

CASE REPORT

Ganglioglioma with glioblastoma component

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Abstract

Ganglioglioma with a glioblastomatous component and high-grade atypia of neuronal cells are extremely rare findings. In this paper, we report the case of a 60-year-old man who presented with a tumor of the left temporal lobe. Hematoxylin–Eosin stained slides revealed a complex tumor with features of glioblastoma and marked atypia of neuronal cells. Glial cells were highlighted by antibodies to GFAP and neuronal cells by chromogranin and synaptophysin markers. There was an accumulation of p53-positive cells. There was a high Ki-67 labelling index (19%).

Keywords: ganglioglioma, glioblastomatous component, neuronal atypia.

□ Introduction

Gangliogliomas are rare tumors in the central nervous system, representing approximately 1% of all brain tumors [1–3]. They occur in both children and adults and are characterized by the presence of ganglion and low-grade glial cells, most cases being grade I or II [4, 5].

Malignant transformation in gangliogliomas is a well-known phenomenon. In most cases, progression leads to an anaplastic (WHO grade III ganglioglioma) [5]. Transformation into a glioblastoma multiforme (WHO grade IV ganglioglioma) is exceptional, about fifteen cases having been published. The correlation of the histological picture with the clinical evolution is still imperfectly established, although its therapeutically implications are obvious.

The case that we studied presented initially with a grade IV ganglioglioma, without prior radiation therapy, and showed anaplastic features of both glial and neuronal cells, a very rare finding.

□ Patient and methods

The patient, a 60-year-old man presented with a tumor of the left temporal lobe, diagnosed clinically and imagistically.

Surgery was done in another medical center and grossly examination revealed a 3/2 cm tumor, whitish, with yellow and hemorrhagic areas.

Paraffin-embedded pieces of tumor were sent to our department for diagnosis. Sections cut at 5-μm were routinely stained with Hematoxylin–Eosin (H&E). Immunohistochemistry analysis was done on slides stained for glial fibrillary acidic protein (GFAP), chromogranin, synaptophysin, p53 protein and Ki-67.

□ Results

The examination of H&E stained slides revealed a complex picture, with glial and neuronal areas (Figure 1). The glial component was dominated by highly anaplastic astrocytic cells. The tumor was hypercellular, the nuclei showed marked atypia and there was a high mitotic index (16 mitoses/10 HPF). Some cells showed gemistocytic features and there was a minor oligodendroglial component. There were areas of coagulative necrosis with pseudo-palisading of neoplastic cells (Figure 2) and microvascular proliferation with glomeruloid structures (Figure 3). The neuronal component was represented by ganglion cells showing cytological atypia (large and bizarre nuclei, hyperchromatism, binucleation) (Figure 4).

GFAP was strongly positive in the glial cells (Figure 5). Neuronal cells were evidenced by chromogranin (Figure 6) and synaptophysin immunohistochemistry. The histological and immunohistochemical data were compatible with a WHO grade IV ganglioglioma, the glial element being represented by a glioblastoma multiforme. Glial cells showed an accumulation of p53 protein (Figure 7) and a high Ki-67 labelling index (29%) (Figure 8).

□ Discussion

Most gangliogliomas are located in the temporal lobes, but have been observed in the frontal lobes, brain stem, cerebellum, spinal cord, pituitary gland and pineal gland [5, 6].

The most common presenting symptom is seizures, noted also in our case.

Anaplastic transformation of gangliogliomas occurs in the glial component, which resembles an anaplastic astrocytoma [2, 6–12].

In the case reported by Suzuki H *et al.* [11] anaplastic neuroglial tissue contained both benign and anaplastic glial components. Adjacent to the anaplastic tissue there was a sarcomatous tissue dominated by pleomorphic fibroblastic cells, which were immunoreactive for smooth muscle actin,

type IV collagen and alpha-1-antitrypsin, but not for desmin and CD34. Interestingly, some of the sarcomatous cells were double positive for smooth muscle actin and GFAP. Ganglioglioma with anaplastic oligodendrogloma component are more rarely encountered [10, 12–14].

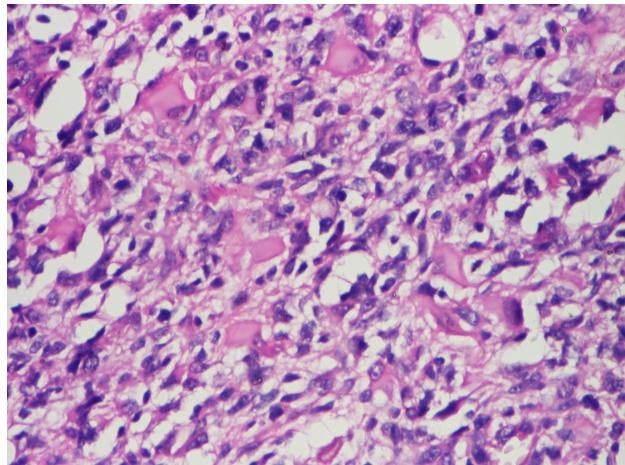


Figure 1 – Dysplastic neuronal and malignant glial cells (H&E stain, $\times 50$)

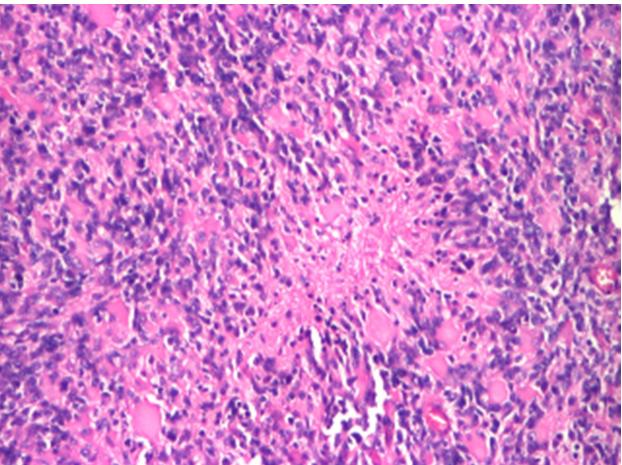


Figure 2 – Pseudopalisading necrosis within the glioblastomatous component (H&E stain, $\times 25$)

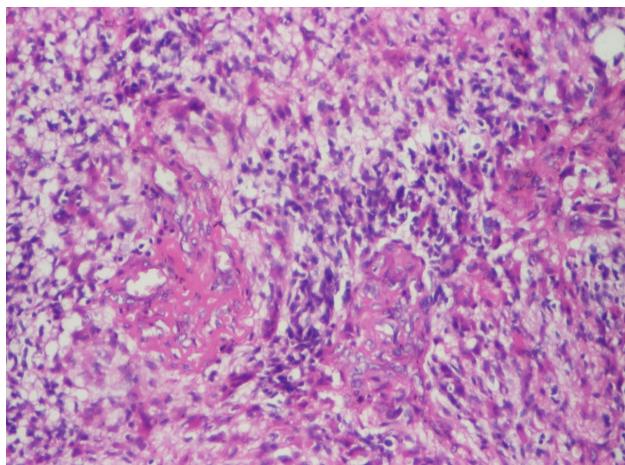


Figure 3 – Vascular proliferation with glomeruloid structures (H&E stain, $\times 25$)

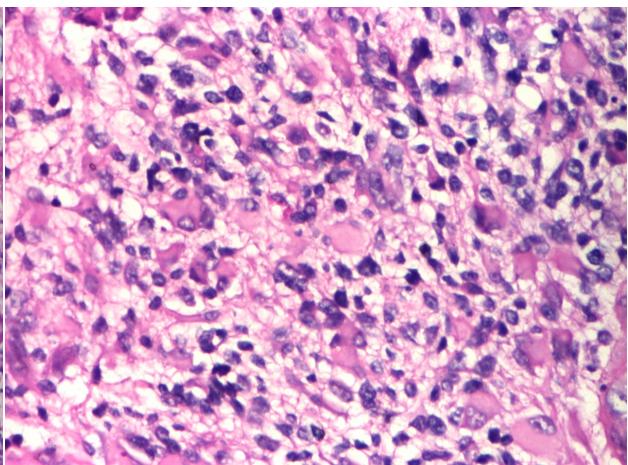


Figure 4 – Marked atypia of ganglionic cells (H&E stain, $\times 50$)

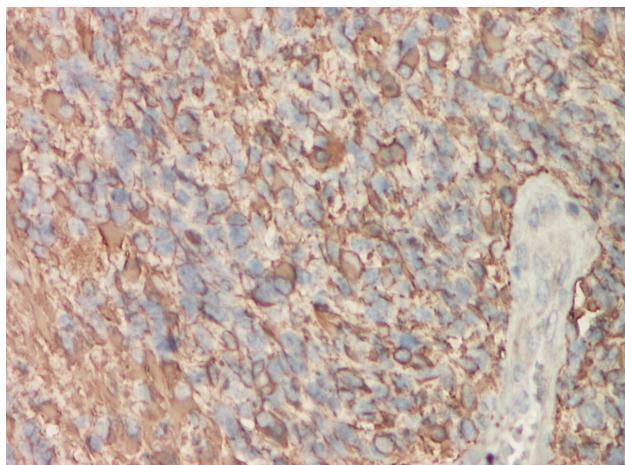


Figure 5 – GFAP positivity of glial cells, $\times 50$

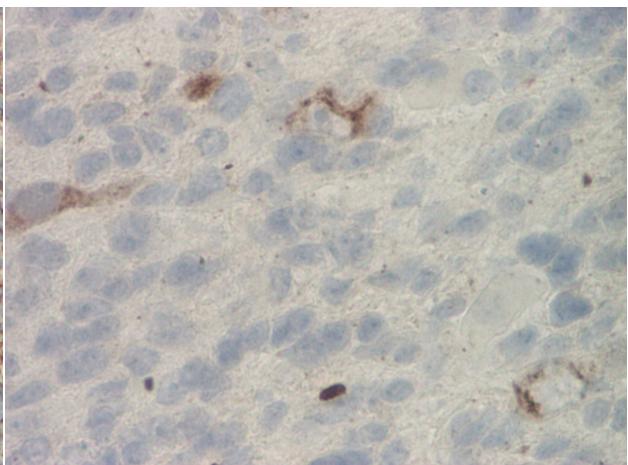


Figure 6 – Neuronal cells were focally positive for chromogranin, $\times 100$

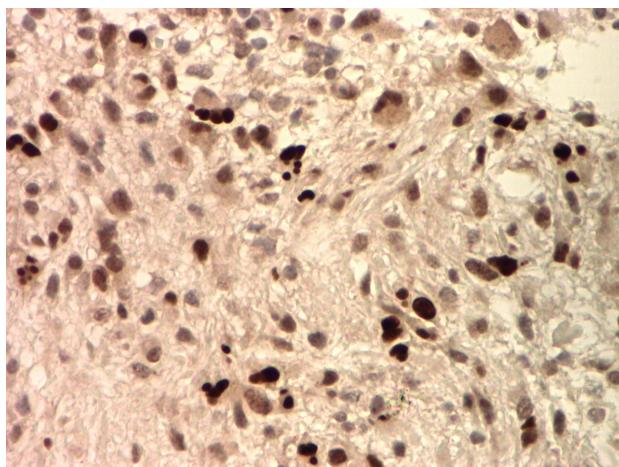


Figure 7 – Immunostaining showing p53 protein-positive cells, $\times 50$

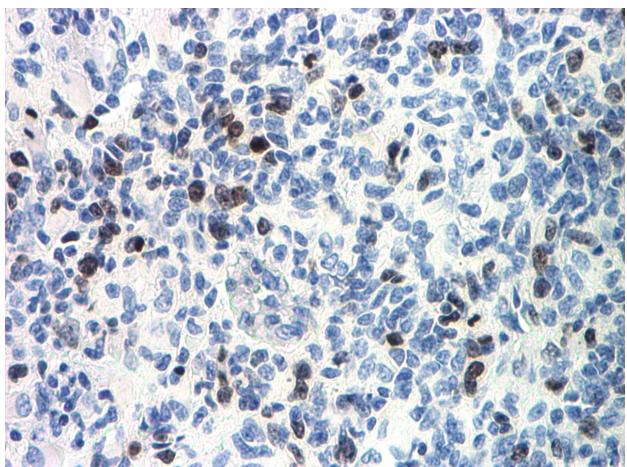


Figure 8 – Numerous cells with Ki-67-positive nuclei, $\times 50$

Ganglioglioma with a glioblastomatous component (WHO grade IV ganglioglioma) are rare findings [1, 15–18]. Mekni A *et al.* [19] found 12 cases having been reported in the literature and added a new one. In most cases malignant component was represented by astrocytes. In rare cases, both astroglial and neuronal cell components showed anaplasia [20–22], a feature that was evident in our case. Gliosarcoma component is usually the result of a malignant transformation of a low-grade ganglioglioma because of a previous radiation therapy [17, 20, 21, 23]. In our case, the patient presented initially with a WHO grade IV anaplastic ganglioglioma, a situation rarely mentioned in the literature [19, 21].

Anaplastic ganglioglioma gain the potential to disseminate to the spinal cord [24] or even in the abdominal and pleural cavities [25].

The correlation of the histological picture with the clinical evolution is still imperfect. Molecular biology studies have shown that Ki-67 index is higher in the anaplastic component than in the benign area [11, 26]. A high Ki-67 labelling index (19%), in accordance with the proliferative capacity of the tumor, was found in our study. Hirose T *et al.* [27] noted that Ki-67 index was significantly higher in recurrent tumors than in the non-recurrent ones, even no examples of anaplastic transformation were encountered. Kim NR *et al.* [18] studied the glioblastomatous transformation of a ganglioglioma and noted that the original tumor exhibited a high proliferation index on flow cytometry, suggesting that application of this technique might play a certain role in predicting biological and clinical behavior of low-grade gangliogliomas.

The accumulation of p53 protein exhibited by the anaplastic glial cells in our case was also mentioned in the literature [11, 18]. The presence of TP53 mutation in progressed gangliogliomas was interpreted as a progression – associated mutation playing a role in the molecular pathway of transformation [17].

These data show that a glioblastomatous component and atypia of neuronal cells may be present initially in a ganglioglioma and that p53 may play a role in the malignant transformation.

Conclusions

Ganglioglioma with a glioblastomatous component and atypia of neuronal cells are extremely rare findings. Anaplastic transformation of gangliogliomas occurs in the glial component which resembles an anaplastic astrocytoma and p53 may play a role in this process.

References

- [1] KALYAN-RAMAN U. P., OLIVERO W. C., *Ganglioglioma: a correlative clinicopathological and radiological study of ten surgically treated cases with follow-up*, Neurosurgery, 1987, 20(3):428–433.
- [2] LANG F. F., EPSTEIN F. J., RANSOHOFF J., ALLEN J. C., WISOFF J., ABBOTT I. R., MILLER D. C., *Central nervous system gangliogliomas. Part 2: Clinical outcome*, J Neurosurg, 1993, 79(6):867–873.
- [3] WOLF H. K., MÜLLER M. B., SPÄNLE M., ZENTNER J., SCHRAMM J., WIESTLER O. D., *Ganglioglioma: a detailed histopathological and immunohistochemical study of 61 cases*, Acta Neuropathol (Berl), 1994, 88(2):166–173.
- [4] LOPEZ M. B. S., VANDENBERG S. R., Tumors of central nervous system. In: FLETCHER C. D. M. (ed), *Diagnostic Histopathology of Tumors*, 2nd edition, Churchill Livingstone, London, 2000, 1643–1645.
- [5] NELSON J. S., BRUNER J. M., Gangliocytoma and ganglioglioma. In: KLEIHUES P., CAVENEY W. K. (eds), *Pathology and Genetics of Tumours of the Nervous System*, IARC Press, Lyon, 1997, 68–69.
- [6] HAKIM R., LOEFFLER J. S., ANTONY D. C., BLACK P. M., *Gangliogliomas in adults*, Cancer, 1997, 79(1):127–131.
- [7] HIROSE T., KANNUKI S., NISHIDA K., MATSUMOTO K., SANO T., HIZAWA K., *Anaplastic ganglioglioma of the brain stem demonstrating active neurosecretory features of neoplastic neuronal cells*, Acta Neuropathol, 1992, 83(4):365–370.
- [8] KROUWER H. G., DAVIS R. L., McDERMOTT M. W., HOSHINO T., PRADOS M. D., *Gangliogliomas: a clinicopathological study of 25 cases and review of the literature*, J Neurooncol, 1993, 17(2):139–154.
- [9] CAMPOS M. G., ZENTNER J., OSTERTUN B., WOLF H. K., SCHRAMM J., *Anaplastic ganglioglioma: case report and review of the literature*, Neurol Res, 1994, 16(4):317–320.
- [10] PRAYSON R. A., KHAJAVI K., COMAIR Y. G., *Cortical architectural abnormalities and MIB1 immunoreactivity in gangliogliomas: a study of 60 patients with intracranial tumors*, J Neuropathol Exp Neurol, 1995, 54(4):513–520.
- [11] SUZUKI H., OTSUKI T., IWASAKI Y., KATAKURA R., ASANO H., TADOKORO M., SUZUKI Y., TEZUKA F., TAKEI H., *Anaplastic ganglioglioma with sarcomatous component: an immunohistochemical study and molecular analysis of p53 tumor suppressor gene*, Neuropathology, 2002, 22(1):40–47.

- [12] NAIR V., SURI V. S., TATKE M., SARAN R. K., MALHOTRA V., SINGH D., *Gangliogliomas: a report of five cases*, Indian J Cancer, 2004, 41(1):41–46.
- [13] ALLEGRENZA A., PILERI S., FRANK G., FERRACINI R., *Cerebral ganglioglioma with anaplastic oligodendroglial component*, Histopathology, 1990, 17(5):439–441.
- [14] JOHNSON M. D., JENNINGS M. T., TOMS S. T., *Oligodendroglial ganglioglioma with anaplastic features arising from the thalamus*, Pediatr Neurosurg, 2001, 34(6):301–305.
- [15] MITTLER M. A., WALTERS B. C., FRIED A. H., SOTOMAYO E. A., STOPA E. G., *Malignant glial tumor arising from the site of a previous hamartoma/ganglioglioma: coincidence or malignant transformation?*, Pediatr Neurosurg, 1999, 30(3):132–134.
- [16] DASH R. C., PROVENZALE J. M., MCCOMB R. D., PERRY D. A., LONGEE D. C., MCLENDON R. E., *Malignant supratentorial ganglioglioma (ganglion cell–giant cell glioblastoma): a case report and review of the literature*, Arch Pathol Lab Med, 1999, 123(4):342–345.
- [17] HAYASHI Y., IWATO M., HASEGAWA M., TACHIBANA O., VON DEIMLING A., YAMASHITA J., *Malignant transformation of a gangliocytoma/ganglioglioma into a glioblastoma multiforme: a molecular genetic analysis. Case report*, J Neurosurg, 2001, 95(1):138–142.
- [18] KIM N. R., WANG K. C., BANG J. S., CHOE G., PARK Y., KIM S. K., CHO B. K., CHI J. G., *Glioblastomatous transformation of ganglioglioma: a case report with reference to molecular genetic and flow cytometric analysis*, Pathol Int, 2003, 53(12):874–882.
- [19] MEKNI A., CHELLY I., HAUQUET S., ZITOUMA M., KCHIR N., *Gangliogliome malin cérebelleux. À propos d'une observation, avec revue de la littérature*, Neuro-chirurgie, 2006, 52(2–3):119–122.
- [20] JAY V., SQUIRE J., BECKER L. E., HUMPHREYS R., *Malignant transformation in a ganglioglioma with anaplastic neuronal and astrocytic components. Report of a case with flow cytometric and cytogenetic analysis*, Cancer, 1994, 73(11):2862–2868.
- [21] TARNARIS A., O'BRIEN C., REDFERN R. M., *Ganglioglioma with anaplastic recurrence of the neuronal element following radiotherapy*, Clin Neurol Neurosurg, 2006, 108(8):761–767.
- [22] MITTELBRONN M., SCHITTENHELM J., LEMKE D., RITZ R., NÄGELE T., WELLER M., MEYERMANN R., BESCHORNER R., *Low grade ganglioglioma rapidly progressing to a WHO grade IV tumor showing malignant transformation in both astroglial and neuronal cell components*, Neuropathology, 2007, 27(5):463–467.
- [23] RUMANA C. S., VALADKA A. B., *Radiation therapy and malignant degeneration of benign supratentorial gangliogliomas*, Neurosurgery, 1998, 42(5):1038–1043.
- [24] NAKAJIMA M., KIDOKA M., NAKASU S., *Anaplastic ganglioglioma with dissemination to the spinal cord: a case report*, Surg Neurol, 1998, 49(4):445–448.
- [25] ARAKI M., FAN J., HARAOKA S., MORITAKE T., YOSHII Y., WATANABE T., *Extracranial metastasis of anaplastic ganglioglioma through a ventriculoperitoneal shunt: a case report*, Pathol Int, 1999, 49(3):258–263.
- [26] SASAKI A., HIRATO J., NAKAZATO Y., TAMURA M., KADOWAKI H., *Recurrent anaplastic ganglioglioma: pathological characterization of tumor cells. Case report*, J Neurosurg, 1996, 84(6):1055–1059.
- [27] HIROSE T., SCHEITHAUER B. W., LOPES M. B., GERBER H. A., ALTERMATT H. J., VAN DEN BERG S. R., *Ganglioglioma: an ultrastructural and immunohistochemical study*, Cancer, 1997, 79(5):989–1003.

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