Correlation between the prognostic value and the expression of the stem cell marker CD133 and isocitrate dehydrogenase1 in glioblastomas

Abstract

Cancer stem cells are thought to be responsible for tumor recurrence and resistance in glioblastomas. An isocitrate dehydrogenase1 (IDH1) mutation, affecting codon132 of the isocitrate dehydrogenase1 gene, has prognostic significance in glioblastomas. We investigated whether stem cell marker expression [CD133, CD34, and vascular endothelial growth factor (VEGF)] and IDH1 mutation correlate with clinical factors and prognosis in glioblastoma. CD133, CD34, and VEGF expression was evaluated by immunohistochemistry in 67 cases of glioblastoma identified between 2005 and 2012. IDH1 mutation was assessed by immunohistochemistry, peptide-nucleic-acid mediated PCR clamping, and direct gene sequencing. Diffuse CD133 expression was detected in 12 (17.9 %) cases and was associated with poor overall survival (OS) \( (P = 0.010) \) and progression-free survival \( (P = 0.017) \). CD34 and VEGF expression were not associated with prognosis in these samples. IDH1 mutation was detected in ten (14.9 %) cases. Eight were clinically secondary tumors and two were primary tumors \( (P < 0.001) \); the mean age of the secondary tumor patients was significantly younger \( (P = 0.001, 41.20 \text{ vs. } 59.14) \). IDH1-positive patients had longer OS than IDH1-negative patients (25.78 vs. 22.95 months), but this difference was not significant. In addition, IDH1 and CD34 expression showed a negative correlation \( (P = 0.024) \). Multivariate analysis showed that age, extent of surgery, and diffuse CD133 expression correlated with OS. CD133 may be a survival marker for glioblastoma. Further characterization of CD133, IDH1, and vascular markers in glioblastoma may help identify new therapeutic targets.
Correlation between the prognostic value and the expression of the stem cell marker CD133 and isocitrate dehydrogenase1 in glioblastomas

Jung Ha Shin · Youn Soo Lee · Yong-Kil Hong · Chang Suk Kang

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Abstract Cancer stem cells are thought to be responsible for tumor recurrence and resistance in glioblastomas. An isocitrate dehydrogenase1 (IDH1) mutation, affecting codon112 of the isocitrate dehydrogenase1 gene, has prognostic significance in glioblastomas. We investigated whether stem cell marker expression [CD133, CD34, and vascular endothelial growth factor (VEGF)] and IDH1 mutation correlate with clinical factors and prognosis in glioblastoma. CD133, CD34, and VEGF expression was evaluated by immunohistochemistry in 67 cases of glioblastoma identified between 2005 and 2012. IDH1 mutation was assessed by immunohistochemistry, peptide-nucleic-acid mediated PCR clamping, and direct gene sequencing. Diffuse CD133 expression was detected in 12 (17.9 %) cases and was associated with poor overall survival (OS) (P = 0.010) and progression-free survival (P = 0.017). CD34 and VEGF expression were not associated with prognosis in these samples. IDH1 mutation was detected in ten (14.9 %) cases. Eight were clinically secondary tumors and two were primary tumors (P < 0.001); the mean age of the secondary tumor patients was significantly younger (P = 0.001, 41.20 vs. 59.14). IDH1-positive patients had longer OS than IDH1-negative patients (25.78 vs. 22.95 months), but this difference was not significant. In addition, IDH1 and CD34 expression showed a negative correlation (P = 0.024). Multivariate analysis showed that age, extent of surgery, and diffuse CD133 expression correlated with OS. CD133 may be a survival marker for glioblastoma. Further characterization of CD133, IDH1, and vascular markers in glioblastoma may help identify new therapeutic targets.

Keywords Glioblastoma · CD133 · CD34 · Vascular endothelial growth factor (VEGF) · Isocitrate dehydrogenase1 (IDH1)

Introduction Cancer stem cells (CSCs) are undifferentiated, self-renewing, and can develop into tumors [1]. They promote resistance to radiotherapy and chemotherapy by preferential activation of the DNA damage response [2]. The fraction of CSCs in tumors could be used to predict response to cancer treatments and facilitate personalized therapy. CSCs should also be the primary therapeutic target to achieve total tumor eradication.

CD133 is a stem cell marker in diverse normal tissues and cancer types [3]. Singh et al. [4] were the first to describe CD133-positive tumor cell population in brain tumors. CD133 is also a marker of glioma stem cells (GSCs), and studies have demonstrated the association between CD133 expression and patient survival [5–7]. Although reports have been inconsistent, many agree that CD133 positive cells have therapeutic resistance; however most of studies have been performed in cell lines or xenograft models [2, 5–8].

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J. H. Shin · Y. S. Lee (✉) · C. S. Kang (✉)
Department of Hospital Pathology, College of Medicine, The Catholic University of Korea, Seoul, Korea
e-mail: lsys908@catholic.ac.kr
C. S. Kang
e-mail: cskang@catholic.ac.kr
J. H. Shin
e-mail: shinjungta@gmail.com
Y.-K. Hong
Department of Neurosurgery, College of Medicine, The Catholic University of Korea, Seoul, Korea

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