Secondary Psychosis Due To Meningioma. A Review About A Case

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Meningiomas are the most frequent primary tumors of the nervous central system. These tend to be benign with slow growth. They may be asymptomatic or even to appear only with psychiatric symptoms, including a psychotic episode. There are no clinical-controlled/randomized studies aimed to investigate the correlation between meningioma and psychotic episodes. Evidence available is based on series and case reports. There is a correlation between the magnitude of the perilesional edema and the presence of psychotic symptoms. On the other hand, the size of the lesion or its specific neuroanatomic location would be less relevant. Surgical resection of the lesion, along with proper psychiatric handling, usually leads to cease of psychotic symptomatology. When evaluating patients with psychotic symptoms there must be high evidence, specially in recent episodes, with atypical treatment resistant manifestations. In these cases, it is recommended to perform a neuroimaging study. This article describes the case of a patient who was evaluated in our hospital and diagnosed with a big left frontal meningioma, with secondary psychotic symptomatology. An updated bibliographic review of this correlation is described.

Key words: meningioma, cerebral tumors, psychosis.

INTRODUCTION

Meningiomas are the most frequent primary tumors of the nervous central system. These may have clinical manifestations at the beginning, only with psychiatric symptomatology. In this review, we shall describe a clinical case of a patient who had a left frontal meningioma with psychotic manifestations, in order to better understand psychiatric manifestations this type of tumors may have, and also its study, prognosis and potential therapeutic strategies.

Clinical case

The patient is a 43-year-old woman. No medical or personal psychiatric background. Three-year clinical picture with a marked evolution marked describing fatigue, lack of energy, weakness in both lower limbs and lack of motivation for her daily activities. Later she started with behavior disturbances that became notorious, both for the patient and for her acquaintances. Social isolation is marked. She stopped sharing with friends and relatives. Even though she performed her labor activities, when she arrived home, she locked herself
in her room, and hardly helped in household chores.

Later she started with irritability, both at work and with her family and friends.

After one year of evolution polymyalgies and bilateral gonalgia are added, so, the patient consults a general physician. The diagnosis was fibromyalgia. She started her treatment with nonsteroidal anti-inflammatory medication with a poor response. Later she quit that treatment.

After two years of evolution, she had progressive decrease of her bilateral visual acuity. Six months later, she started to neglect her personal care and accumulate garbage in her room, at an extreme that it was difficult to move around inside. This was remarkable for her acquaintances, as previously she was very concerned about her personal care and cleanliness. At that time, she started to provide wrong answers to simple questions, such as her age, her son’s birthday. She had unreasonable laughter, occasional kinesthetic hallucinations, and she said she was shivering. When she told her relatives about this situation, they denied such assertion. She looked puzzled and did not know what to do.

Her family took her to various physician of assorted specialties and no clear diagnosis was obtained. She had a medical leave for more than 6 months with a fibromyalgia diagnosis.

Two weeks before she entered the Neurosurgery Institute she started with damaging delirious ideas, where she said her father wanted to poison her with sour milk and garbage in her room caused some influence on her by means of “energies”. She also had visual hallucinations of a black man who was permanently by her side. These situations caused her an intense anguish, as she had a feeling, he could harm her.

Despite the foregoing symptomatology, the patient was taken to consultation, as her visual acuity got much worse. In the ophthalmologic evaluation papilledema was found. A brain magnetic resonance (MR) was made reporting a 7.7 x 6.7 x 5.5 cm diameter left dural frontal extra axial based mass, conditioning a significant mass effect on the surrounding structures, displaced to the right from the medium line structures, subfalcial herniation, obliteration of local convexities grooves and collapse of the lateral ventricles frontal eminence, with deformity and compression of the back portion of the corpus callosum (Fig. 1 and 2)

Due to the findings, she was referred to the Neurosurgery Institute. She was evaluated and later a full resection of the expansion process and of the dural margin of the implantation. The anatomicopathological diagnosis reported findings matching an atypical meningioma, grade II, as per WHO.

Given persistence of psychotic symptoms after the surgery she was medicated with Haloperidol, 4 mg a day, for 7 days and then gradual elimination. She had a good psychiatric response, no significant symptomatology during further controls.

BIBLIOGRAPHIC REVIEW

Meningiomas
A brain tumor is a mass with abnormal cells growth which may have a wide variety of symptoms. It may be classified, according to its histopathological characteristics or anatomic location. If the origin of the tumor comes from brain tissue, it is a primary brain tumor. If it has cerebral metastasis from tumors located in other body tissues, it is a secondary cerebral tumor. Primary brain tumors originated by glial cells are named as gliomas, within which astrocytomas, oligodendrogliomas and ependymomas are found. Within brain tumors not originated from the glial tissue, meningiomas, schwannomas, craniopharyngiomas, tumors of germ cells, pituitary adenomas and pineal region tumors are found.(1)

Meningiomas are the most frequent primary tumors in the central nervous system, with around 37%, with a yearly incidence of 7.61 every 100,000 individuals(2)

Meningiomas are intracranial extra-axial tumors originated in the meningotheelial cells of the arachnoids(3)(4)(5). Meningiomas can be found on any dural intracranial or spinal surface. They may appear in any place where arachnoid cells are present, being most frequent on parasagittal locations (20.8%), of the cerebral convexity (15.2%) and sellar tuberculum (12.8%). Parasagittal meningiomas are most frequent in the lobe front.(5) These are most frequent in women, with a frequency of 2-4: 1 against
Figure 1. Magnetic resonance axial encephalon and coronal axial cuts. Sequence T2 SE. It is evident the big mass effect on the left/right front lobe. Apart from major perilesional edema in the left frontoinsular region.

Figure 2. Magnetic resonance with axial/coronal/sagittal encephalon cuts. Sequence T1 with gadolinium. A left frontal extra axial lesion is observed with homogeneous enhancement after contrast administration.
men and incidence increases with age. Other risk factors are presence of type 1 and type 2 neurofibromatosis, and also exposition to ionizing radiation\(^6\). Its peak of incidence is at 45 years old and age diagnosis average is at 65 years. The risk increases with age, although 1.5% occur during childhood and adolescence, in general between at 10 to 20 years old and are associated to neurofibromatosis type 1.\(^7\)

Meningiomas are generally lone, benign lesions, with a slow growth. They may be multiple in around 8% of all cases, being this finding most frequent in patients who have neurofibromatosis. Many are incidentally discovered with neuroimaging. Even though they have a pathognomonc symptomatolgy, typical symptoms are cephalae due to increasing intracranial pressure, focal neurologic deficit or convulsions caused by the mass effect.\(^8\) Papilledema and homonymous hemianopsia were typical traits of the increasing meningiomas at the anterior parasagittal.\(^5\)

Magnetic resonance imagery is often enough to perform a diagnosis. Frequency of meningiomas is probably underestimated, as the systematic exploration with magnetic resonance showed that prevalence of undiagnosed meningiomas is 0.5% in people aged 45 to 59 years old; 1.6% after 75 years old\(^9\), according to WHO histopathological classification \(^10\) 94% are grade I (typical), 4% grade II (atypical), and 1% is grade III (anaplastic). \(^11\)

**Psychiatric Presentation in Brain Tumors**

Metastatic brain tumors may be associated with a higher incidence of psychiatric symptoms than primary brain tumors, quite likely due to the diffused distribution of metastasis on brain parenchyma\(^12\). Between 50 to 78% of patients with brain tumors have psychiatric manifestations.\(^13\)(\(^14\)). However, Keschner's et al study, took a sample of 530 patients who had a brain tumor. Only 18% of them had psychiatric symptomatology as a first clinical manifestation.\(^14\) A change in mental status may be the first sign in around 15 to 20% of patients who have a brain tumor, which may appear as a change in personality, emotional disturbances or intellectual deficit\(^15\).

Some old studies report there is no correlation between tumor histology and psychiatric symptomatology.\(^14\) This has been confirmed with more recent studies, reporting that 44% of patients with brain tumors have affective symptomatology, regardless of tumor histology\(^17\).

Some studies reported that psychiatric symptomatology may depend on localization of the tumor\(^18\). Frontal/temporal brain tumors tend to cause more psychiatric symptomatology than parietal or occipital tumors.\(^15\) A tumor in the prefrontal dorsolateral region tend to cause executive dysfunction; at an orbitofrontal level, it tends to cause disinhibition. A tumor located in the medifrontal region may cause abulia or apathy\(^18\). Limbic temporal tumors se may cause psychosis.\(^19\) There is a correlation between anorexia and hypothalamic tumors; a possible correlation between psychotic symptoms and hypophysis tumors; cognitive symptoms and thalamic tumors; and affective symptoms and frontal tumors.\(^18\)

Psychotic symptomatology in brain tumors tend to be mostly visual; more frequently with simple rather than complex characteristics\(^20\) Madhusoodanan et al. state that affective symptoms are the most common. These have been reported in 36% of cases. Psychotic symptoms are reported in 22% of patients. In case of patients with psychotic symptoms, many of them had pituitary tumors. In another study temporal lobe tumors were mostly related with psychotic manifestations.\(^18\)

The fact that tumors located in the same brain areas may cause similar psychiatric symptoms suggests these are altering relatively specific connections within the cerebral cortex.

Meningiomas are tumors in the meninges, not in the brain parenchyma; however, they may affect the cortex by creating a mass effect, which may interrupt connectivity within and between cortical lobes; therefore, they may cause these documented psychiatric symptoms.\(^21\) Peritumoral edema has also been considered as the cause of such interruption in the neuronal cerebral connectivity\(^22\). In this sense, there is evidence that alterations of the corticothalamic connectivity may be related with appearance of psychotic symptoms. However, no identification has been made about what specific corticothalamic circuits are involved\(^23\). There is a bidirectional correlation between psychiatric pathology and brain tumors. In this sense,
patients with psychiatric pathology have up to 10 times higher frequency in brain tumors. In this sense, a study proved that one out of 323 psychiatric patients who were subject to a brain computed tomography had a brain tumor.

**Meningiomas and General Psychiatric Symptoms**

Meningiomas may be clinically silent or may only appear with psychiatric manifestations that were not previously present. In this sense, 21% of the meningiomas has been observed to have psychiatric symptomatology in absence of neurologic symptoms. Affective symptoms are the most frequent ones and there is no correlation between laterality of the tumor and psychiatric manifestations. In another study psychiatric episodes in 44% of meningiomas of the convexity were diagnosed.

Cephalgia, papilledema or focal neurologic signs often appear only when a meningioma has reached an advanced stage. Psychiatric changes attributed to meningiomas include depression, anxiety, apathy, mania, psychosis and personality changes. Meningiomas compressing frontal lobes from outside could not cause any type of symptoms or else a progressive change in personality and intellectual functions only when reaching a big size. Intensity and course of the symptoms will depend on evolution time of the tumor and its velocity of growth.

Gyawali et al. in 2019 made a review on meningiomas and psychiatric symptoms. 48 case reports studies, cases series (maximum 3 cases) and letters to the Editor, were analyzed, with a total of 52 cases. The most frequent location of tumors was found at the lobe front with nearly 30 cases. Most frequent symptoms reported for frontal meningiomas were depressive symptoms. Right frontal meningiomas were associated to bipolar disorder, alcohol abuse and musical hallucinations. Capgras and Anton Syndrome were also described in frontal tumors. Case of meningioma of the olfactory sulcus that compromised both frontal lobes had symptoms of affective flattening, abulia, decreasing personal care for 3 years, which was initially diagnosed as schizophrenia. A right temporoparietal meningioma was associated to depressive symptoms which later turned into symptoms compatible with an acute schizomorph syndrome. Similarly, the right parasagittal region of the parietal lobe was associated to schizophrainform psychosis.

**Psychosis**

The term "psychosis" does not have a unified definition, but it denotes a syndrome made up of several symptoms. Psychotic symptoms are common and unleash many psychiatric episodes on neurodevelopment, neurologic and medical; it is a significant objective of evaluation and treatment in neurologic and psychiatric practice. Definition and characterization of psychosis as a concept is complex and has changed in time. It was first used by the Austrian physician Ernst von Feuchtersleben, in 1845. In the first editions of the Diagnostic & Statistic Manual of Mental disorders (DSM) of the American Association of Psychiatry (APA), psychosis was defined in general terms as a "severe alteration in the reality test" or "loss of the limits of the self" interfering with the capacity to comply with usual aspects of life. In current diagnosis classification systems, both that of APA and of the WHO, alteration in the reality test is still conceptually relevant for psychosis. Unlike the previous diagnosis classification system, the objective is to rationalize such alteration. In this sense, in DSM-5, Chapter "Spectrum of Schizophrenia and other Psychotic Disorders " states that these disorders are defined by abnormalities in one or more of the following five domains: delusions, hallucinations, disorganized thinking, disorganized or abnormal behavior (including catatonia) and negative symptoms. Still it is not possible to determine the exact mechanisms working on individual cases of psychotic manifestations. Therefore, psychosis is still defined by its clinical picture, not with lab/ genetic/neuroimage investigations.
Meningiomas and Psychosis

Meningiomas located at the right parietal lobe, pineal gland, lateral ventricle and bilateral occipital lobe have been found associated with psychosis.\(^{(18)(37)}\) Same situation at temporal medial level, specifically, at the hippocampal complex, gyri parahippocampalis, tonsils and superior temporal gyri, preferably the left side.\(^{(38)(39)(40)(41)}\) Regarding lateralization of the lesion, frontal right meningiomas are associated to psychiatric symptoms mostly at the left side.\(^{(22)}\)

Particularly, right parietal meningioma is related with paranoid delusions and hallucinations.\(^{(37)}\) Meningiomas of the cerebral convexity are associated to delirious symptomatology.\(^{(22)}\)\(^{(42)}\) It has been observed that compression and perilesional edema at the right temporal lobe, caused by meningiomas at such location have been associated with loss of facial recognition and familiarity, and also delusions and violent behavior, similar to Capgras syndrome.\(^{(43)}\) It has been observed there is no correlation between the volume of the meningioma and psychotic symptoms, but such correlation between the volume of perilesional edema and such symptoms has been observed.\(^{(22)}\) However, the mechanisms by which meningioma causes such psychotic symptoms still remain blurred.\(^{(21)}\)

Regarding treatment there is some evidence based on case reports, regarding use of low doses of olanzapine in order to decrease psychotic symptomatology in this group of patients, which is safe and has good effectiveness indexes.\(^{(44)}\)

According to the cases review made by Gyawali et al, patients treatment consisted of full/partial resection of the meningioma, along with treatment of psychiatric symptoms using antidepressants, antipsychotics and anticonvulsivants. Usually with resection of the tumor, psychiatric manifestations are reduced, and many times did not require to continue psychopharmacological treatment. However, some case reports described a new appearance of psychiatric symptoms after resection of the tumor. Most case reports are not clear to specify if psychotropic agents remained or not after the resection of the tumor.\(^{(1)}\)

DISCUSSION

There is poor evidence with respect to correlation between meningiomas and psychotic symptomatology, being predominantly based on reports and cases series. There are no controlled/randomized/double blind clinical studies for this clinic correlation.

We think this poor level of evidence may be caused by continuity loss between psychiatric anamnesis of the case and then its surgical resolution. Probably in case a Psychiatrist, as part of the study of a psychotic episode, requests a neuroimage whose result is finding a brain tumor, will immediately refer the case to a neurosurgery team. These will find the best way to remove the tumor and will proceed with surgery. The priority to surgically intervene a case like the one we introduced, reduces the importance of how psychiatric symptoms appear in time and the way how such diagnosis was obtained.

The case presented by us is exceptional, as it shows a young patient with a left frontal meningioma and psychotic symptomatology. This case is highly suggestive of a correlation between meningioma and psychosis manifestation, considering that surgical resolution caused a significant clinical improvement of the symptoms, where the use of a antagonistic dopaminergic drug probably acted as a adjuvant.

In the light of the foregoing, we think this work may be a contribution to the body of evidence stating that meningiomas may appear associated to psychotic symptomatology.

There is no clear reason why a patient specially one who has a left frontal meningioma may remain asymptomatic, to have psychotic symptoms or any other type of psychiatric manifestations. However, we think that perilesional edema, the mass effect caused by the tumor or the interruption of corticothalamic pathways may be related in this manifestation.

Regarding associated symptomatology, psychotic symptoms in the presence of brain tumors would have no location value for the lesion in specific neuroanatomic regions.

Present psychiatric symptomatology is not related with the histopathological type of the tumor.\(^{(18)}\) Therefore, presence of a meningioma would not be different than other types of primary brain tumors.

There is no information available that relates
the size of the tumor with the severity of the symptomatology. However, there would be a directly proportional correlation between the cerebral edema caused by the tumor and severity of psychiatric symptoms\(^{(22)}\). Some subtle neurologic signs that may be found before or along with psychiatric manifestations are: apraxia, visual field deficit and anomia. Then some personality changes, sleep disturbances, apathy, loss of weight, anorexia and lack of concentration may appear. After that a psychiatric episode may appear which may not easily match the existing category diagnosis, and also atypical/refractory/recurrent symptoms\(^{(18)}\).

We agree with Madhusoodanan et al, in the sense that when having a high level of suspicion, we must request a neuroimaging study before a new psychotic episode, recent loss of memory, first time appearance of anxious/depressive symptoms in elderly people. Same thing, before appearance of atypical symptoms, personality changes and anorexia without dimorphic symptoms, such as body self-image alteration. We would suggest to obtain a neuroimage in case of patients who have a torpid evolution or resistance to psychiatric treatment, despite having good adherence and compliance of given indications.

It is important to state the need of a multi-disciplinary solution, looking for a good participation among all specialists. It is necessary to work as a team and to have feedback regarding referrals or interconsultations made. We think it is advisable that in the training programs for general physicians and specialists these topics are addressed, mainly regarding psychiatric episodes of neurosurgical symptoms.

There are no randomized/double blinded studies on treatment of psychotic symptoms in meningiomas. It is necessary to perform more investigations in order to have more evidence, as still there are many questions to be answered. For instance, is it necessary to continue with psychopharmacological treatment tumor resection? If so, for how long?

As a conclusion, we may say it is necessary that before a first psychotic episode or atypical manifestation of a psychiatric episode, a neuroimaging study is requested. In this way, in case of chasing a brain tumor, there are more possibilities of getting early diagnosis and timely neurosurgical treatment, along with psychiatric treatment, if necessary.

**BIBLIOGRAPHY**


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