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Case Study

Glioblastoma Multiforme

Jardson Peixinho*

Nove de Julho University – UNINOVE, São Paulo, SP- Brazil

***Corresponding Author:** Nove de Julho University – UNINOVE, São Paulo, SP- Brazil.

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Abstract

Neoplasia is the proliferation of cells of a given tissue, which are out of the control of the organism and tend to autonomy, causing serious damage to its host.

Tumors can be classified as: benign and malignant. Benign tumor cells grow more slowly while malignant tumor cells grow faster and disorderly.

In the case of brain tumors, we can classify them according to their aggressiveness, where the degree can vary from I to IV, and the higher the degree, the greater the aggressiveness of the tumor.

Gliomas is the term used to designate tumors (neoplasms) originating from brain glial cells.

Glioblastoma Multiforme (GBM) fits in Grade IV tumors, originates in glial cells, has no defined form, and is highly lethal and in cases of removal there is recurrence.

Imaging methods are used to locate the lesion extremely useful to determine the extent of the disease.

Keywords: Glioblastoma; Staging; Technicians and Technologists in Radiology; Cancer; Neoplastic Metastasis; Neurosurgery

Concept

Glioblastoma Multiforme is the most common malignant tumor found in thebrain. It presents general focal symptoms and signs related to size, location, and tumor growth rate, and generally affects the cerebral hemispheres.

This tumor fits grade IV tumors according to the World Health Organization (WHO), having a high degree of lethality. It is characterized by the presence of neoplastic astrocytes with areas of vascular proliferation and/or necrosis.

Histologically characterized by having high cellularity; nuclear atynations (pleomorphism, which is the variety of size and shape of tumor cells, and hyperchromatic nucleus); mitoses, oftenatypical; vascular proliferation, and areas of necrosis, small or extensive, which may show pseudopaliçadas of surrounding nuclei that is another aspect of glioblastoma, being defined as areas of irregular necrosis, of geographical contours, surrounded by neoplastic cells arranged more densely, forming the so-called pseudopaliçadas. Tumor peri edema and midline deviation occur with hernias. In some cases, the tumor infiltrates the callous body, passing into the contralateral hemisphere (butterfly wing tumor).

Glioblastoma multiforme can occupy any site of the Central Nervous System (CNS), being more common in the frontal temporal region, forming a large tumor tissue with interconnections with

both lobes. Rarely affects the posterior fossa region, where 0.24% of multiform glioblastomas affect the cerebellum (Figure 1) [1-3].

Figure 1: Glioblastoma Multiforme [4].

Glioblastomas may also present meningeal dissemination. The survival rate for the patient who has GBM is greatly reduced, reaching 10% in 10 years.

Epidemiology

The epidemiology of GBM shows that there are two different subgroups of the disease. Approximately 20% of patients develop GBM from a low-grade astrocytic tumor. In the next 80% of patients, who are usually older than patients with secondary GBM, the disease is diagnosed again, in its primary form [5].

Incidence

Glioblastoma Multiforme has a higher incidence in adults, with higher frequency in men than women, which is higher in the range between45 and 70 years, being less frequent under 30 years of age [1].

Risk factors

People with a specific genetic tendency may be more susceptible to the development of brain tumors earlier than those who do not have the gene.

Neoplasms such as the name of gliomas in most cases originate from a spontaneous mutation in genes that control the cell cycle or cell division. These genes when in normal function stops the proliferation of the cell or control its division harmoniously. This mutation is sporadic and has no hereditary character.

Only in rare cases of family tumors do genes pass from one generation to another.

The triggering factors such a mutation is not yet well known for most cases. The only clear factor that triggers mutations is ionizing radiation. Environmental factors such as viruses, hormones and trauma are being investigated, but nothing is yet conclusive. Therefore, there is no way to define risk groups for this type of disease.

Currently researchers have associated the development of GBM with the presence of Cytomegalovirus (CMV), which is a type of herpes present in 80% of the population. But it has not yet been proven that the presence of CMV is really the triggering factor for the appearance of GBM [6-9].

Symptomatology

Patients have different focal or general signs and symptoms, depending on the size, location, and growth rate of the tumor. General signs and symptoms include headache, nausea, jet vomiting, papillaedema, vision disorders or abnormal eye movements, as a result of intracranial hypertension syndrome, changes in level of consciousness, epileptic seizures, weakness in the arms or legs, difficulties in speech or movement, lack of coordination while walking, hemiparesis (partialparalysis on one side of the body), paresthesia's (feeling of cold, heat, tingling and/or pressure),apits (partial- or total loss of language, and speech capacity),hemianopsia (loss of object vision covering half of the visualfields, or only from single quadrant), location allocated signs according to the area reached drowsiness and changes in memory or personality [1,9-12].

Etiology

GBM has no known etiology and emergence in the brain itself, more specifically astrocytes being defined as an astrocytoma. It is assessed as an advanced grade (grade IV) astrocytoma, with a high lethality rate.

Diagnosis

The clinical diagnosis is made from questions asked by the doctor. Neurological examination will check reflexes, coordination, sensitivity, response to pain and muscle strength. He will examine the eyes with an illuminated device for possible signs of increased intracranial pressure or brain swelling. Depending on the symp-

toms or physical examination, he may request other laboratory, radiological and complementary tests.

Radiological examinations

In Brazil, technical professionals and technologists in radiology perform important functions in the Unified Health System (SUS) and private institutions, as they are responsible, for example, for carrying out radiographic examinations and preparing patients who will undergo exams. Imaging itself encompasses different segments such as: X-rays, mammography, computed tomography, magnetic resonance imaging, fluoroscopy, nuclear medicine, radiotherapy, ultrasound, among others. In this sense, the initial examination for the diagnosis of glioblastoma multiforme (GBM) are plain radiographs of the skull and brain, which are of little use in the diagnosis of brain tumors.

Computed tomography ends up being more used because it is more accessible, different from magnetic resonance imaging, which has a high cost, but has characteristics that make them useful. It can be used in some cases where resonance is not a good option, as inner cities that do not have this modality, for overweight patients or who have claustrophobia. Tomography also provides better detailing of bone structures near the tumor. Some CT scans are performed in two stages: without and with contrast. Intravenous administration of contrast should be performed when one wishes to better outline the structures of the body, making the diagnosis more accurate. In tomography angiography an intravenous contrast is injected during the examination. Scanning creates detailed images of blood vessels in the brain, which can help plan the surgery. TOMography angiography may, in some cases, provide more details of blood vessels around a tumor than MRI angiography.

Magnetic Resonance (RNM)

This scan provides an image of the brain using a powerful magnet, a radiofrequency transmitter and a computer. On MRI it is possible to better visualize some parts of the brain compared to CT imaging. Among the main advantages of magnetic resonance imaging is its enormous contrast between the various organs, such as veins, arteries, nerves, and tumors, which do not generate shade on radiographs. Gadolinium contrast can be injected to intensify the images and make them clearer.

Spectroscopic MRI: This scan is like MRI but intensifies signals from different substances in the body that sometimes gives a clearer picture of a tumor. The use of this method for brain tumors is still experimental and is not commonly used (Figure 2).

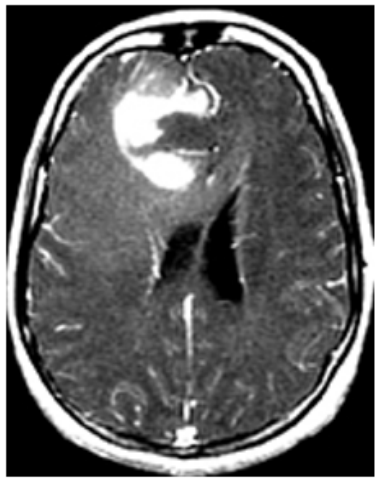

Figure 2: Spectroscopy of a GBM [15].

Positron Emission Tomography (PET-CT): This test identifies a tumor through the use of a sugar orother substances other than those found in normal brain tissue, can identify variations in biochemical processes when altered by a disease, and that occur before visible signs of it are present on computed tomography or magnetic resonance imaging. The PET-CT examination is a combination of nuclear medicine and biochemical analysis, which allows a visualization of human physiology by electronic detection of radiopharmaceuticals emitting short-lived pósitrons. Radiopharmaceuticals, or molecules marked with a radioactive isotope, are administered to the patient intravenously before the examination. As cancer cells reproduce very quickly, and consume a lot of energy to reproduce and stay active, the test takes advantage of this property. Glucose molecules, which are pure energy, are marked by a radioisotope and injected into patients. As tumor cells are awed by the energy coming from glucose, it will focus on cancer cells, where cell metabolism is more intense. A few minutes after glucose ingestion it is possible to map the body, producing images of the inside of the body. PET scan is useful after treatment, to determine if tumor cells have been destroyed, since dead cells do not absorb glucose. This examination can help determine whether an abnormal area, visualized on MRI, remnant of the tumor is just scar tissue.

This test is most often used to assess treatment success, distinguishing the tumor from the scar tissue. For this exam, a very low dose of radioactive sugar is injected into a vein, which will be highlighted in the exam image (Figure 3).

Figure 3: GBM in an image acquired through PET [16].

Complementary exams

Histopathological examination: This is the study of the body tissues under a microscope. Histopathological examination makes it possible to safely affirm the nature of a lesion.

In histopathological examination, a fragment of the tissue is examined, thus evaluating its entire composition, being, therefore, more accurate than the cytological examination.

The material can be obtained through a small surgery, called open biopsy (Figure 4-7).

Lumbar puncture /Spinal puncture: A sample of the spinal fluid (csleb) is taken from the lower part of the spine with a needle. The liquid is checked for signs of infection or cancer cells. This test is usually done when the neurologist has seen computed tomography or mri.

Cerebral angiography: is sometimes used for further evaluation of the size and location of the tumor if surgery was planned. It is an x-ray of the veins and arteries, using an iodinated contrast to define the outlines of blood vessels.

Figure 4: Surgically removed tumor fragment [2].

Figure 5: Cellular atypia, characteristic of Glioblastoma Multiforme [2].

Usually in brain tumors metastasis may occur. If this is suspected, X ray examinations of other organs may also be performed.

Features of images

The computed tomography (CT) without contrast is a very heterogeneous lesion, usually with central areas of low density, which

Figure 6: Vascular Proliferation [2].

Figure 7: Pseudorabies necrosis [2].

show necrosis or cyst formation. Calcification is rare. Hemorrhage at different stages is frequent. There is peripheral edema, which surrounds the tumor and extends along the white matter. The reinforcement after contrast is strong and heterogeneous, and a thick disc of capture of contrast in the periphery of the tumor is common (Figure 8 and Figure 9).

In MRI, the aspect is also heterogeneous. In T1, a mixed signal mass is observed, poorly delineated, with formation of cysts or necrosis, and a thick irregular wall, with marked and heterogeneous reinforcement after contrast (Figure 10 and Figure 11). As

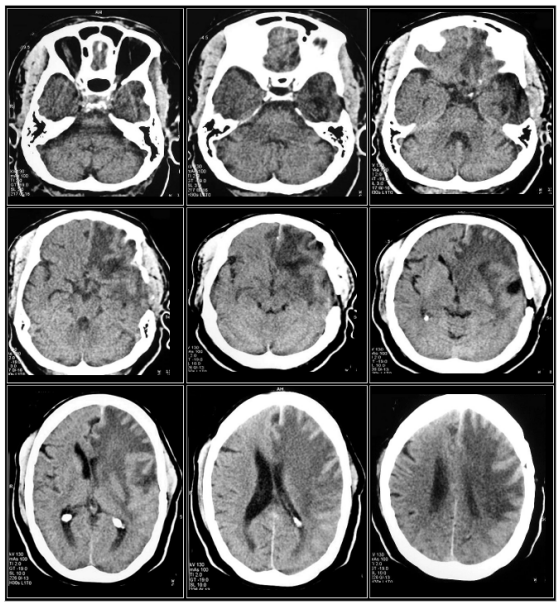

Figure 8: Non-contrast-snag SkullCT, axial cut [17].

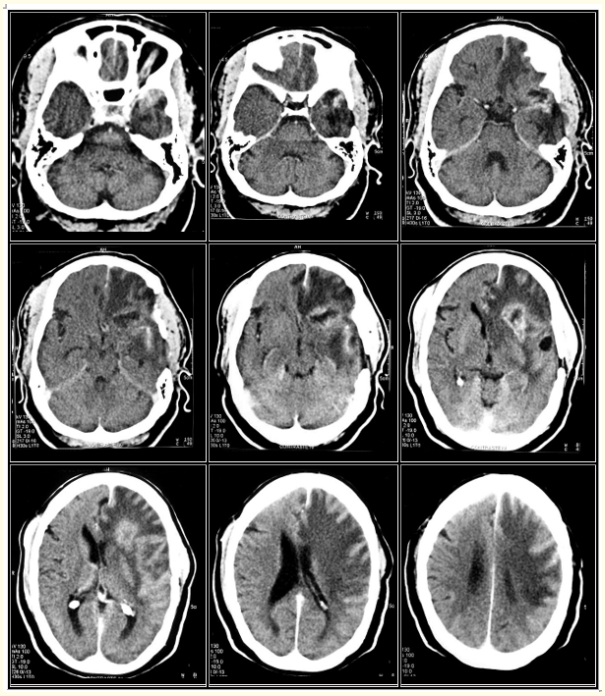

Figure 9: Skull CT image with contrast, axial cut [17].

they are highly vascularized tumors it is possible to observe vessels with absence of signal and hemorrhages in various stages.

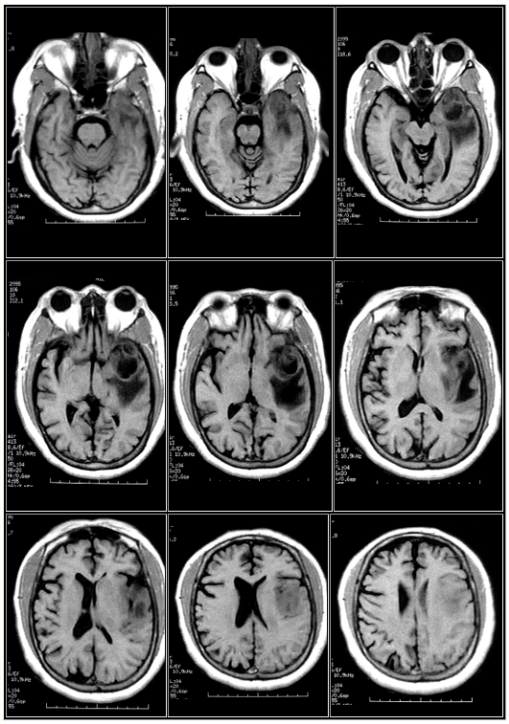

Figure 10: Mri image in T1 withoutcontrast, axial cut [17].

In T2 also stands out the heterogeneous aspect, with areas of hypo-, iso- and hypersignal. The areas of necrosis correspond to hypersignal. The margins of the tumor are confused with the surrounding edema, and it is not possible to differentiate tumor edema (Figure 12 and Figure 13) [13].

Secondary diseases

The secondary diseases that appear after the diagnosis of GBM are: headache, changes in the level of consciousness, epilepticta-ttoos, dyslalia, hemiparesis (partialparalysis on one side of the body), paresthesia (feeling cold, heat, tingling and/or pressure), aphasias (partial or total loss of language, and speech) ability, hemianopsia (loss of object vision covering half of the visual fields or only from a single quadrant).

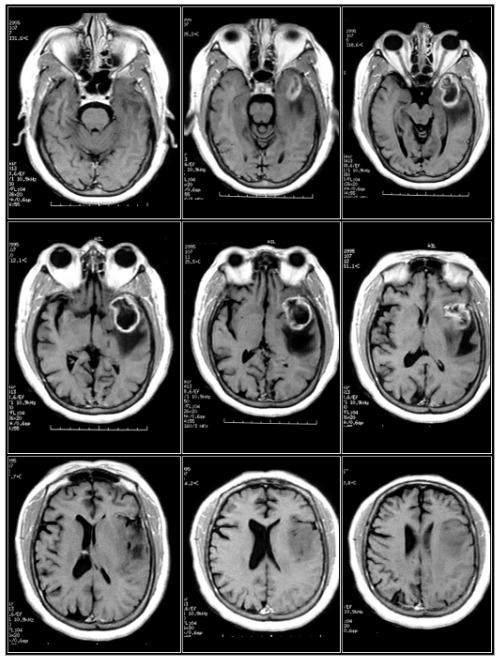

Figure 11: Mri image in T1 with contrast, axial cut [17].

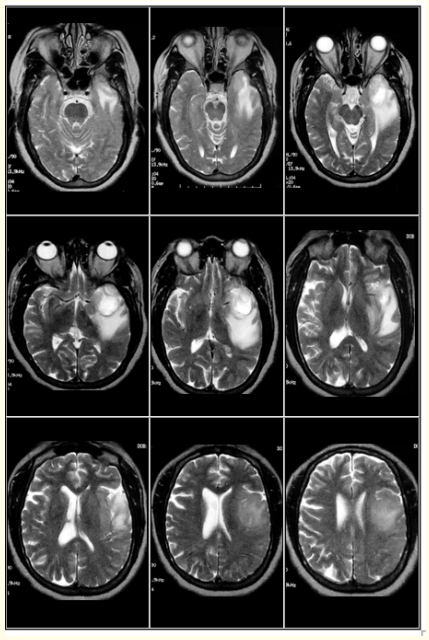

Figure 12: Image of MrI of Skull in T2, axial section [17].

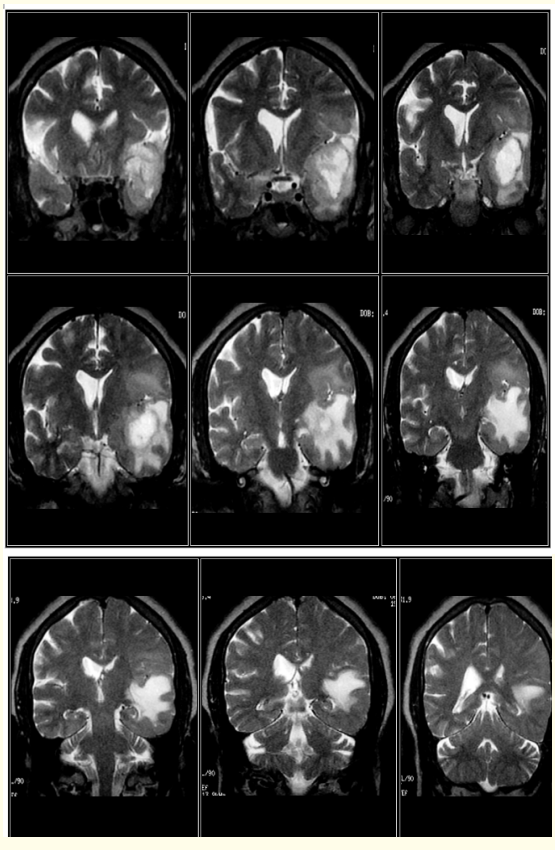

Figure 13: Mri image in T2 with contrast, coronal cut [17].

Treatment

There is no cure for this type of tumor, but alternative therapies in conjunction with standard surgery + chemotherapy +radiotherapy treatment may increase patient survival.

The use of drugs is also an option for the treatment of GBM. Currently, the most used chemotherapy for this case is TEMODAL® (Temozolomide),whose basic action is to "intoxicate" the body, including tumor cells. There are other medicines such as Avastin (Bevacizumab) and CPT11 (Irinotecan), with which in many cases of GBM tumors decrease or disappear and the toxicity of Avastim + CPT11 is greater than that of Tumoral but seem to be more efficient since Temodal can at most bar tumor growth for a while.

Another current technique is incisionless surgery, the so-called Gamma Knife. Basically it is a "localized radiotherapy", but for it to be performed, the tumor must have a specific, small size [18].

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