests that prevention may be considered, should HPV be recognized as a causative agent in gliomagenesis.

KEYWORDS: HPV, glioblastoma multiforme, prognosis

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