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Case Report

Intramedullary glioblastoma multiforme in young patients: A case report and brief review

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ABSTRACT

Cervical glioblastoma multiforme (GBM) is rare, and its early diagnosis and management is crucial to patient survival. In the young population, it's even more difficult to diagnose. The main challenges in GBM therapy are associated with the location of the disease and its complex and heterogeneous biology. Here, we present a case of a 35-year-old female patient admitted due to complain of pain in her right lower limb. She reported the evolution of the condition for dysesthesia in upper limbs and lower limbs 4 weeks ago. MRI showed an intramedullary lesion extending from C2 to C5. The patient was managed surgically. The purpose of this report is to document this rare condition, especially in the young age group, and reveal the current knowledge regarding intramedullary GBM.

Keywords: Glioblastoma multiforme, Neuro-oncology, Neurosurgery, Spinal cord

INTRODUCTION

Glioblastoma multiforme (GBM) is a malignant astrocytic tumor classified by the World Health Organization (WHO) as Grade IV and presents itself as one of the most aggressive and lethal brain neoplasms. It is possible to subdivide GBM into primary and secondary. The primary tumor appears without clinical and histopathological evidence of a precursor lesion, while the secondary one progresses from a pre-existing lower grade astrocytoma.[1,2]

GBM affects a population group of 55–65 years old, predominantly male.[1-4] So far, exposure to high doses of ionizing radiation is the only confirmed risk factor for GBM. GBM is located mainly in the subcortical white matter. The regions most commonly affected are – temporal lobe followed by parietal lobe. GBM represents 7.5% of all intramedullary gliomas and 1–3% of all tumors of the spinal cord.[1-4]

The clinical presentation of GBM is variable, depending on the location of the tumor, with headache being the most common symptom. In regard to cervical GBM, the symptoms are varied, and patients may develop sensory and/or motor alterations. In severe cases, respiratory symptoms may appear.[4-6] Statistics about the prevalence of the symptoms is scarce in the literature.

We describe a case of cervical GBM in a young patient. This article sought to reveal the current knowledge regarding intramedullary GBM clinical features as a form to early diagnosis and appropriate treatment.

CASE REPORT

A 35-year-old female patient was admitted in the service complaining of pain in her right lower limb. She reported the evolution of the condition for dysesthesia in upper limbs and lower limbs 4 weeks ago, since the onset of the clinical condition.

On examination of motricity, the patient presented limb movement with Grade 2/5 strength in the right dimidium. On the left dimidium, there was movement of the limb against gravity, but without resistance, representing a Grade 3/5 strength. MRI showed an intramedullary lesion extending from C2 to C5 [Figures 1 and 2].

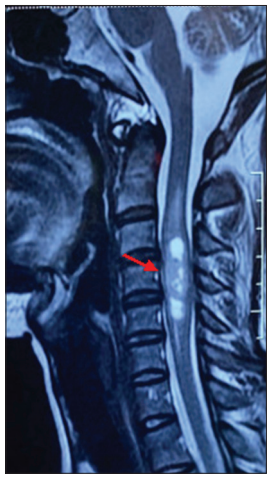

Figure 1: T2-weighted MRI showed hyperintense lesion in the sagittal section (red arrow).

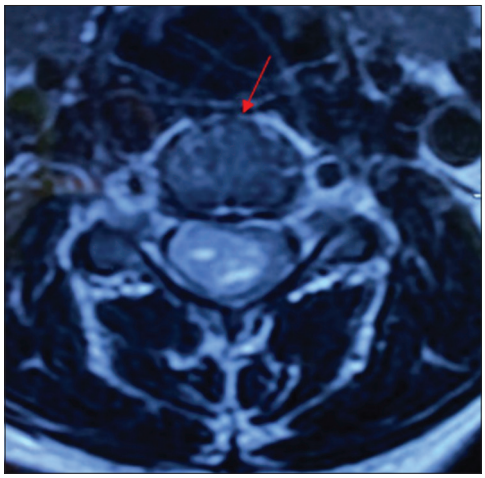

Figure 2: T2-weighted images showed iso-hyperintense lesion in the axial section (red arrow).

The patient underwent surgical treatment, under electroneurophysiological monitoring, to perform the tumor excision. In surgery, laminotomy was performed from C3 to C6 for posterior cervical access. For cervical spine exposure, the median durotomy was performed followed by median myelotomy guided by neurophysiological monitoring and finally, total macroscopic resection [Figures 3 and 4]. The biopsy confirmed the diagnosis of GBM.

After a slight worsening in the post-operative segment, the patient evolved with stability and complete remission of symptoms 6 weeks after surgery.

DISCUSSION

Epidemiology and pathophysiology

GBM can occur at any age, but the peak incidence is between 55 and 65 years.[7] The occurrence of GBM is low, reaching 2–3 cases in every 100,000 individuals. This tumor is more common in male and it is twice as common in Caucasians versus African-Americans.[7-10] Glioblastomas can affect various parts of the central nervous system, however, they appear more rarely (1–3%) in the spinal cord.[3,5,7-10]

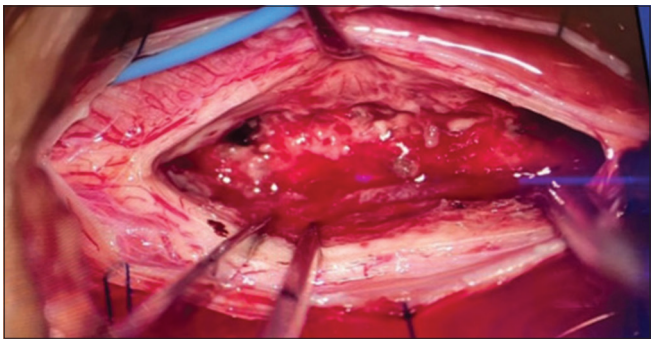

Figure 3: Operative cavity after tumor excision.

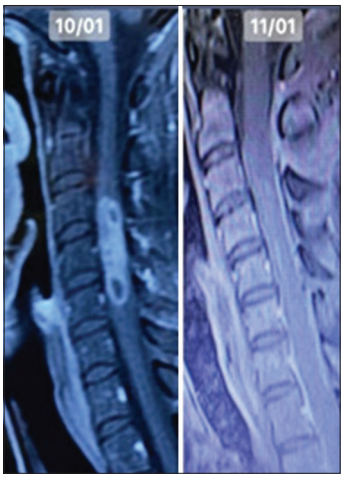

Figure 4: Image of cervical MRI in sagittal view pre-operative (left) and post-operative (right).

The etiology of Grade IV astrocytoma is unknown. So far, exposure to high doses of ionizing radiation is the only confirmed risk factor.[11,12] No evidence has been found between development of GBM and routine exposure to diagnostic radiation in children and adults.[13] No conclusive association has been found between GBM and environmental factors such as smoking, diet, and cell phones.[7-10] As per literature, infections and allergic diseases may have a protective effect on GBM, which may be due to the activation of the immune surveillance mechanism. In addition, the probability of developing glioblastoma may be associated with the inheritance of a dominant gene for the p53 protein (tumor suppressor gene).[14-16]

GBM is an anaplastic tumor that has poorly differentiated cells, round or pleomorphic, occasional multinucleated cells, nuclear atypia, and anaplasia. According to the WHO classification, GBM differs from anaplastic astrocytomas by the presence of necrosis observed under microscopy. The tumor is usually represented by a single irregular lesion, which can be large and which usually appears in white substance.[16-18] The development of a Grade IV astrocytoma is believed to be derived from neural stem cells or glial precursor cells.[16-18]

GBM holds pleomorphic cells, ranging from small, poorly differentiated tumor cells to large multinucleated cells with multifocal necrosis and predominant mitotic activity.[18,19] There are genetic changes that explain the origin of GBM. In the case of the tumor without existing precursor lesions, the modifications include an increase in the epidermal growth factor receptor, the deletion of the p16 gene, and, in addition, the amplified expression of the negative regulator of the p53 tumor suppressor, MDM2. Regarding the genetic changes in GBM with pre-existing lower grade astrocytoma, there is an increase in factor derived from type A platelets, in addition to an increase in alpha receptors (PDGFA/PDGFRa), retinoblastoma, and mutation of the isocitrate dehydrogenase gene 1 and 2.[18-20]

Glioblastoma is divided into primary and secondary tumor. The appearance of the primary tumor is not associated with clinical changes or precursor lesions. In the secondary tumor, Grade IV astrocytoma is due to a pre-existing neoplasm.[7,9] In the present case, the patient had a cervical GBM without previous injury, characterizing a primary tumor.

Clinical features

Most patients with GBM generally have a short medical history, ranging from 3 to 6 months; however, if the tumor develops from a low-grade astrocytoma, the clinical history extends over several years.[7,17,18]

GBM patients may have different signs and symptoms, which can be produced by three different factors – direct effect, increased intracranial pressure, and tumor location. Directly, the brain tissue may be destroyed by necrosis, causing focal neural deficit and cognitive impairments. It is usually unilateral, with progressive severity and there is no specific pattern for pain. It may be associated with vomiting and papilledema. About 20–40% of patients may also have seizures, usually with focal onset, which can be simple partial, partial complex, or generalized.[7,17]

When located in the cervical region, GBM can present with limb pain, paresis, paresthesia, urinary incontinence, and dyspnea.[2,14,20] In our case, the patient reported pain in the right lower limb, which evolved to dysesthesia in the upper limbs and lower limbs. In addition, he presented changes in motor strength. When assessed on the strength scale, the patient expressed Grade 2/5 in the right dimidium and Grade 3/5 in the left dimidium.

Diagnosis

Imaging techniques performed on individuals suspected of having brain tumors include procedures such as catheter angiography and non-invasive tests, such as CT scan and the gold standard for tumor detection, which MRI.[7,17,18]

On CT scan, GBM lesions usually appear as hypointense areas in comparison to the surrounding tissue and may be associated with midline deviation. In MR, hypointense lesions are seen in T1-weighted images, while hyperintense lesions are seen in T2-weighted images.[7] GBM has a heterogeneous, poorly delimited macroscopic presentation, and may present with multifocal hemorrhage, necrosis, and cystic areas. The tumor is usually represented by a single lesion with an irregular shape and relatively large.[6,8,14,21] In the present case, the MRI evaluation did not detect hemorrhagic or necrosis.

It may be impossible to distinguish, on imaging studies, a high-grade astrocytoma from other tumors, such as ependymoma. There are some reports that suggest that high-grade neoplasms have less spinal cord enhancement, especially those in the conus medullaris region.[17]

The diagnosis of Grade IV astrocytoma is confirmed by biopsy. Histological analysis shows cell atypism and pleomorphism, justifying the existence of the tumor.[20] In our case, the biopsy confirmed the diagnosis of GBM after surgical excision.

Treatment

The main challenges in GBM therapy are associated with the location of the disease and its complex and heterogeneous biology. Although most treatments fail to reach all tumor cells, the surgical procedure is the main method for treating GBM followed by the association with systemic therapy and radiotherapy.[7,8] The standard of care for patients

with newly diagnosed GBM includes maximum and safe resection of the tumor, followed by radiation therapy with concomitant systemic therapy, using the alkylating agent temozolomide.[9]

Depending on the location and size of the tumor, surgery can bring numerous benefits with GBM resection or complete excision, such as pain control, neurological deficit regression, and normalization of motor strength.[3] Extensive resection is more complex in intramedullary GBM, due to the poorly defined tumor margin in the spinal cord and adjacent tissues and poor overall prognosis, regardless of therapeutic intervention.[20] Surgical treatment may be followed by radiotherapy, which may be associated with better life expectancy in patients with high-grade gliomas.[16]

Post-operative irradiation is generally recommended in cases of partial resection of high-grade malignant astrocytomas and has been shown to result in increased survival and neurological improvement. Despite the disappearance of the tumor mass on imaging studies after complete resection of an intramedullary GBM, given the high rates of recurrence, brain metastasis, and leptomeningeal involvement, post-operative chemoradiotherapy is indicated.[20]

Chemotherapy is associated with several limitations. Many chemotherapeutics are not able to cross the blood–brain barrier and, consequently, the administration of drugs for the cerebral/medullary parenchyma and the tumor itself is compromised.[7]

In our case, a complete macroscopic resection of the cervical GBM was performed. The patient underwent clinical follow-up with oncologist, radiotherapist, and motor physiotherapy. After the surgical procedure, the patient was stable with significant improvement in motor and pain.

Prognosis

The prognosis of GBM depends on factors intrinsic to the tumor, such as location and size. In addition, the strategy for carrying out the various therapeutic techniques is decisive in patient's follow-up.[21]

The prognosis of intramedullary GBM is very low (median 15 months; range 6–18 months) and leptomeningeal dissemination occurs in approximately 60% of patients.[20] Extraneural metastases from GBM are rare.[1,6,7,18] The chances of recurrence are approximately 80% of cases and usually occur within 2–3 cm of the original lesion margin.[16]

CONCLUSION

Intramedullary GBM of the spinal cord is rare. Despite aggressive intramedullary tumor resection, followed by clinical therapy, the patient's ultimate long-term outcomes are less impacted. This article aimed to report a rare case of successfully treated intramedullary GBM at our service and brief review in regarding this poorly understood disease.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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