Expression, association with clinicopathological features and prognostic potential of CEP55, p-Akt, FoxM1 and MMP-2 in astrocytoma

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Abstract. Centrosomal protein 55 (CEP55) is a member of the centrosomal-associated protein family and participates in the regulation of cytokinesis during cell mitosis. However, aberrant CEP55 protein expression has been observed in human tumors. In addition, CEP55 regulates the biological functions of tumors by inducing the Akt pathway and upregulating forkhead box protein M1 (FoxM1) and matrix metalloproteinase-2 (MMP-2). In the present study, the levels, clinicopathological features and prognostic potential of CEP55, phosphorylated Akt (p-Akt), FoxM1 and MMP-2 in astrocytoma were evaluated. CEP55, p-Akt, FoxM1 and MMP-2 levels were examined in 27 normal brain tissues and 262 astrocytoma tissues by using immunohistochemistry. Furthermore, Kaplan-Meier analysis and Cox proportional hazards models were applied to predict the prognosis of patients with astrocytoma. The results indicated that expression levels of CEP55 and other proteins were elevated in human astrocytoma compared with those in normal brain tissue. The levels of the selected proteins were increased as the tumor grade increased. Furthermore, CEP55 expression was positively correlated with p-Akt, FoxM1 and MMP-2 levels in astrocytoma. Overall survival analysis revealed that patient prognosis was associated with CEP55, p-Akt, FoxM1 and MMP-2 levels, as well as with the tumor grade and patient age. Furthermore, CEP55, FoxM1, tumor grade and patient age were independent prognostic factors in astrocytoma according to multivariate analysis. Taken together, the present results suggested that CEP55, p-Akt, FoxM1 and MMP-2 have crucial roles in the progression and prognosis of human astrocytoma and that CEP55 and FoxM1 may be potential therapeutic targets.

Introduction

Astrocytoma is a common type of human glioma and a primary lethal central nervous system (CNS) tumor. High invasion and poor prognosis are typical features of this tumor type. In particular, patients with glioblastoma, the most aggressive form of malignant astrocytoma, only have a median survival time of 9-12 months (1,2). Despite multimodal treatment, including surgical resection followed by chemotherapy and radiotherapy, no significant improvements in clinical outcomes have been observed in patients with astrocytoma. Therefore, novel molecular markers or targets may contribute to the diagnosis and treatment of malignant brain tumors.

Isocitrate dehydrogenase (IDH) mutations are commonly detected in low-grade diffuse gliomas and evidence supports that this mutation is a driver of gliomagenesis. IDH1 mutations represent a distinguishing feature of low-grade glioma and secondary glioblastoma (GBM) (3). Of note, patients with IDH1 mutations have a significantly better prognosis than patients with wild-type IDH1 (4). Based on the updated 2016 edition of the World Health Organization (WHO) classification of CNS tumors, IDH1 has become a necessary marker for analysis of tumor classification (5). Therefore, IDH1 mutations are important reference indices for the pathological diagnosis and prognostic evaluation of patients with glioma.

Centrosomal protein 55 (CEP55) is a member of the CEP protein family and was initially identified as a centrosome- and midbody-associated protein that regulates cytokinesis (6). Overexpression of CEP55 leads to cytokinesis defects and increased multinucleated cells, which may cause tumorigenesis. In recent years, high CEP55 expression has been indicated in certain types of human tumors and to be correlated with poor prognosis in patients with malignancies (7-9). A study also indicated that overexpression of CEP55 enhances the cell proliferation and aggressiveness in gastric carcinoma, whereas CEP55 knockdown inhibits these processes (10). Furthermore, numerous studies have indicated that CEP55 regulates the biological behaviors of tumors through the phosphatidylinositol 3-kinase (PI3K)/Akt signaling pathway (11,12). For instance, in osteosarcoma and lung cancer, CEP55 promoted the proliferation, migration and invasion of tumor cells via the...
PI3K/Akt signaling pathway (13,14). In addition, CEP55 has been indicated to combine with the catalytic subunit α of PI3K, also known as p110. This interaction enhances the stability of the subunit, resulting in increased Akt activation, as demonstrated by an increase in S473 phosphorylation (11,13).

Forkhead box protein M1 (FoxM1) is a member of the Fox family and is expressed mainly as a transcription factor in normal proliferating cells (15). Furthermore, FoxM1 is upregulated in most human solid malignant tumor types, including cervical carcinoma, lung cancer and glioma (16-18). FoxM1 is localized in the nucleus of tumor cells and is regulated by multiple cytokines and signaling pathways, including the PI3K/Akt pathway. Cross-talk between the Akt and FoxM1 pathways has been demonstrated (19-21). Various studies suggested that Akt upregulates FoxM1 expression in osteosarcoma and that downregulation of Akt by small interfering RNA inhibits FoxM1 expression in prostate cancer and melanoma (20-22). In addition, FoxM1 is able to increase the expression of matrix metalloproteinase-2 (MMP-2) in various human tumor types, thereby promoting the invasion and metastasis of tumors. For instance, downregulation of FoxM1 expression in esophageal squamous cell carcinoma cells may cause a significant decrease in MMP-2 expression (23). Ahmad et al (24) reported that upregulation of FoxM1 expression in breast cancer cells markedly increased MMP-2 expression and promoted tumor invasion and metastasis. Furthermore, FoxM1/MMP-2 and CEP55 are correlated in certain tumors. Indeed, in oral squamous cell carcinoma, CEP55 increases the expression of FoxM1 and MMP-2 proteins, thereby promoting tumor cell migration and invasion (25). However, the possible roles and putative associations among CEP55, phosphorylated (p-)Akt, FoxM1 and MMP-2 in astrocytoma remain to be fully elucidated.

Accordingly, in the present study, the levels of CEP55, p-Akt, FoxM1 and MMP-2 in astrocytoma were determined and the associations of these proteins with the clinicopathological features of astrocytoma were investigated. In addition, survival analysis was performed to identify factors that affect the prognosis of patients with astrocytoma.

Materials and methods

Tissue specimens and clinical data. The present study was a retrospective study. A total of 262 cases were included and their archival paraffin-embedded astrocytoma tissue specimens collected between May 2011 and February 2016 at the Department of Pathology of the Second Hospital of Hebei Medical University (Shijiazhuang, China) were obtained. The present study was approved by the Ethics Committees of the Second Hospital of Hebei Medical University (Shijiazhuang, China) and informed consent for the use of these tissues and the use of the 27 normal brain tissue specimens was also approved by the Ethics Committee of the Second Hospital of Hebei Medical University (Shijiazhuang, China). The overall survival time was calculated from the date of diagnosis to the date of death or the date of the last follow-up or last time-point the patient was known to be alive, defined as censored (last evaluated November 30, 2017).

Immunohistochemical staining. Immunohistochemical staining for CEP55, p-Akt, FoxM1, MMP-2 and IDH1 proteins in astrocytoma sections was performed using a ready-to-use Biotin-Streptavidin/Horseradish peroxidase (HRP) Detection system (OriGene Technologies, Inc.). Paraffin sections (4 μm) were deparaffinized in xylene and then rehydrated with alcohol; heat-induced antigen recovery was performed in citrate buffer (pH 6.0) for 5 min at 120°C or EDTA antigen retrieval solution (pH 8.0) for 5 min at 120°C, followed by quenching of the endogenous peroxidase using 3% H2O2 for 20 min at room temperature. Goat serum (OriGene Technologies, Inc.) was used for blocking nonspecific binding sites for 3-4 h at room temperature. Slides were then incubated with primary antibodies [anti-CEP55 (1:400 dilution; Abcam; ab214302); anti-p-Akt (1:150 dilution; Gene Tex; GTX28932); anti-FoxM1 (1:600 dilution; Abcam; ab207298); anti-MMP-2 (1:200 dilution; Gene Tex; GTX104577); mouse anti-IDH1R132H (working solution; OriGene Technologies, Inc.; ZM-00447)] at 4°C overnight. After washing with PBS, a Biotin-Streptavidin HRP Detection system (working solution; OriGene Technologies, Inc.; SP-9000/9001/9002) was used for detection of the antigen-antibody complex, which was visualized with diaminobenzidine as the chromogen. Finally, counterstaining was performed using Mayer’s hematoxylin and the sections were dehydrated in alcohol prior to mounting. As a negative control, the primary antibody was omitted; no staining was observed.

Scoring of staining. Immunohistochemical staining was assessed using semi-quantitative scoring by two independent investigators (YL and JC) who were blinded to the histopathological features and clinicopathological data of the samples. Before the scoring was performed, a set of criteria were
established based on the literature with minor modifications in terms of the percentage scores of positive cells and the final score (27-30). The degree of staining was determined by the percentage of positive cells and the staining intensity. Cells that were stained with yellow or brown color were considered as positively-stained cells. Necrotic areas and areas with extensive bleeding were not included. Positive expression of CEP55, p-Akt and MMP-2 proteins was identified in the cytoplasm and/or nucleus. Sections were observed and five high-power fields (magnification, x40) were randomly selected under a light microscope. The percentage of positive cells was divided into four grades (percentage scores), as follows: 1, ≤10%; 2, 11-50%; 3, 51-80%; and 4, >80%. The staining intensity was divided into four grades (intensity scores), as follows: 0, no staining; 1, light yellow; 2, brown; and 3, dark brown. The staining degree was calculated as follows: Overall score=percentage score x intensity score. If the overall score was 0-4, the sample was classified as having low expression; if the overall score was 5 or more, the sample was classified as having high expression. FoxM1 protein was localized in the nucleus. Percentage scoring for FoxM1 protein was as follows: 0, ≤5%; 1, 6-25%; 2, 26-50%; 3, 51-75%; and 4, >75%; while the intensity scoring was as follows: 0, no staining; 1, light yellow; 2, brown; and 3, dark brown. The staining degree was calculated as follows: Overall score=percentage score x intensity score. Overall scores of 0-4 indicated low expression, whereas overall scores of 5 or more indicated high expression. Based on this, the patients were divided into low and high expression groups.

Figure 1. CEP55, p-Akt, FoxM1, MMP-2 and IDH1 proteins in astrocytoma were detected by immunohistochemistry. CEP55 and IDH1 were localized in the cytoplasm of tumor cells. p-Akt and MMP-2 protein were mainly expressed in the cytoplasm, with a small amount in the cell nuclei. FoxM1 protein was observed only in the cell nuclei. Low expression of CEP55, p-Akt, FoxM1 and MMP-2 was present in normal brain tissue and DA, while high expression was observed in AA and GBM. Staining for IDH1 was negative in normal brain tissue and GBM and strongly positive in DA and AA (magnification, x200; scale bar, 100 µm). DA, diffuse astrocytoma; AA, anaplastic astrocytoma; GBM, glioblastoma; FoxM1, forkhead box protein M1; MMP-2, matrix metalloproteinase-2; p-Akt, phosphorylated Akt; CEP55, centrosomal protein 55; IDH, isocitrate dehydrogenase.
Statistical analysis. All statistical analyses were performed using SPSS 21.0 software (IBM Corp.). $\chi^2$ tests were used to compare the staining results for target proteins in different groups and for comparisons with clinicopathological characteristics. The correlations between CEP55 and other proteins were determined using nonparametric Spearman's correlation tests. Kaplan-Meier analysis was performed to draw overall survival curves and statistical significance was assessed using log-rank tests. Univariate and multivariate analysis were performed using the Cox proportional hazard regression model. P<0.05 was considered to indicate statistical significance.

Results

CEP55, p-Akt, FoxM1 and MMP-2 levels in normal brain tissues and astrocytoma tissues. Immunohistochemical analyses were performed to determine the expression levels and distributions of target proteins. Representative images and the results are provided in Fig. 1 and Table I, respectively. For the 27 normal brain tissues, high expression of CEP55, p-Akt, FoxM1 and MMP-2 was observed in 2 (7.4%), 2 (7.4%), 0 (0.0%), and 1 (3.7%) cases, respectively. For the 262 astrocytoma tissues, high expression of these proteins was observed in 170 (64.9%), 145 (55.3%), 136 (51.9%), and 156 (59.5%) of cases, respectively. Thus, high expression of these markers was significantly more frequent in astrocytoma than in normal brain tissue (P<0.05).

Clinicopathological characteristics of CEP55, p-Akt, FoxM1 and MMP-2 in astrocytoma. Next, the associations of protein levels and clinicopathological features in patients with astrocytoma were assessed by $\chi^2$ tests and Spearman correlation analysis. As presented in Table II, the expression levels of CEP55, FoxM1 and MMP-2 in astrocytoma were positively associated with patient age (P<0.05); however, sex and tumor size were not significantly associated with the expression levels of the three proteins (CEP55, FoxM1 and MMP-2).
MMP-2; P>0.05; Table II). High levels of p-Akt were not associated with age, sex or tumor size in patients (P>0.05; Table II). Furthermore, Spearman correlation analysis indicated that the levels of CEP55, p-Akt, FoxM1 and MMP-2 were correlated with the tumor grade (r_{CEP55}=0.540, P<0.05; r_{p-Akt}=0.526, P<0.05; r_{FoxM1}=0.585, P<0.05; r_{MMP-2}=0.482, P<0.05; Fig. 2). As the tumor grade increased, the levels of all of the four proteins also increased (P<0.05; Table II). However, IDH1 mutations were not associated with the expression of CEP55, p-Akt, FoxM1 and MMP-2 in astrocytoma (P>0.05; Table II). Taken together, these results indicated that CEP55, p-Akt, FoxM1 and MMP-2 may have roles in astrocytoma progression.

**Prognostic value of CEP55, p-Akt, FoxM1 and MMP-2 in patients with astrocytoma.** As presented in Fig. 3, overall survival analysis indicated that higher expression levels of CEP55, p-Akt, FoxM1 and MMP-2 were associated with significantly poorer overall survival than that for patients with lower levels of these proteins. Indeed, CEP55, p-Akt, FoxM1 and MMP-2 levels were positively correlated in astrocytoma and DA (P<0.05). In AA, correlations were observed between all proteins (P<0.05), except for the correlation between FoxM1 and MMP-2, which was not significant. In GBM, a positive correlation was observed for all comparisons (P<0.05). In GBM, a positive correlation was observed for all comparisons (P<0.05); however, there was no significant correlation between p-Akt and FoxM1 and between FoxM1 and MMP-2. These results suggested that CEP55 may interact with the other proteins to mediate invasive growth of astrocytoma.

**Discussion**

Astrocytoma is a common type of brain tumor in humans. Diffuse astrocytoma (also known as low-grade astrocytoma) and anaplastic astrocytoma frequently progress to glioblastoma with highly proliferative and invasive phenotypes. Despite advanced therapeutic strategies, the prognosis of malignant
Table III. Correlations among CEP55, p-Akt, FoxM1 and MMP-2 levels in astrocytoma.

A, Astrocytoma

| Protein | p-Akt | FoxM1 | MMP-2 |
|---------|-------|-------|-------|
|         | High  | Low   |       | High  | Low   |       | High  | Low   |       |
|         |       |       |       |       |       |       |       |       |       |
| **CEP55** |       |       |       |       |       |       |       |       |       |
| High    | 0.594 | <0.001 |       | 0.508 | <0.001 |       | 0.501 | <0.001 |       |
| Low     | 131   | 39    |       | 120   | 50    |       | 132   | 38    |       |
| p-Akt   |       |       |       | 0.365 | <0.001 |       | 0.464 | <0.001 |       |
| High    | 99    | 46    |       | 116   | 29    |       | 116   | 29    |       |
| Low     | 37    | 80    |       | 40    | 77    |       | 40    | 77    |       |
| **FoxM1** |       |       |       |       |       |       |       |       |       |
| High    | 0.405 | <0.001 |       |       |       |       |       |       |       |
| Low     |       |       |       |       |       |       |       |       |       |

B, DA (WHOII)

| Protein | p-Akt | FoxM1 | MMP-2 |
|---------|-------|-------|-------|
|         | High  | Low   |       | High  | Low   |       | High  | Low   |       |
|         |       |       |       |       |       |       |       |       |       |
| **CEP55** |       |       |       |       |       |       |       |       |       |
| High    | 0.531 | <0.001 |       | 0.492 | <0.001 |       | 0.556 | <0.001 |       |
| Low     | 16    | 10    |       | 11    | 15    |       | 15    | 11    |       |
| p-Akt   |       |       |       | 0.338 | 0.002 |       | 0.448 | <0.001 |       |
| High    | 8     | 14    |       | 12    | 10    |       | 12    | 10    |       |
| Low     | 5     | 54    |       | 7     | 52    |       | 7     | 52    |       |
| **FoxM1** |       |       |       |       |       |       |       |       |       |
| High    | 0.393 | <0.001 |       |       |       |       |       |       |       |
| Low     |       |       |       |       |       |       |       |       |       |

C, AA (WHOIII)

| Protein | p-Akt | FoxM1 | MMP-2 |
|---------|-------|-------|-------|
|         | High  | Low   |       | High  | Low   |       | High  | Low   |       |
|         |       |       |       |       |       |       |       |       |       |
| **CEP55** |       |       |       |       |       |       |       |       |       |
| High    | 0.494 | <0.001 |       | 0.312 | 0.001 |       | 0.240 | 0.016 |       |
| Low     | 55    | 21    |       | 54    | 22    |       | 61    | 15    |       |
| p-Akt   |       |       |       | 0.216 | 0.030 |       | 0.284 | 0.004 |       |
| High    | 42    | 17    |       | 50    | 9     |       | 50    | 9     |       |
| Low     | 21    | 21    |       | 25    | 17    |       | 25    | 17    |       |
| **FoxM1** |       |       |       |       |       |       |       |       |       |
| High    | 0.150 | 0.133 |       |       |       |       |       |       |       |
| Low     |       |       |       |       |       |       |       |       |       |

D, GBM (WHOIV)

| Protein | p-Akt | FoxM1 | MMP-2 |
|---------|-------|-------|-------|
|         | High  | Low   |       | High  | Low   |       | High  | Low   |       |
|         |       |       |       |       |       |       |       |       |       |
| **CEP55** |       |       |       |       |       |       |       |       |       |
| High    | 0.490 | <0.001 |       | 0.323 | 0.003 |       | 0.277 | 0.013 |       |
| Low     | 60    | 8     |       | 55    | 13    |       | 56    | 12    |       |
|         | 4     | 8     |       | 5     | 7     |       | 6     | 6     |       |
astrocytoma remains poor (1,2). Therefore, early diagnosis and prognostic evaluation of astrocytoma are critical for early treatment and improved survival.

CEP55 is a member of the CEP family and has important roles in mediator-dependent cellular functions, including centrosome replication, cell cycle progression and cytokinesis (6). CEP55 exhibits high expression in numerous human tumor types and high expression of CEP55 is associated with the degree of malignancy (12). Similarly, in the present study, it was demonstrated that CEP55 was upregulated in patients with astrocytoma, suggesting important roles of CEP55 in the progression of this tumor type.

After stimulation by growth factors, hormones and cytokines, Akt is phosphorylated, resulting in activation of the protein. p-Akt promotes the growth, proliferation, invasion and metastasis of cancer cells. p-Akt has been detected in various tumor types, including prostate cancer (31) and colorectal cancer (32). The levels of p-Akt were also increased in the study, indicating that Akt activation may be involved in the development or progression of astrocytoma.

FoxM1 is a key transcription factor that has important roles in embryo development, mature tissue homeostasis and carcinogenesis. Upregulation of FoxM1 has been observed in numerous malignant tumor types, including lung cancer, oropharyngeal squamous cell carcinoma and ovarian cancer (33-35). It was also revealed that FoxM1 was upregulated in astrocytoma, similar to CEP55 and p-Akt.

MMP-2 is a gelatinase that degrades the extracellular matrix and has important roles in tumor cell growth and differentiation, invasion, metastasis and tumor angiogenesis. MMP-2 is closely linked to the occurrence and development of various types of tumor, including breast cancer, ovarian cancer and lung cancer (36-38). In the present study, overexpression of MMP-2 was also observed in astrocytoma, further highlighting the importance of this proteinase in cancer.

Overall, the present results suggested that CEP55, p-Akt, FoxM1 and MMP-2 were involved in the development of astrocytoma. CEP55, FoxM1 and MMP-2 were positively associated with the age of patients in astrocytoma, but sex and tumor size were not associated with the three proteins.

### Table III. Continued.

| Protein | p-Akt | FoxM1 | MMP-2 |
|---------|-------|-------|-------|
|         | High  | Low   |       |
| p-Akt   |       |       |       |
| High    | 49    | 15    | 54    |
| Low     | 11    | 5     | 8     |
| FoxM1   |       |       |       |
| High    | 49    | 11    | 49    |
| Low     | 13    | 7     | 13    |

CEP55, centrosomal protein 55; p-Akt, phosphorylated Akt; FoxM1, forkhead box protein M1; MMP-2, matrix metalloproteinase-2; DA, diffuse astrocytoma; AA, anaplastic astrocytoma; GBM, glioblastoma.

### Table IV. Univariate and multivariate analysis of the prognostic factors of patients with astrocytoma.

| Variable                      | Univariate analysis | Multivariate analysis |
|-------------------------------|---------------------|-----------------------|
|                               | HR (95% CI)         | P-value               | HR (95% CI)         | P-value               |
| CEP55 (Low vs. high expression)| 3.958 (2.724-5.751) | <0.001                | 2.406 (1.496-3.869) | <0.001                |
| p-Akt (Low vs. high expression)| 2.543 (1.855-3.485) | <0.001                | 1.174 (0.801-1.722) | 0.410                 |
| FoxM1 (Low vs. high expression)| 3.423 (2.482-4.721) | <0.001                | 1.871 (1.298-2.696) | 0.001                 |
| MMP-2 (Low vs. high expression)| 2.492 (1.798-3.454) | <0.001                | 0.827 (0.560-1.221) | 0.339                 |
| Tumor grade (DA/AA vs. GBM)   | 2.097 (1.728-2.545) | <0.001                | 1.477 (1.161-1.879) | 0.002                 |
| Age (<50 years vs. ≥50 years) | 2.230 (1.647-3.020) | <0.001                | 1.860 (1.348-2.567) | <0.001                |
| Sex (Female vs. male)         | 1.224 (0.908-1.649) | 0.184                 |                     |                       |
| Tumor size (<5.0 cm vs. ≥5.0 cm)| 1.020 (0.763-1.365) | 0.893                 |                     |                       |

HR, hazard ratio; CEP55, centrosomal protein 55; p-Akt, phosphorylated Akt; FoxM1, forkhead box protein M1; MMP-2, matrix metalloproteinase-2; DA, diffuse astrocytoma; AA, anaplastic astrocytoma; GBM, glioblastoma.
addition, the levels of all four proteins increased as the tumor grade increased, further supporting the conclusions regarding the roles of these targets in astrocytoma progression.

CEP55 promotes the growth and invasion of gastric carcinoma, oral cancer, osteosarcoma and lung cancer by inducing the PI3K/Akt pathway and upregulating FoxM1 (10-14, 25). Chen et al (25), indicated that oral cancer cell motility is promoted by CEP55/FoxM1-induced MMP-2 overexpression and activation. In addition, FoxM1 is regulated by numerous signaling pathways, including the Akt signaling pathway. For instance, in melanoma and osteosarcoma, Akt modulates FoxM1 protein expression (19, 20, 22). Inhibition of Akt activity or expression results in decreased FoxM1 expression. In prostate cancer, the expression levels of Akt and FoxM1 are also positively correlated (21). In addition, FoxM1 is involved in the invasion of glioma cells as an upstream regulator of MMP-2. When FoxM1 expression is downregulated in glioma cells, MMP-2 expression also decreases, affecting tumor invasion and metastasis (39). In the present study, Spearman’s rank correlation analysis revealed that CEP55 protein expression was positively correlated with p-Akt, FoxM1 and MMP-2 levels in astrocytoma. These results suggested that CEP55 may...
interact with the other three proteins to regulate the invasive growth of astrocytoma.

High expression of CEP55 and FoxM1 is linked to the occurrence, development and malignancy of tumors and to poor prognosis. For instance, Jiang et al (40) indicated that patients with non-small-cell lung cancer with higher CEP55 expression had a less favorable prognosis than patients with lower CEP55 expression. In breast cancer, the expression levels of CEP55 were positively associated with the degree of malignancy and high expression of CEP55 was indicated to be associated with poor prognosis (41,42). In addition, Dai et al (43), indicated that FoxM1 expression was significantly increased in solid malignant tumors (including breast, gastric and pancreatic cancer) and was associated with poor prognosis. Furthermore, Wen et al (35) reported that FoxM1 promotes the proliferation, invasion and metastasis of ovarian cancer cells, resulting in poor prognosis. The present study indicated that high levels of CEP55, p-Akt, FoxM1 and MMP-2 were associated with shorter overall survival. Further multivariate analysis confirmed that CEP55 and FoxM1 expression, tumor grade and patient age were independent prognostic factors in patients with glioma.

In conclusion, CEP55, p-Akt, FoxM1 and MMP-2 levels were increased in astrocytoma and these targets may have important roles in the progression of this disease. Furthermore, strong correlations were observed among CEP55, p-Akt, FoxM1 and MMP-2 in patients with astrocytoma. It may therefore be proposed that CEP55 upregulates MMP-2 expression, which promotes the invasion of astrocytoma cells by mediating the Akt/FoxM1 signaling pathway. The results of the overall survival analysis revealed that CEP55, p-Akt, FoxM1 and MMP-2 levels, as well as tumor grade and patient age were associated with patient prognosis. Furthermore, CEP55 and FoxM1 expression, tumor grade and patient age were independent prognostic factors predicting poor outcomes in patients with astrocytoma. Taken together, the present results indicated that these four targets have crucial roles in the progression and prognosis of human astrocytoma. CEP55 and FoxM1 may be potential therapeutic targets.

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Availability of data and materials

The datasets used during the present study are available from the corresponding author upon reasonable request.

Authors’ contributions

YL, SN and JW were responsible for the conception and design of the study and critically revised the manuscript for important intellectual content. SN, JC, WG and YC were responsible for the data acquisition, selection and analysis and clinical interpretation of the data. SN, LL, QZ, YL, HS, LX, LS and WW performed the experiments and analyzed the data. All authors contributed to the writing of the manuscript. All authors read and approved the final version of manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of The Second Hospital of Hebei Medical University. All patients or their guardians provided written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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