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CLINICAL AND ANATOMOPATHOLOGICAL CORRELATIONS IN GLIOBLASTOMA MULTIFORME

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Abstract: *Described in the literature as a characteristic feature of adulthood, glioblastoma is the most common malignant brain tumour of this age group, accounting for less than 20% of all intracranial tumours and about 80% of all astrocytic neoplasms. Risk factors involved in the development of this type of tumour include certain genetic disorders such as Li-Fraumeni syndrome (an autosomal dominant syndrome, fortunately extremely rare but predisposing to various forms of cancer), Turcot syndrome or neurofibromatosis. On the other hand, radiotherapy in the past also seems to be a factor in the development of glioblastoma. It is predominantly found in the cerebral hemispheres, is rarely found in the brainstem and occurs exceptionally in the cerebellum. Scientific studies conducted globally have shown a male:female ratio of 1.26 in the US and 1.28 in Europe. The peak incidence is between 40 and 70 years of age, but cases have also been observed, less frequently, in children with predominantly brainstem involvement. In what follows I would like to present the case of a 68-year-old patient, admitted with the suspicion of a tumour formation with right temporo-parietal location, which was found to be a glioblastoma multiforme after CT, anatomopathological and immunohistochemical examinations.*

INTRODUCTION

Glioblastoma (1,2,3,4,5,6,7) is one of the most aggressive forms of neoplasm that can develop even in the spinal cord. Clinically, it is manifested by epileptic seizures, headaches (8), vomiting, progressive loss of brain functions, the most affected being speech, muscle strength, attention span, memory and behavioural disorders. In the absence of adequate treatment, symptoms progress rapidly within a few weeks. In the literature there have been described both primary or de novo glioblastomas (9) (due to embryonic remains of glial cells), which interest the elderly adult and have a clinical history under 3 months, but also secondary glioblastomas (10), which affects young adults and has a possible clinical history of several years. Secondary forms arise by the malignancy of a second or third degree astrocytoma, and two well-known pathologists, James Watson Kernohan (11) and Hans-Joachim Scherer, also contributed to the advancement of this idea. Glioblastoma grows rapidly, is invasive and produces metastases both locally and remotely. The treatment consists in the removal of the tumour formation, a procedure followed by radiotherapy (12) and chemotherapy. The prognosis depends on the presence or absence of the aforementioned treatment. In the absence of any form of therapy, the survival rate is somewhere around 3 months.

CASE REPORT

In the following, I have proposed to present the case of a 68-year old patient presenting to the Emergency Room with intense headache, vomiting and speech difficulties. The active cranial MDCT examination performed on the same day reveals the presence of a tumour mass with right temporo-parietal location, with peripheral irregular iodophilia, with dimensions of about 4/4.5/5.5 cm, with peripheral digitiform edema and mass effect, characteristic aspect for a glioblastoma multiforme. The CT examination was complemented with a radiological, overall chest examination which revealed the following features: Loose lateral costo-diaphragmatic sinuses. Prominent, opaque, fluid-contoured pulmonary hilum. Moderately accentuated bilateral diffuse pulmonary interstitial reticular (fibrotic) type. Non-homogeneous, flu conturated opacity, of costal intensity, projected left lateral-thoracic. Cord with elongated left lower arch. Old fracture of the middle 1/3 of the left clavicle. On the basis of these aspects and especially the CT scan, it is proposed to admit the patient to the Neurosurgery Department for further investigations and specialized therapy. The neurological examination on admission shows a conscious, cooperative patient with cephalalgic syndrome and developmental speech and language disorders. In the clinical and imaging context, surgery is recommended, the patient knowingly accepting. Surgery is performed under general anaesthesia, with right temporo-parietal skin incision, right temporo-parietal craniotomy, ablation of the tumour formation and bone flap replacement. Postoperatively, the patient is transferred to the Intensive Care Unit (ICU) for surveillance. Following the establishment of a favourable evolution, he is moved to a ward on the neurosurgery section. A few days after the surgery, the CT examination is repeated, which reveals the following aspects: right temporo-parietal craniotomy area. Heterogeneous right temporo-insular and lenticular area (with hypodense areas and presence of acute hematic inclusions), with diameters of 75x50 mm, with minimal mass effect on the medial structures. Digitiform edema in the temporo-parietal white matter. Midline structures are discreetly deviated to the left. Discrete asymmetric ventricular system, compensatory enlargement, normotensive.

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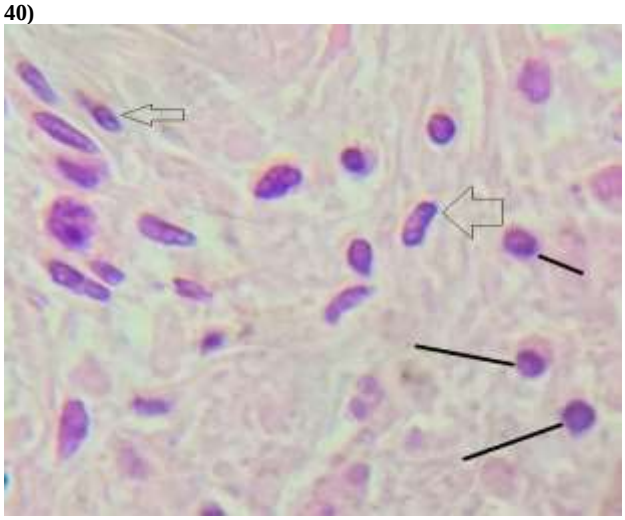
Bilateral frontal hygroma with a maximum thickness of 6 mm on the right. A few air inclusions underlying the skull cap. Bilateral right frontotemporal and parietal epicranial hematoma, maximum 11 mm thick.

Conclusions: postoperative right temporo-insular inhomogeneous area with minimal mass effect; small epicranial haematoma. Evolution on section is favourable, with improvement of neurological symptoms. In the second decade of May, another CT examination reveals: right temporo-parietal craniotomy with underlying CSF density and postoperative hematic content. Discrete diffuse cerebral edema right hemisphere. Ventricular system with minimal asymmetry without deviation of midline structures. Remaining edema in right temporoparietal white matter. Right temporal epicranial edema. The patient is discharged with improving symptoms, but after about 1 month, he returns to the ICU with intense headache. Native cranial MDCT examination, with contiguous sections, reveals; right temporo-parietal craniotomy, with extensive area of vasogenic F-T-P-O edema, centered on superficial temporo-parietal hypodense image, with dense, irregular contour and dimensions of about 5. 3/3.7 cm in the axial plane, minimal mass effect on midline structures with a subfalcine right-left herniation of about 3.5 mm (most likely a tumour relapse/relict). No acute haematological densities present. No pathological sinus collections. Eyeballs, orbits without pathological changes. Right acute mastoiditis changes. On readmission, the patient is conscious, cooperative, without motor or sensory deficit, but with cephalalgic syndrome. Under conservative treatment, the evolution is favourable. He is discharged slightly neurologically improved, afebrile, with recommendations.

DISCUSSIONS

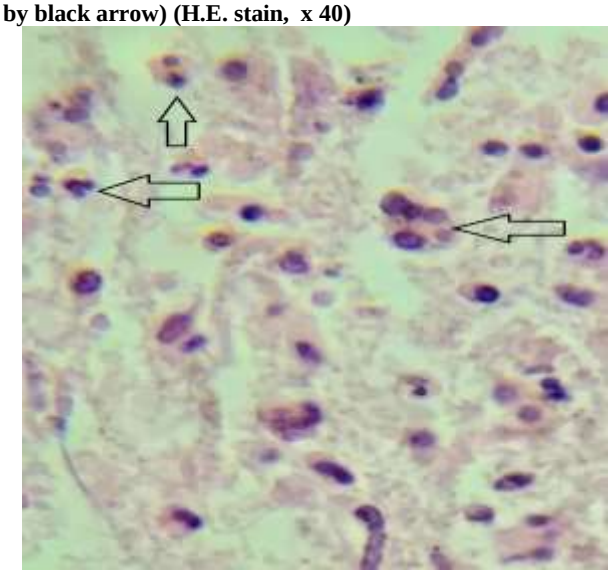
Macroscopically - glioblastoma appears as a greyish, soft, rapidly growing and infiltrative formation.(13) The tumour tends to invade along the corpus callosum (14) and the contralateral hemisphere, creating a characteristic "butterfly" image.(15) On section it shows an irregular outline, whitish-yellowish appearance, accompanied by frequent haemorrhages and necrosis (16,17), giving it a cystic character. Corresponding to this case, multiple fragments were received in the Pathology Department with dimensions between 8/5/4 mm and 20/20/14 mm.

Figure no. 1. The histopathology of glioblastoma multiforme shows cells of various sizes, round-oval (indicated by black lines) and spindle-shaped (indicated by black arrows) (H.E. stain, x 40)



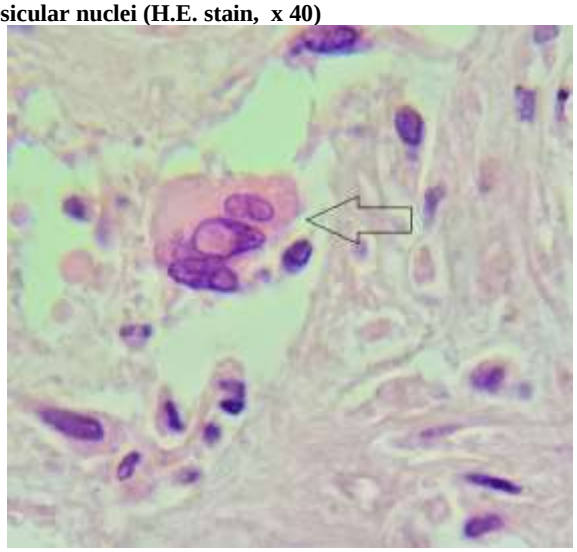
Microscopically - Fragments of brain tissue were found, with the presence of cell proliferation of astrocytic origin with atypical characters, with cells of varied size, round-oval and fusiform shape (reminiscent of astroblasts and spongioblasts (figure no.1) (18), alternating with irregularly shaped cells with pleomorphic, incised, vesicular nuclei, with coarse chromatin, with increased rate of mitosis (figure no. 2).(19) The cytoplasm of smaller cells appears regular, but in larger cells it acquires a polymorphic character. Cell distribution appears uneven and irregular. Sometimes they are densely arranged (20), at other times paucicellular fibrillar structures are recognised which stain eosinophilically pale, similar to normal nervous tissue.

Figure no. 2. Histopathology of glioblastoma multiforme shows the presence of an increased rate of mitosis (indicated by black arrow) (H.E. stain, x 40)



Focally, multinucleated giant cells are present (21) (figure no. 3).

Figure no. 3. Histopathology of glioblastoma multiforme, showing the presence of a multinucleated giant cell (indicated by black arrow), with variable size, polymorphic, vesicular nuclei (H.E. stain, x 40)



Stroma shows sprouts of vascular (figure no. 4) (22) or vascular-endothelial proliferation accompanied or not by hyperplasia of surrounding connective tissue. with the outline of a palisade (figure no. 5).(23,24,25) Some neoplastic cells are placed perivascularly, mimicking a rosette pattern. The presence of areas of necrosis and scattered foci of haemorrhage are noted.

The peritumoral nerve tissue stains paler, while the periglial and pericapillary spaces are enlarged due to edema.

Figure no. 4. Histopathology of glioblastoma multiforme, showing the presence of vascular proliferation sprouts (indicated by dark arrows) (H.E. stain, x 40)

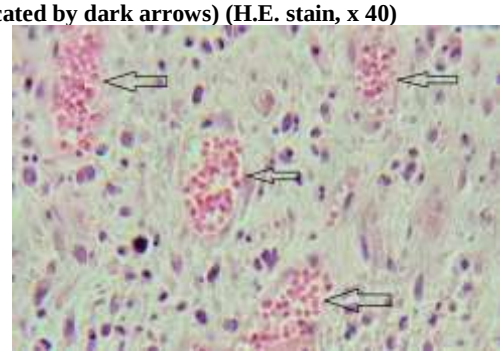
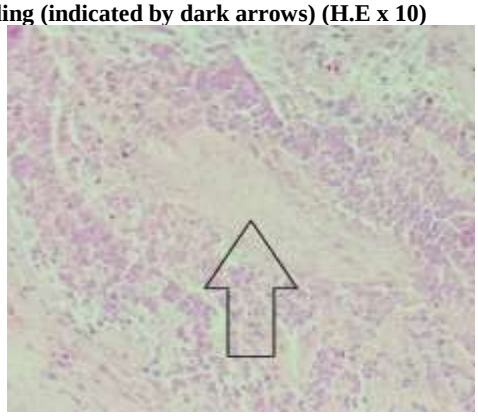


Figure no. 5. Histopathology of glioblastoma multiforme shows the presence of a foci of necrosis, with the onset of palisading (indicated by dark arrows) (H.E x 10)



CONCLUSIONS

Neurological and imaging examinations are essential and provide important information about the location of this type of tumour formation, but histopathological examination gives us more details about the tumour type. As usual, the first stain used is haematoxylin-eosin, but for a more accurate diagnosis, immunohistochemistry provides important data on the final diagnosis. Immunohistochemistry is a combination of histochemistry and immunology and aims to detect the antigenic properties of substances contained in different tissues. This method uses polyreactive sera and monoclonal antibodies and helps, as mentioned above, to refine both the diagnosis of certainty and the differential diagnosis. In the present case the following antibodies were analysed:

- *Cytokeratin AE 1-3* - This is a combination of antibodies used in the detection of possible metastases. It is also used as a method to exclude the presence of epithelial tumours. It is negative in this case.
- *Human Melanoma Black or HMB45* - Negative in this case, it is a monoclonal antibody used to exclude the presence of melanocytic tumours.
- *Vimentin* - Confirms mesenchymal origin in certain tumour formations. In this case it is positive in stroma.
- *Ki67* - Is a nuclear protein associated with cell proliferation. It is an index of mitotic proliferation. In this case it is as a valuable prognostic biomarker for adult patients with glioblastoma - 30%.

The histopathological and immunohistochemical findings are consistent with glioblastoma multiforme (WHO gr. IV).

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