



The Intralesional Hemorrhage Risk for Meningiomas and Dural Metastasis: Is There a Prostaglandin's Receptors Role in Its Pathogenesis? Case Report

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Abstract

Background: Many hemorrhage's risk factors have been listed for brain meningiomas, but intracerebral hemorrhage often occurs for malignant or secondary brain tumors. Maybe that these two eventualities are combined for the histopathological expression of the same hormonal receptors.

Case Report: We present three cases of patients treated for intracerebral hemorrhage occurred on brain tumors. Pathological findings of the tumors revealed two cases of meningioma I WHO and a breast cancer metastasis: The prostaglandins' receptors presented over expression in the all the cases.

Conclusion: This correlation could support the hypothesis that the prostaglandin receptor's expression favorites the intracerebral hemorrhage insurgence.

Keywords: Meningioma; Breast cancer; Prostaglandin receptors; Dural metastasis

Abbreviations

MRI: Magnetic Resonance Imaging; CT: Computed Tomography

Background

Intracranial hemorrhage from a brain tumor is well known but not so common. The incidence of hemorrhage from intracranial tumors is around 5% [1]. Dural metastasis is rarely reported: Represents less than 1% of intracranial metastases [2]. According to Nayak et al., breast cancer was the most common primary tumor associated with dural metastasis [1]. However, reports of patients with intracranial hemorrhage from dural metastasis of breast cancer are rare [3]: Most of them were patients with subdural hematoma [4,5]. Meningiomas are the most common, benign intracranial tumor, accounting for 19% of all primary intracranial neoplasms [6]; they are slow growing and potentially highly vascularized, but hemorrhage of these tumors is rare. We present three cases of intralesional hemorrhage occurred on brain tumors radiologically mimicking meningiomas, which presented histopathological findings united by well-represented prostaglandin's receptors [7-9].

Case Series

Case 1

An 81-years old woman came to our attention for gait disturbance and repeated episodes of falling to the ground. An MRI Siemens MAGNETOM SKYRA 3-T examination revealed an extra-axial mass adherent to right parieto-occipital convexity dura mater with internal hemorrhagic nodules; after gadolinium administration, there was a homogeneous enhancement except for hemorrhagic images within the mass (Figure 1). The size of the lesion was about 4.5 cm × 5.7 cm × 3.5 cm. Imaging findings were suggestive for hemorrhagic meningioma. The day before planned surgery, she presented an episode of loss of consciousness and the Computed Tomography (CT) General Electric revolution 64 scan performed in emergency proved a new mass bleeding with 3 cm of brain-shift. Emergency craniotomy was performed. A very large hematoma and a well-demarcated and mild-consistency lesion have been removed piecemeal within the convexity dural-attachment. No tumor infiltration has been observed on the surrounding brain. Pathological examination revealed a fibroblastic meningioma I WHO (EMA +, Progesterone receptor +, GFAP-, OLIG2-). The patient during immediate postoperative time was transferred in Intensive Care Unit (ICU) under general anesthesia. Despite the postoperative CT General Electric revolution 64

OPEN ACCESS

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Received Date: 16 Jan 2024

Accepted Date: 28 Jan 2024

Published Date: 02 Feb 2024

Citation:

Fazzolari B*, Zambuto MR, Gammone V, Richiello A, Brunori A, Menniti A, et al. The Intralesional Hemorrhage Risk for Meningiomas and Dural Metastasis: Is There a Prostaglandin's Receptors Role in Its Pathogenesis? Case Report. *Clin Oncol.* 2024; 9: 2055.

ISSN: 2474-1663

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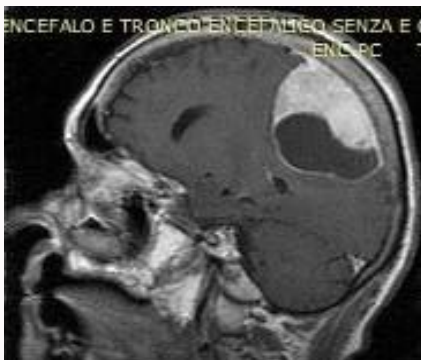


Figure 1: Case 1: MRI Siemens MAGNETOM SKYRA 3-T examination revealed an extra-axial mass adherent to right parieto-occipital convexity dura mater with internal hemorrhagic nodules, suggestive for hemorrhagic meningioma.

scan demonstrated the complete hemorrhage and tumor removal without brain-shift, the patient's clinical outcome got worse, a tracheotomy has been performed to the perduring of anesthesia. After one month, the sedative reduction arose eyes opening and facial mimicking response with slight verbalization. Patient keep severe left hemiparesis. The next step would be the return to Neurosurgery ward to income a rehabilitation route.

Case 2

A 75-years old woman presented to first-aid for right hemiparesis just occurred. An MRI Siemens MAGNETOM SKYRA 3-T examination revealed an extra-axial mass sited in correspondence with left frontal motor convexity, that seemed adherent to the dura mater with bone erosion; after gadolinium administration, there was a homogeneous enhancement (Figure 2); in its context were some hemorrhagic spots. The size of the intradural lesion was about 4.3 cm × 2.3 cm × 1.7 cm; the extradural part measured 4 cm × 2.3 cm × 0.8 cm. Imaging findings were suggestive for frontal meningioma with bone erosion. Ten years before this patient suffered a breast cancer removal still in follow-up. The patient has been transferred to Neurosurgery Unit and surgical removal has been planned. After skin incision, the tumor was immediately exposed as pericranium's invasion, then the boundaries of bone erosion have been identified. Bone seemed as infiltrated by the tumor as eroded; a little craniotomy was necessary to complete the bone removal and expose the intradural portion of lesion. The tumor consistency was soft and few demarcated: Total

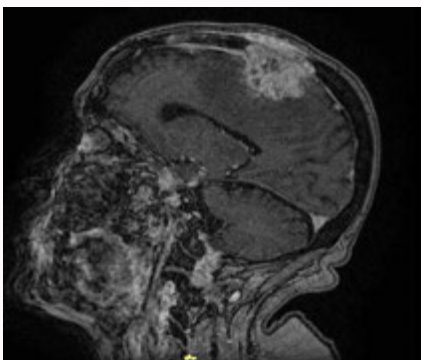


Figure 2: Case 2: MRI Siemens MAGNETOM SKYRA 3-T examination revealed an extra-axial mass sited in correspondence with left frontal motor convexity, that seemed adherent to the dura mater with bone erosion, suggestive for frontal meningioma.

removal have been carried out including the eroded bone. There were some hemorrhagic spots into the tumor and no brain invasion. After en bloc removal, bone reconstruction has been carried out by resin substitute modeled to fit the remaining hole. After surgery there was an immediate recovery of motility in the right side but, in the second postoperative day the patient had an epileptic seizure with worsening of right arm motility, the emergency CT General Electric revolution 64 scan revealed a hemorrhage in correspondence of surgical field. Emergency hematoma removal have been done: A cortical artery bleeding has been cauterized and the patient recovered the right arm motility into 7 days from that time. Pathological examination revealed a tumor with soft consistency with mucinous and grey-red cells, consistent with poorly differentiated carcinoma, bone and brain infiltrating (E-Cadherin +, Estrogen receptor SP1 +, Progesterone receptor 1E2 +, HER 2 receptor 4B5 -) which origins from the breast carcinoma. Hemiparesis improved and postoperative course was uneventful; she was discharged two weeks after second surgery. The postoperative 1 month-later MRI Siemens MAGNETOM SKYRA 3-T shows total removal with no tumor regrowth; the patient has started whole brain irradiation therapy and concomitant chemotherapy.

Case 3

A 77-years old woman has presented to first-aid for loss of consciousness episode with motor aphasia. An MRI Siemens MAGNETOM SKYRA 3-T examination revealed an extra-axial mass adherent to left frontal convexity dura mater in correspondence Broca's area. Into the mass there were some internal hemorrhagic nodules (n=3); after gadolinium administration, there was a homogeneous enhancement except for hemorrhagic images within the mass (Figure 3). The size of the lesion was about 5 cm × 4.3 cm × 3.2 cm. Imaging findings were suggestive for hemorrhagic meningioma. The patient has been transferred to Neurosurgery Unit for surgery. Fronto-temporal craniotomy was performed. The lesion appears totally adherent to the convexity dura mater and has been removed en-bloc within its dural-attachment. Tumor did not show brain invasion. Pathological examination revealed an angiomatous meningioma I WHO (EMA +, Progesterone receptor +, GFAP-). The patient during immediate postoperative time was transferred in Intensive Care Unit (ICU) under general anesthesia. On the second postoperative day have been detected on lung CT General Electric revolution 64 scan a pneumonia and the patient have been transferred

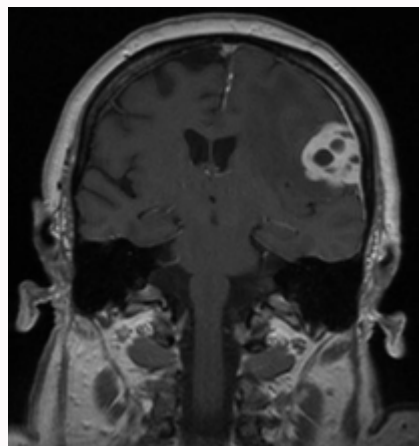


Figure 3: Case 3: MRI Siemens MAGNETOM SKYRA 3-T examination revealed an extra-axial mass adherent to left frontal convexity dura mater in correspondence Broca's area, suggestive for hemorrhagic meningioma.

to Medicine Unit for treatment. She was recovering preoperative aphasia. Postoperative CT General Electric revolution 64 scan demonstrated the complete tumor removal without brain-shift.

Discussion

Many authors identified clinicopathological features which favor the onset of intralesional hemorrhagic events: The tumor vasculature in meningiomas is heterogeneous, and undifferentiated vessels may play a pivotal role in the spontaneous intra-tumoral bleeding of meningiomas [10]. The largest literature review to date was published by Bosnjak et al. in 2005 [11] who state that there are many significant risk factors for hemorrhage in a meningioma: the age older than 70 or younger than 30; the location of meningioma being intraventricular or convexity; the histopathology consistent with being malignant, fibrous, or angioblastic; and presence of hypertension, anticoagulation therapy, and traumatic brain injury. As Bosnjak's statement confirmation, our cases represent one angiomatous meningioma and one fibroblastic meningioma. Pressman et al. [6] suggest the role of other two risk factors for the hemorrhagic onset of meningiomas: First, the use of Selective Serotonin Reuptake Inhibitors (SSRIs) or other antidepressants increases the risk of spontaneous hemorrhage of meningiomas as increased risk of other abnormal bleeding; second, the high-dose estrogen replacement therapy [12]. The role of female hormones (estrogens and progestogens) is recognized to be correlated with hemorrhagic/thrombotic events, especially in the post-menopausal period. A study in 2016 by Qureshi et al. [13] found that the rate of subarachnoid hemorrhage was higher among women on active hormonal replacement therapy compared with those without. On the other hand, most reported cases of dural metastasis with hemorrhage showed subdural hematoma due to the location of the tumor in the subdural space [4,5,14,15]. The second case described presented the hemorrhagic spots into the tumor's portion adjacent to the brain spreading to the space between the tumor and frontal lobe with wide peritumoral edema; the surrounding sagittal venous sinus maybe thrombosed inducing venous infarction into the lesion. Grasso et al. [16] reported the tumor vessels' features which make them inadequately permeable to macromolecules and allow the leakage of both water and an exudate, which is very similar in composition to plasma. Authors comment a molecular analysis carried out by Wang et al. [17] on markers' expression on endothelial vessel: They state that mean number of differentiated vessels in hemorrhagic meningiomas was 49.7-12.1, compared with 54.2-14.6 in controls, a none statistically significant difference ($P>0.05$) but the mean number of undifferentiated vessels was significantly higher in hemorrhagic meningiomas than in controls (15.3-4.9 vs. 6.4-3.6; $P<0.01$). Our findings suggest a possible role of progesterone receptors in the pathogenesis of intralesional hemorrhage, given the already well-known role of these hormones in hemorrhagic and thrombotic activation in the postmenopausal period. In all three cases we found a large expression of these receptors in the histological nature of the three lesions, despite their different histopathological nature (meningioma and breast cancer metastases). Despite the limitation of this work, it is intended as a food for thought for further studies on the matter.

Conclusion

Taking into account the limitations of this study which presents the histological characteristics of only three cases, the aim of our work

is to be understood as a proposal to identify the presence of hormone receptors responding to progesterone in the context of the lesion as a risk factor for intralesional bleedings.

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