대한방사선종양학회지 2007;25(3):145~150

Impact of Cyclooxygenase-2 Expression on the Survival of Glioblastoma

Youngmin Choi, M.D.*, Dae-Cheol Kim, M.D.†, Ki-Uk Kim, M.D.‡, Young-Jin Song, M.D.‡, Hyung-Sik Lee, M.D.*, Won-Joo Hur, M.D.*, Sun-Seob Choi, M.D.§ and Su-Yeong Seo, M.D.‖

Departments of *Radiation Oncology, †Pathology, ‡Neurosurgery, §Diagnostic Radiology, ‖Microbiology, Dong-A University School of Medicine, Busan, Korea

Purpose: To investigate the degree and effect of cyclooxygenase (COX)-2 expression on the survival of patients with glioblastoma multiforme (GM).

Materials and Methods: Between 1997 and 2006, thirty consecutive GM patients treated with surgery and postoperative radiotherapy (dose range: 44~65.1 Gy, median dose: 61.2 Gy) were included in the study. Three patients were excluded that discontinued radiotherapy before receiving a dose of 40 Gy due to mental deterioration. The expression of the COX-2 protein in surgical specimens was examined by immunohistochemical analysis. Survival analysis and verification were performed with respect to sex, age, performance status, resection extent, radiotherapy dose, and degree of COX-2 expression using the Kaplan-Meier method and the log rank test.

Results: The median length of follow-up was 13.3 months (range: 6~83 months). Staining for COX-2 was positive in all patient samples. Staining for COX-2 that was positive for over 75% of the tumor cells was found in 24 patients. Staining for COX-2 that was positive in less than 25% of tumor cells was found in 3 patients (10.0%), staining for COX-2 that was positive in 25 to 50% of tumor cells was found in 1 patient (3.3%), staining for COX-2 that was positive in 50 to 75% of tumor cells was found in 2 patients (6.7%) and staining for COX-2 that was positive in 75 to 100% of tumor cells was found in 24 patients (80.0%). The median survival and two-year survival rate were 13.5 months and 17.5%, respectively. The survival rate was influenced significantly by the degree of resection (tumor removal by 50% or more) and radiotherapy dose (59 Gy or greater) ($p<0.05$). The median survival of patients with staining for COX-2 that was positive in less than 75% of tumor cells and in at least 75% of tumor cells was 15.5 and 13.0 months, respectively ($p>0.05$), and the two-year survival for these groups was 33.3 and 13.3%, respectively ($p>0.05$).

Conclusion: The absence of a statistical correlation between the degree of COX-2 expression and survival in GM patients, despite the high rate of COX-2 positive tumor cells in the GM patient samples, requires further studies with a larger series to ascertain the prognostic value of the degree of COX-2 expression in GM patients.

Key Words: Glioblastoma, Cyclooxygenase-2, Radiotherapy, Survival

Introduction

Glioblstoma is the most common type of primary malignant brain tumors in adults. Standard treatment for GM is surgical resection followed by postoperative radiotherapy. Complete surgical resection of GM is usually impossible due to its infiltrative growth, resulting in a high recurrence rate. In spite of state-of-the-art therapies, the median survival rate ranges from 12 to 15 months, and most patients die within two years.[1,2] Therefore, new targets to improve outcomes should be pursued.

Cyclooxygenase (COX) is the key enzyme required for the conversion of arachidonic acid to prostaglandins. Its two isoforms are known as COX-1 and COX-2. COX-1 expression is constitutive in most mammalian tissues, but COX-2

Submitted June 27, 2007, accepted August 27, 2007
Reprint requests to Youngmin Choi, Department of Radiation Oncology, Dong-A University School of Medicine, 1 Dongdaesin-dong 3-ga, Seo-gu, Busan 602-715, Korea
Tel: 051)240-5343, Fax: 051)254-5889
E-mail: cymin00@dau.ac.kr
This Paper was supported by Dong-A University Research Fund in 2006.

expression is inducible and increases in response to various stimuli, including inflammatory signals, mitogens, cytokines, and growth factors. Although the precise mechanism remains to be determined, increased COX-2 expression has been associated with carcinogenesis by inhibiting apoptosis[3,4] promoting cell division,[5,6] enhancing metastasis,[7,8] and stimulating neovascularization.[9,10]

Unlike most normal tissues in which COX-2 is expressed at undetectable or low levels, COX-2 is constitutively expressed in the central nervous system, kidneys, and seminal vesicles.[11~13] Although COX-2 is typically expressed in a normal brain, the degree of COX-2 expression in GM was significantly higher compared to low-grade glioma and normal brain specimens.[14~16] Therefore, COX-2 is a likely candidate for a treatment target in GM patients. The prognostic significance of COX-2 expression in GM has been evaluated in several studies. Shono *et al.*[16] reported that the survival of patients with high COX-2 expression was lower compared to those with low COX-2 expression in GM, as well as in glioma. Buccoliero *et al.*[17] found that the median survival of GM patients who were COX-2 positive was more than double of that for who were COX-2 negative. Their findings, however, were statistically insignificant. And the profile of COX-2 expression in GM specimens was heterogenous according to studies.[14~18]

The results documenting the relationship between COX-expression and survival in GM patients are scarce and the degrees of COX-2 expression are various. Thus, this study is an attempt to assess the correlation between COX-2 expression and the survival in GM patients. Another goal is to evaluate the degree of COX-2 expression in GM specimens.

Materials and Methods

Between 1997 and 2006, thirty consecutive patients of GM who were treated with surgery and postoperative radiotherapy at Dong-A university hospital, in Busan, South Korea were included. Three additional patients who discontinued radiotherapy before 40 Gy due to mental deterioration were excluded. In these three patients, radiotherapy was stopped at 12.6, 23.4, and 37.8 Gy. The thirty patients for whom data was fully collected received radiotherapy of 44~65.1 Gy (median: 61.2 Gy) in daily fractions of 1.8~2.0 Gy for five days a week. Clinical data were obtained by a retrospective chart review. The mean and median ages of the patients were 52.6 and 52 years, respectively. Seventeen were male and 13 female. At least 50% of the initial tumor volume was removed by operation in 26 patients, and less than 50% was resected by operation in the remaining four. Twenty seven patients received 59 Gy or more radiation, and the remaining three received less than 59 Gy (Table 1).

Table 1. Patient Characteristics

	Number of patients
Age (year)	
Mean	52.6
Median	52
Sex	
Male	17
Female	13
Extent of resection	
Less than 50%	4
50% or more	26
Radiotherapy dose	
Less than 59 Gy	3
59 Gy or more	27

Immunohistochemical staining was performed with a DAKO EnVision Kit (Dako, Denmark). Immunoperoxidase studies were performed on sections prepared from formalin-fixed and paraffin-embedded specimens that were dewaxed and rehydrated with graded alcohols. Endogenous peroxidase was blocked by dipping sections in 3% aqueous hydrogen peroxide for 10 min, and antigen retrieval was performed with 10 min of microwave treatment in a 10 mM/L citrate buffer at a pH of 6.0. For immunohistochemical staining of COX-2, a Target Retrieval Solution (Dako, Denmark) was used for antigen retrieval. Diluted primary antibodies for COX-2 (1 : 100, Santa Cruz Biotechnologies, CA) were treated at room temperature for 30 min. After the primary antibody incubation, the sections were incubated with the secondary antibody. The sections were then lightly counterstained with hematoxylin. The percentage of COX-2 positive cells in a section was scored by counting at least 50 cells in 10 high-power fields and categorizing to the one of following groups: less than 25%; 25% to less than 50%; 50 to less than 75%; 75% or more (Fig. 1).

Survival time was determined from the date of initial surgery and analyzed by the Kaplan-Meier method (SPSS for

Windows version 12.0.1). The statistical significance of the association between the survival time and variables was verified using a log-rank test that included the degree of COX-2 expression, sex, age, performance status, resection extent, and radiotherapy dose.

Results

The median duration of follow-up was 13.3 months (6~83 months). The median survival and two-year survival rates were 13.5 months and 17.5%, respectively. Expression of COX-2 was detected in all patients with immunohistochemistry. COX-2 positive results for the under 25%, 25~50%, 50~75%, and more than 75% tumor cell groups were found in 3, 1, 2, and 24 patients, respectively. Thus, 80% of the GM patients had 75% or more COX-2 positive tumor cells (Table 2). Median survivals of patients with COX-2 positive in at least 75% tumor cells and less than 75% tumor cells were 13.0 and 15.5 months, respectively ($p>0.05$), and the two-year survival rates of these groups were 13.3 and 33.3%, respectively ($p>0.05$) (Fig. 2. and Table 3).

Survival of patients younger than 50 years did not differ from that for those 50 years or older. Additionally, there was no difference in terms of survival according to the sex and

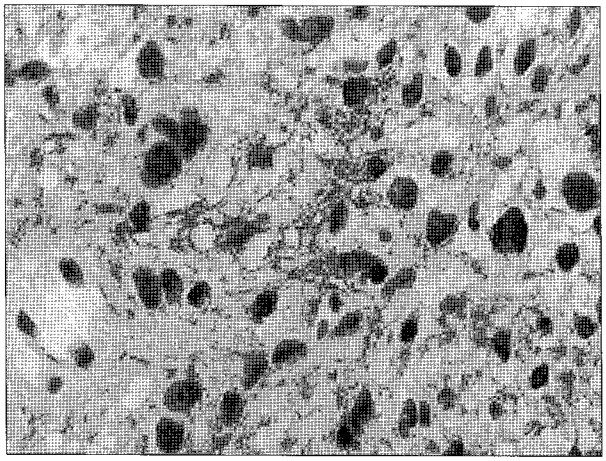

Fig. 1. COX-2 expression in the cytoplasm of a glioblastoma (GM) specimen. More than 75% of GM cells were stained with COX-2 (brown color). Original magnification ×400.

Table 2. The Percentage of COX-2 Positive Cells in the GM Specimens

COX-2 staining	Number of patients (%)
Less than 25%	3 (10.0)
25~50%	1 (3.3)
50~75%	2 (6.7)
75~100%	24 (80.0)

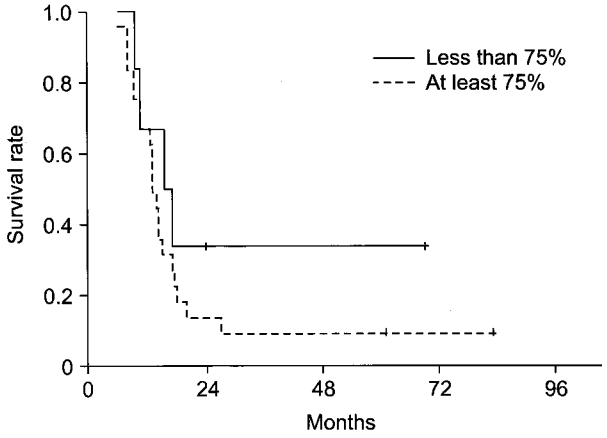

Fig. 2. Kaplan Meier survival curves of patients with glioblastoma according to cyclooxygenase-2 (COX-2) expression. The 2-year survival rates of the patients with COX-2 positive in at least 75% tumor cells and less than 75% tumor cells were 13.3% and 33.3%, respectively ($p>0.05$).

Table 3. Survivals according to the Patients' Characteristics

	No. of patients	Median survival (months)	2-year survival rate (%)	p value
Age (years)				0.87
Younger than 50	15	13.5	20.0	
50 or older	15	14.0	14.8	
Sex				0.55
Male	17	13.5	26.1	
Female	13	14.0	7.7	
Performance status				0.37
ECOG 1	21	14.0	14.29	
ECOG 2	5	13.5	40.0	
ECOG 3	4	6.0	0	
Degree of resection				0.02
Less than 50%	4	8.0	0	
50% or more	26	14.0	20.4	
Radiotherapy dose				0.01
Less than 59 Gy	3	10.0	0	
59 Gy or more	27	14.0	19.5	
Degree of COX-2 expression				0.27
Less than 75%	6	15.5	33.3	
At least 75%	24	13.0	13.3	

performance status of patients. A greater extent of resection and a higher radiotherapy dose resulted in a higher survival rate in patients in general. The median survival and two-year survival rate of patients whose tumor volumes were reduced to less than 50% of the original volume after surgery were significantly better than those whose remaining tumor volumes were more than 50% (14 months and 20.4% versus 8 months and 0%, respectively, p=0.02) after surgery. The median survival and two-year survival rates of patients receiving 59 Gy or higher were 14.0 months and 19.5%, respectively, while these figures for patients receiving less than 59 Gy were 10.0 months and 0%, respectively (p=0.01) (Table 3).

Discussion

The incidence of a COX-2 positive result in GM patients and the extent of COX-2 positive tumor cells in GM specimens are relatively different among studies. Positive staining of COX-2 in the GM patients ranged from 63% to 100% according to the referenced studies.[14~18] The extent of COX-2 staining among tumor cells varies considerably in the studies. Deininger *et al.*[14] reported that the percentage of COX-2-labeled cells among GFAP (glial fibrillary acidic protein) positive GM cells was at most 20% in all GM patients. Prayson *et al.*[18] found that 12 out of 47 GM patients were not stained for COX-2, COX-2 staining in 5% or less of tumor cells was observed in 20 patients, and COX-2 positive results in more than 50% of tumor cells was observed in only two patients. However, higher COX-2 positive results are reported here compared to results published in other studies. Joki *et al.*[15] and Shono *et al.*[16] reported that more than 50% COX-2-immunopositive tumor cells were found in 24 out of 25 GM patients (96%) and in 22 out of 31 (71%), respectively. In present study, COX-2 was expressed in all GM patients, and more than 50% and 75% COX-2 positives among tumor cells were found in 86.7% and 80.0% of GM patients, respectively. As this considerable variation in terms of the percentage of cells expressing COX-2 in the referenced studies may have resulted from the different antibodies used in the immunohistochemical staining, more sensitive antibodies to the COX-2 protein are needed in order to verify the proportion of GM cells that express the COX-2 protein.

The degree of COX-2 expression in gliomas was reported to be directly proportional to the pathologic grade. Thus, the harmful effect of COX-2 expression in GM patients could be inferred. Shono *et al.*[16] found that GM patients with tumors having a high percentage of COX-2 expression (>50% of cells stained positive) had a statistically poorer prognosis compared to those with tumors having a low percentage of COX-2 expression. Buccoliero *et al.*[17] found that the median survival of GM patients with COX-2 positive lesions was shorter compared to those with COX-2 negative lesions (10 months versus 15 months, respectively), although their findings were statistically insignificant. In the present study, the median survival and two-year survival rates were poorer in patients with tumors having a high COX-2 expression (≥75% of cells stained positive) compared to those having a low COX-2 expression. This finding, however, was also statistically insignificant.

In addition to the clinical data concerning the expression and prognostic value of COX-2 in GM patients, further studies targeting COX-2 in glioma cells were conducted. Selective COX-2 inhibitors have been found to inhibit the growth of glioma cell lines[15,19]: additionally, Nam *et al.*[20] revealed in their in vivo study that a COX-2 inhibitor known as celecoxib reduced the size of gliosarcomas significantly in rats. Furthermore, it has been suggested that selective COX-2 inhibitors enhanced the radiosensitivity of GM cells.[21~23] From these results, COX-2 has potential as an additional target for GM management.

The influence of the extent of a surgical resection on the survival of GM patients has been controversial. A number of studies have posited that aggressive resection improved the survival rate of GM patients,[24~26] while others have insisted that the extent of surgery was not a significant prognostic factor.[27,28] In the present study, a greater extent of surgical resection was found to be associated with longer survival rates.

The survival rate of high-grade glioma patients receiving 60 Gy was longer compared to those receiving 45 Gy, showing an increase of three months.[29,30] Irradiation with 58 to 60 Gy in 1.8 to 2.0 Gy fractions for five days is considered as the standard radiotherapy at present. In the present study, the patients irradiated with at least 59 Gy showed better survival compared to those irradiated at less than 59 Gy. With the conventional treatment of surgery and radiotherapy, the survival of GM patient remains poor; most recurrence occurs

in the immediate area 2 to 3 cm from the site of the original tumors.[26,31] Improvements related to local tumor control are necessary, but studies that used a radiation dose of up to 70 Gy or higher did not show a higher survival rate.[32] Therefore, treatments that involve the development of more sophisticated radiotherapy methods and additional targeted therapies are required to improve the survival rate of GM patients.

In summary, COX-2 was expressed in all the GM patients in this study, with more than 75% COX-2 positivity in the tumor cells found in 80% of the patients. Furthermore, the survival rate associated with high-COX-2 expression was lower compared to that associated with low-COX-2 expression, though this finding was statistically insignificant. Further large-scale studies are necessary to ascertain the prognostic value of COX-2 in GM patients.

References

1. **Stupp R, Mason WP, van den Bent MJ, et al.** Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med 2005;352:987-996
2. **Souhami L, Seiferheld W, Brachman D, et al.** Randomized comparison of stereotactic radiosurgery followed by conventional radiotherapy with carmustine to conventional radiotherapy with carmustine for patients with glioblastoma multiforme: report of Radiation Therapy Oncology Group 93-05 protocol. Int J Radiat Oncol Biol Phys 2004;60:853-860
3. **Lin MT, Lee RC, Yang PC, Ho FM, Kuo ML.** Cyclooxygenase-2 inducing Mcl-1-dependent survival mechanism in human lung adenocarcinoma CL1.0 cells. Involvement of phosphatidylinositol 3-kinase/Akt pathway. J Biol Chem 2001; 276:48997-49002
4. **Sheng H, Shao J, Morrow JD, Beauchamp RD, DuBois RN.** Modulation of apoptosis and Bcl-2 expression by prostaglandin E2 in human colon cancer cells. Cancer Res 1998;58: 362-366
5. **Chinery R, Coffey RJ, Graves-Deal R, et al.** Prostaglandin J2 and 15-deoxy-delta12,14-prostaglandin J2 induce proliferation of cyclooxygenase-depleted colorectal cancer cells. Cancer Res 1999;59:2739-2746
6. **Sawaoka H, Kawano S, Tsuji S, Tsujii M, Murata H, Hori M.** Effects of NSAIDs on proliferation of gastric cancer cells in vitro: possible implication of cyclooxygenase-2 in cancer development. J Clin Gastroenterol 1998;27(Suppl 1):S47-52
7. **Tomozawa S, Tsuno NH, Sunami E, et al.** Cyclooxygenase-2 overexpression correlates with tumour recurrence, especially haematogenous metastasis, of colorectal cancer. Br J Cancer 2000;83:324-328
8. **Kakiuchi Y, Tsuji S, Tsujii M, et al.** Cyclooxygenase-2 activity altered the cell-surface carbohydrate antigens on colon cancer cells and enhanced liver metastasis. Cancer Res 2002; 62:1567-1572
9. **Uefuji K, Ichikura T, Mochizuki H.** Cyclooxygenase-2 expression is related to prostaglandin biosynthesis and angiogenesis in human gastric cancer. Clin Cancer Res 2000; 6:135-138
10. **Masferrer JL, Leahy KM, Koki AT, et al.** Antiangiogenic and antitumor activities of cyclooxygenase-2 inhibitors. Cancer Res 2000;60:1306-1311
11. **Yamagata K, Andreasson KI, Kaufmann WE, Barnes CA, Worley PF.** Expression of a mitogen-inducible cyclooxygenase in brain neurons: regulation by synaptic activity and glucocorticoids. Neuron 1993;11:371-386
12. **Yasojima K, Schwab C, McGeer EG, McGeer PL.** Distribution of cyclooxygenase-1 and cyclooxygenase-2 mRNAs and proteins in human brain and peripheral organs. Brain Res 1999;830:226-236
13. **Kirschenbaum A, Liotta DR, Yao S, et al.** Immunohistochemical localization of cyclooxygenase-1 and cyclooxygenase-2 in the human fetal and adult male reproductive tracts. J Clin Endocrinol Metab 2000;85:3436-3441
14. **Deininger MH, Weller M, Streffer J, Mittelbronn M, Meyermann R.** Patterns of cyclooxygenase-1 and -2 expression in human gliomas in vivo. Acta Neuropathol 1999;98: 240-244
15. **Joki T, Heese O, Nikas DC, et al.** Expression of cyclooxygenase 2 (COX-2) in human glioma and in vitro inhibition by a specific COX-2 inhibitor, NS-398. Cancer Res 2000;60: 4926-4931
16. **Shono T, Tofilon PJ, Bruner JM, Owolabi O, Lang FF.** Cyclooxygenase-2 expression in human gliomas: prognostic significance and molecular correlations. Cancer Res 2001;61: 4375-4381
17. **Buccoliero AM, Caldarella A, Gheri CF, et al.** Inducible cyclooxygenase (COX-2) in glioblastoma--clinical and immunohistochemical (COX-2-VEGF) correlations. Clin Neuropathol 2006;25:59-66
18. **Prayson RA, Castilla EA, Vogelbaum MA, Barnett GH.** Cyclooxygenase-2 (COX-2) expression by immunohistochemistry in glioblastoma multiforme. Ann Diagn Pathol 2002; 6:148-153
19. **Kardosh A, Blumenthal M, Wang WJ, Chen TC, Schonthal AH.** Differential effects of selective COX-2 inhibitors on cell cycle regulation and proliferation of glioblastoma cell lines. Cancer Biol Ther 2004;3:55-62
20. **Nam DH, Park K, Park C, et al.** Intracranial inhibition of glioma cell growth by cyclooxygenase-2 inhibitor celecoxib. Oncol Rep 2004;11:263-268
21. **Petersen C, Petersen S, Milas L, Lang FF, Tofilon PJ.** Enhancement of intrinsic tumor cell radiosensitivity induced by a selective cyclooxygenase-2 inhibitor. Clin Cancer Res 2000;6: 2513-2520
22. **Pyo H, Choy H, Amorino GP, et al.** A selective cyclooxygenase-2 inhibitor, NS-398, enhances the effect of radiation in vitro and in vivo preferentially on the cells that express cyclooxy-

genase-2. Clin Cancer Res 2001;7:2998-3005
23. **Karim A, McCarthy K, Jawahar A, Smith D, Willis B, Nanda A.** Differential cyclooxygenase-2 enzyme expression in radiosensitive versus radioresistant glioblastoma multiforme cell lines. Anticancer Res 2005;25:675-679
24. **Simpson JR, Horton J, Scott C, et al.** Influence of location and extent of surgical resection on survival of patients with glioblastoma multiforme: results of three consecutive Radiation Therapy Oncology Group (RTOG) clinical trials. Int J Radiat Oncol Biol Phys 1993;26:239-244
25. **Lacroix M, Abi-Said D, Fourney DR, et al.** A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. J Neurosurg 2001;95:190-198
26. **Cho JH, Lee CG, Kim KJ, et al.** Radiation dose-escalation trial for glioblastomas with 3D-conformal radiotherapy. J Kor Soc Ther Radiol Oncol 2004;22:237-246
27. **Sandberg-Wollheim M, Malmstrom P, Stromblad LG, et al.** A randomized study of chemotherapy with procarbazine, vincristine, and lomustine with and without radiation therapy for astrocytoma grades 3 and/or 4. Cancer 1991;68:22-29
28. **Kowalczuk A, Macdonald RL, Amidei C, et al.** Quantitative imaging study of extent of surgical resection and prognosis of malignant astrocytomas. Neurosurgery 1997;41:1028-1036
29. **Walker MD, Strike TA, Sheline GE.** An analysis of dose-effect relationship in the radiotherapy of malignant gliomas. Int J Radiat Oncol Biol Phys 1979;5:1725-1731
30. **Bleehen NM, Stenning SP.** A Medical Research Council trial of two radiotherapy doses in the treatment of grades 3 and 4 astrocytoma. The Medical Research Council Brain Tumour Working Party. Br J Cancer 1991;64:769-774
31. **Wallner KE, Galicich JH, Krol G, Arbit E, Malkin MG.** Patterns of failure following treatment for glioblastoma multiforme and anaplastic astrocytoma. Int J Radiat Oncol Biol Phys 1989;16:1405-1409
32. **Chang CH, Horton J, Schoenfeld D, et al.** Comparison of postoperative radiotherapy and combined postoperative radiotherapy and chemotherapy in the multidisciplinary management of malignant gliomas. A joint Radiation Therapy Oncology Group and Eastern Cooperative Oncology Group study. Cancer 1983;52:997-1007

Abstract

다형성아교모세포종 환자에서 Cyclooxygenase-2 발현이 생존율에 미치는 영향

동아대학교 의과대학 방사선종양학교실*, 병리학교실†, 신경외과학교실‡, 영상의학교실§, 미생물학교실‖

최영민* · 김대철† · 김기욱‡ · 송영진‡ · 이형식* · 허원주* · 최순섭§ · 서수영‖

목 적: 다형성아교모세포종 환자들에서 cyclooxygenase-2 (COX-2) 단백의 발현 정도와 생존율에 미치는 영향을 조사하고자 한다.

대상 및 방법: 1997년부터 2006년까지 다형성아교모세포종으로 수술 및 방사선치료를 받은 환자들 중에서, 의식 상태의 악화로 40 Gy 전에 방사선치료가 중단된 3명을 제외한 30명을 대상으로 하였다. 조직에서의 COX-2의 발현은 면역조직화학염색으로 검사하였다. 생존 분석과 성별, 나이, 활동도, 수술 정도, 방사선량, COX-2 발현 정도 등이 생존율에 미치는 영향을 Kaplan Meier 법과 log rank test로 분석 및 검증하였다.

결 과: 중앙추적관찰기간은 13.3개월이었다(6~83개월). 전체 환자들에서 COX-2의 발현이 관찰되었고, 종양 세포의 75% 이상에서 COX-2가 양성이었던 환자가 24명이었다: 종양 세포의 25% 미만, 3명(10.0%); 25~50%, 1명(3.3%); 50~75%, 2명(6.7%); 75~100%, 24명(80.0%). 중앙생존기간이 13.5개월이었고, 2년 생존율은 17.5%였다. 수술 정도(50% 이상 종양 제거)와 방사선량(59 Gy 이상 조사)이 생존율에 유의하게 영향을 주었다($p<0.05$). 종양 세포의 75% 미만에서 COX-2가 발현되었던 환자군과 75% 이상에서 발현되었던 환자군에서 중앙생존기간은 각각 15.5개월과 13.0개월이었고($p>0.05$), 2년 생존율은 각각 33.3%와 13.3%였다($p>0.05$).

결 론: 다형성아교모세포종에서의 COX-2 양성도는 높았지만, 다형성아교모세포종 환자들에서 COX-2 발현의 정도와 생존율 간에는 통계적인 유의성이 없었으므로, 향후 보다 많은 환자들을 대상으로 COX-2 발현 정도가 생존율에 미치는 영향에 대한 연구가 필요하다.

핵심용어: 다형성아교모세포종, Cyclooxygenase-2, 방사선치료, 생존율