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PRIMARY CEREBRAL GLIOSARCOMA: ABOUT TWO CASES AND REVIEW OF THE LITERATURE

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ABSTRACT

Gliosarcoma is a very rare primary mixed tumor in the central nervous system, accounting for 1,8 -8% of all glial tumors. It has been classified by the World Health Organization as a variant of glioblastoma. Gliosarcoma is characterised by a biphasic growth pattern, composed of glialcontingentand sarcomatous contingent. Conventionally, this tumor is localized at the supratentorial floor. clinical picture is polymorphic, imaging data are evocative, His diagnosis is based on histology. Treatment is always surgical. The prognosis of gliosarcoma does not differ from other glioblastomas. We here report two clinical cases treated in our service with the aim of assessing the diagnostic, therapeutic and prognostic features of this rare tumor.

KEYWORDS: Primary Gliosarcoma, Central Nervous System, Diagnosis, Treatment, Prognosis.

INTRODUCTION

Gliosarcoma is considered by the World Health Organization (WHO) as a variant of glioblastoma and is classified as Grade IV. These tumors are characterized by a biphasic proliferation associating glioblastoma glial contingent and a sarcomatous contingent. Gliosarcoma is a very rare brain tumor accounting for 1.8 to 8% of all glial tumors. We report two cases of gliosarcoma treated in our department through which we will discuss the anatomoclinical, radiological and diagnostic, therapeutic and prognostic features of this rare tumor.

OBSERVATION 1

Mr Z.A, 71 years old, diabetic since 5 years on oral antidiabetic drugs, who was consulting for a right hemiparesis evolving since one month. The cerebral CT showed a left occipital tumor process of 6.5x 4cm, having a tissue component with low cystic component, raised in an annular and heterogeneous manner after intavenous injection of the contrast agent, with perilesional edema and sub-cortical variable size calcifications exerting a mass effect on the medial structures which are slightly deviated to the right evoking a high grade cystic astrocytoma. The patient had a complete surgical excision of the tumor.

The macroscopic study of the operative specimen revealed an oval formation of 7x5x4cm, yellowish-white in appearance, remodeled by haemorrhage. Histologically, the analysis of the operative specimen showed poorly limited, unencapsulated tumor proliferation of essentially fusiform and elongated cells with irregular nuclei and the presence of sometimes normal mitoses. The cytoplasm of the cells is of moderate eosinophilic mean abundances. The cytoplasmic limits are not very clear. Within proliferation there are foci of tumor necrosis and dystrophic calcifications. The adjacent glial tissue is infiltrated at the periphery.

The immunohistochemical study showed positive labeling of the glial component by GFAP. The other sarcomatous cells expressed the anti-vimentin antibody. Faced with these arguments, the diagnosis of gliosarcoma was retained.

The patient was referred to our service and he received concomitant radio-Chemotherapy according to the Protocol Stupp: 60 Gy radiotherapy in 30 fractions in six weeks, combined with Temozolomide at the dose of 75 mg / m2 / day for 42 consecutive days, then six cycles of 150- 200mg / m2 / day from day 1 to day 5 starting every 28 days. The evolution is good after 8 months of decline.

OBSERVATION 2

A 55-year-old patient with no notable pathological antecedents who, two months before admission, presented a progressive worsening of intracranial hypertension syndrome complicated by convulsive seizures.

CT showed an exponential frontal left temporo-occipital tumor process without perilesional edema. The patient

had undergone surgical resection of the tumor. Histological examination showed a malignant tumor proliferation organized into diffuse layers. The tumor cells are pleomorphic. They are sometimes round, sometimes fusiform. The cytoplasm is abundant and eosinophilic, associated with these tumoral cells a gemistocytic contingent of subnormal morphology, with presence of numerous ranges of micro-cystic degeneration, palissadic-type tumor necrosis, and presence of numerous calcifications. The immunohistochemical study showed positive labeling of the glial component by GFAP. The sarcomatous component had positive labeling for vimentin and negative for GFAP. These arguments were in favor of a primitive Gliosarcoma. The patient benefited in our formation of a concomitant radio-chemotherapy adjuvant according to the Protocol Stupp. The evolution was good after a 6-month follow-up, then the patient was lost to follow-up.

THE DISCUSSION

Gliosarcoma is a rare primary central nervous system malignancy, accounting for 2% of all glioblastomas and 0.59-0.76% of all brain tumors.[1] It is a variant of glioblastoma, characterized by biphasic proliferation involving both glial tissue and malignant mesenchymal tissue.[2] The glial component is often of the glioblastoma type or exceptionally oligodendrioglioma type. This tumor was described for the first time by Stroebe in 1895,[3] it is an adult tumor that affects subjects aged between 40 and 60 years old with an average age of 52.1 years. The man as the woman with a sex ratio male / female of 1.8.[4]

Gliosarcomas have predominantly supratentorial localization, affecting the temporal region in more than 65% of cases. Frontal, parietal and occipital localizations are rarer.[5] Rarely can the disease affect the posterieur cerebral fossa and the spinal cord.[4,6]

The clinical history is usually short, with a duration ranging from one week to 3 months,[6] as was the case for our patients. The symptoms are not specific, depend on the location of the tumor.

Nevertheless, it remains dominated by intracranial hypertension syndrome, motor deficit and seizures.[7] Because of the presence of the sarcomatous contingent, gliosarcomas metastasize more than glioblastomas and are sometimes discovered at the metastatic stage.[8]

The CT features of gliosarcoma are similar to those of glioblastoma. Gliosarcoma normally occurs as a well-circumscribed, hyperdense, heterogeneous mass surrounding central hypodensity corresponding to plaques of necrosis and peritumoral edema disproportionate to tumor size.

If the mesenchymal component is important, the appearance is that of a hyperdense mass taking the contrast homogeneously and simulating a meningioma, but without implantation base in the skull.[9]

On MRI, gliosarcoma appears to be a well-limited, intradaxial mass, coming into contact with the dura with areas of cystic reworking and vasogenic edema. In T2, the intensity of the signal is intermediate, but hypointense in comparison with other glial tumors. After injection of gadolinium, in T1, the tumor shows a significant ring enhancement. These enhancement zones are iso-intense in T2.[10]

From an anatomopathological point of view, the macroscopic appearance of gliosarcoma is firm, lobulated, well circumscribed If the mesenchymal contingent is predominant, the tumor is of hard, well-limited consistency, possibly suggestive of the diagnosis of metastasis or, when it is attached to the dura, that of a meningioma.[2]

Histologically, the gliosarcoma has a two-phase appearance with a mixture of two contingents. The glial component is essentially of high-grade astrocytic type, glioblastoma type with a variable degree of anaplasia.[2] The sarcomatous component, made of atypical fusiform cells with a high mitotic index.[1]

The distinction between these two components is often facilitated by the combined use of histochemical and immunohistochemical techniques. The anti-GFAP antibody makes it possible to highlight the glial component while the mesenchymal component expresses the anti-Vimentin antibody and is negative for the anti-GFAP antibody. The clear demonstration of the malignant nature of the GFAP-negative mesenchymal contingent is important in order to distinguish a true gliosarcoma from a glioblastoma with fibroblastic proliferation.[12]

The histogenesis of gliosarcoma remains obscure. The most commonly accepted theory is that

Sarcomatous component appears to originate from the vessels of a pre-existing glioblastoma.

Westphall et al. 74 evoke a "common cellular ancestor from which glial and sarcomatous cells were derived. This hypothesis is opposed to the concept of simultaneous transformation of two distinct tissues.

Genetically, gliosarcomas have a profile that is closer to secondary glioblastomas than primary glioblastomas such as chromosome 9 short arm deletion, chromosome 7 gain, chromosome 10 and 17 loss, p53 and PTEN gene mutations.[14] On the other hand, only one difference was noted between gliosarcoma and glioblastoma; found in most studies and relates to the lower frequency of amplification of the gene encoding the Epidermal Growth Factor (EGFR) receptor in gliosarcoma compared to primary glioblastoma multiforme.

The therapeutic modalities of gliosarcoma include tumor resection, radiotherapy and postoperative chemotherapy.[15]

Surgical resection may be partial or total depending on the extent of the tumor.

According to Chang CH et al. The mean overall survival of patients receiving adjuvant radiotherapy is better than those treated by surgery alone (10.6 months vs 6.2 months).[16] Radiation therapy should be started within 4 to 6 weeks after surgery. The standard treatment consists in administering a dose of 60 Gy (in daily fractions of 1.8 to 2 Gy) on the tumor bed and / or tumor residue with a margin of safety of 2 cm.

Gliosarcoma is chemo-resistant but studies report a slight improvement in survival for patients who received Temozolamide concomitant with radiotherapy (according to the stupp protocol), at a dose of 75 mg / m2 per day and then adjuvant at 150 mg / m2 in 6 cycles.[17]

The evolutionary profile of gliosarcomas is characterized by a much more frequent metastatic extension compared with glioblastomas.[4] In a review of the literature, Maiuri et al.[18] report a rate of metastatic gliosarcomas in 15 to 30%. These metastases can be pulmonary, pleural, medullary, hepatic or spinal (18). In our series no patient has developed metastases.

The prognosis of gliosarcomas does not differ from other glioblastomas. It is usually unpleasant, with an average survival of less than 8 to 24 months after the onset of symptoms.

THE CONCLUSION

Gliosarcomas are biphasic tumors associating to glioblastoma glial contingent and a sarcomatous contingent. The clinical profile is polymorphic.

The imaging data (CT, MRI) are evocative. His diagnosis is based on data from the pathological examination completed by the immunohistochemical study. The treatment is essentially based on surgery and radiotherapy. The prognosis of gliosarcomas is dark and does not differ from other glioblastomas and is closely related to the quality of exeresis.

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