Brain Abscess as Initial Presentation of Metastatic Adenocarcinoma and Melanoma

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ABSTRACT

Introduction: Case reports of the coexistence of brain abscesses and neoplastic processes are scarce, being its pathophysiology still unclear. In this paper, we report two cases of metastatic brain tumors mimicking brain abscesses. Cases presentation: A 65-year-old woman with neurological deficit and a brain MRI showing a 3.3x3x4 cm left frontal annular lesion and a halo of extensive ipsilateral frontotemporoparietal edema, suggestive of brain abscess. She was submitted to trepanopuncture with aspiration of 20 ml of purulent secretion and, due to persistence of the symptoms, she underwent surgical resection of the frontal lesion with anatomopathological and immunohistochemistry analyses showing a metastatic lung adenocarcinoma, keratin expression profile (CK7+/CK20-) and co-expression of TTF-1 and Napsin. In the second case, a 58-year-old man with sudden neurological deficit and brain MRI showing a 1.9x1.5 cm right thalamic lesion suggestive of a brain abscess. Due to failed response to empirical antibiotic therapy and evolution with sensory loss, a thalamic lesion biopsy and external ventricular shunt were performed. Anatomopathological and immunohistochemistry analyses reported metastatic melanoma with positive HMB45, S-100 and Melan-A antibodies. Conclusion: This is a report of the second confirmed case of an abscess mimicking a brain tumor in the supratentorial region and the first case describing a metastatic melanoma with initial diagnosis of a brain abscess.

Keywords: Brain metastasis; Brain abscess; Melanoma; Lung adenocarcinoma

RESUMO

Introdução: Relatos de casos da coexistência de abscessos cerebrais e processos neoplásicos são escassos, sendo sua fisiopatologia ainda incerta. Neste artigo, relatamos dois casos de tumores cerebrais metastáticos mimenizando abscessos cerebrais. Relatos de Casos: Mulher de 65 anos com déficit neurológico e ressonância magnética cerebral mostrando lesão anular frontal esquerda de 3,3x3x4 cm e halo de extenso edema frontotemporoparietal ipsilateral, sugestivo de abcesso cerebral. Foi submetida a trepanopunção com aspiração de 20 ml de secreção purulenta e, devido à persistência dos sintomas, foi submetida à ressecção cirúrgica da lesão frontal com análise anatomopatológica e imuno-histoquímica evidenciando adenocarcinoma pulmonar metastático, perfil de expressão de queratina (CK7+/CK20-) e co-expessão de TTF-1 e Napsina. No segundo caso, homem de 58 anos com déficit neurológico súbito e...
INTRODUCTION

Brain abscesses have an incidence of around 0.3 to 1.3 per 100,000 people per year, being most common in men. In about 95% of cases, the etiologic agent responsible is a bacterium. This diagnosis can be challenging due to a nonspecific and varied clinical findings, and the classical triad of headache, fever and focal neurological deficit is present in only 20% of the patients. Among its main differential diagnoses are brain tumors. Brain metastases are the most common type of brain tumor, being, in most cases of pulmonary origin. The main imaging test to perform the differential diagnosis between abscess and brain tumor is the Magnetic Resonance Imaging (MRI), however both pathologies may present with similar characteristics on MRI, requiring biopsy for etiological confirmation.

Most cases of abscessed brain tumors occur in the intra or parasellar region, being rare in other regions of the brain. A literature review indicated the presence of only 20 case reports of abscesses associated with extrasellar intracranial tumors, being only five of these associated with brain metastasis, and one of them, the first report in the literature of an abscessed parietal lobe tumor, and the others located in the posterior fossa. Only one case of adenocarcinoma mimicking a brain abscess has been reported in the literature, this one located in the posterior fossa.

In this article, we present two cases of patients initially diagnosed with brain abscesses and, later, immunohistochemistry analysis confirmed brain metastases.

CASES PRESENTATION

Case 1

Sixty-five-year-old woman, hypertensive, diabetic and smoker, was admitted to the emergency due to sudden motor deficit in the right hemibody and dysarthria for three weeks then, brain MRI showing a left frontal annular lesion measuring 3.3x3x4cm, an estimated volume of 75ml, and extensive halo on the left frontotemporoparietal edema, suggestive of brain abscess (Figure 1).

She presented with Glasgow 15, isochoric and photoreactive pupils, horizontal nystagmus, and strength on the right lower limb grade 4. It was, then, decided to perform a frontal trepanopuncture on the left side for drainage and diagnosis of the lesion, with the drainage of 20ml of purulent secretion (Figure 2).

Cultures were requested and empirical antibiotic therapy was initiated. She improved clinically and all the cultures were negative. After three weeks, she evolved with motor aphasia, right hemiparesis, headache, vomiting and mental confusion. Head CT showed recurrence of the lesion and worsening of the edema. Corticosteroid therapy was, then, started, antibiotic therapy was extended, and a new MRI was made for surgical planning. Again, the aspect studied (spectroscopy, and weightings) indicated a brain abscess as a hypothesis. The patient and family members chose not to perform the resection of the lesion, so a new drainage was performed through the previous burr hole, aspirating 20ml of serosanguineous secretion.

She evolved with clinical improvement, however, after six weeks she presented worsening again, with mental confusion and right hemiparesis, a new MRI was performed with persistence of the lesion. Thus, it was discussed again with the patient and family about craniotomy for resection of the brain abscess capsule.
Case Report

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The intraoperative appearance was that of a purulent lesion, without an organized capsule, being, then, resected and sent for analysis. The anatomopathological and immunohistochemistry diagnoses of metastatic adenocarcinoma (Figure 3) mainly considered the possibility of metastatic lung adenocarcinoma due to histological aspects, Keratin (CK7+/CK20-) expression profile, co-expression of TTF-1 and Napsin. Screening of primary neoplastic focus and staging was performed, and chest CT showed a tumor in the right lower lung lobe measuring 2.9cm. Patient was diagnosed with stage IV metastatic adenocarcinoma of the lung (T3N1bM1), then, being sent for radiotherapy and palliative chemotherapy.

The patient was hospitalized for treatment of complicated pneumonia after 3 months of hospital discharge, evolving to death in the same hospitalization.

Case 2

Fifty-eight-year-old man, chronic alcoholic, no previous comorbidities, with a history of excision of a non-malignant skin lesion six years before, was admitted to the emergency department due to left hemiparesis since the previous day, associated with a parieto-occipital headache.

He was afebrile, in Glasgow 15, with isochoric and photoreactive pupils, with labial commissure deviation to the right side, positive Romberg with a tendency to fall to the left and Babinski sign on the left side was present. Brain MRI revealed a right thalamic lesion measuring 1.9x1.5cm and the image analysis (weighting and spectroscopy) was suggestive of a brain abscess (Figure 4). Empirical antibiotic therapy and investigation follow-up were started.

Echocardiogram, chest CT and CSF analysis were unaltered, and with negative blood cultures. Abdominal CT showed hepatic nodules, suggestive of Hemangioma, and a 3cm right inguinal lymph node enlargement. A hypopigmented skin lesion with a bluish-black core measuring 1.5x1cm was identified in the lumbar region on the right, and a biopsy was performed, and its anatomopathological analysis suggested a melanocytic lesion with complete regression.

After one week, the patient evolved with sudden lowering of the level of consciousness. A new head CT showed intraparenchymal hemorrhage adjacent to the lesion, associated with an 8mm midline shift. It was, then, decided to perform a biopsy of the lesion and external ventricular shunt, and along with the general surgery team, excisional biopsy of the inguinal lymph node (Figure 5).
During the biopsy, it was observed drainage of a purulent secretion, which was sent for analysis. The chemocytological analysis showed 25,380 cells with a predominance of neutrophils, 20,000 erythrocytes, glucose < 5mg/dl and 414mg/dl of proteins, besides of isolating a gram-positive culture.

Histopathological and immunohistochemistry analyses of the biopsies indicated the diagnosis of Metastatic Melanoma, containing areas of necrosis and hemorrhage, with positive HMB45, S-100 and Melan-A antibodies (Figure 6). The patient evolved with clinical improvement.

Three weeks after being discharged from the hospital, he required hospitalization due to pulmonary thromboembolism, with a favorable outcome, and is currently undergoing chemotherapy treatment with the oncology team, with a Karnofsky score of 70%.

Brain abscess is a focal intracerebral collection composed mainly of pus, immune cells, and microorganisms. The most affected region is the frontal lobe. Its etiology is associated with hematogenous dissemination or with a contiguous focus of infection.
infection, especially pulmonary infections, endocarditis, otitis media, and mastoiditis, or, more rarely, trauma and invasive procedures, mainly dental and neurosurgical. Among its main complications are ventriculitis, hydrocephalus, secondary bacterial meningitis, seizures, persistence of neurological deficits and death, with a mortality of 5 to 15%.

In immunocompetent individuals, such as the patients reported, the most associated etiologic agent to the brain abscess is the bacterium. In immunocompromised individuals, such as people living with HIV, fungal infections, atypical bacteria, and toxoplasmosis should be considered.

The diagnosis of brain abscess can be challenging, as it is associated with a nonspecific clinical picture. Its main differential diagnoses are bacterial meningitis, primary or secondary brain tumors, encephalitis, demyelination lesions and fungal infections.

The imaging test of choice for its diagnosis is MRI, using spectroscopy, diffusion weighting (DWI) and diffusion tensor (DTI). However, the differential diagnosis with brain metastases is still difficult, not excluding the need of biopsy for etiological confirmation. Brain abscesses usually present on T1-weighted MRI as a hyperintense annular sign around a central hypointensity, on T2- as a hypointense sign and a central hyperintensity. However, these findings may also be present in cystic or necrotic tumors, as in the cases reported in this article.

The treatment of brain abscesses is initially performed with intravenous antibiotic therapy for six to eight weeks, which may be associated with surgical drainage in cases of lesions measuring from 2-2.5cm in diameter, significant perilesional edema, cases that are refractory to antibiotic therapy or clinical worsening of the patient. In cases that are refractory to the surgical drainage, craniotomy is indicated for resection of the abscess capsule, which can be assisted by neuronavigation.

The use of corticosteroids, such as dexamethasone, for a short period of time, can be associated with the treatment in cases of increased intracranial pressure associated with perilesional edema. Although its use is related to an improvement in the symptoms, it tends to delay the encapsulation process, increase necrosis, and decrease antibiotic penetration into the abscess. A meta-analysis indicated that most studies do not demonstrate a significant increase in mortality in patients using dexamethasone.

In the first case, the patient used dexamethasone, and, during the lesion resection surgery, it was observed the absence of an organized capsule in the lesion.

Figure 6. A-D. Histological slide of brain injury and inguinal lymph node with demonstrate areas of abundant melanin.
Despite of the suggestive characteristics of a brain abscess both on MRI and during the surgical procedures performed, after the anatomopathological and immunohistochemical results, the misdiagnosis was detected. Case reports in the literature related to the coexistence of brain abscess with a neoplastic process are scarce and the associated pathophysiology is unclear. One study showed that the occurrence of tumor with extracranial abscess is more commonly described in cases of lung tumor and ovarian tumor.15-17

Regarding the intracranial abscessed brain tumor, we found that most cases occur in the intra- or parasellar region, being rare in other regions. A literature review indicated the presence of only 20 case reports of abscesses associated with extrasellar intracranial tumors, being only five of these associated with Brain Metastases, and one of them, the first report in the literature of an abscessed parietal lobe tumor, associated with Salmonella bacteria,9,10, and the others located in the posterior fossa.9,11

Regarding the presence of adenocarcinoma with brain abscess, one confirmed case9 and a possible case of metastatic lung adenocarcinoma were reported18, both located in the posterior fossa. This report is the second confirmed case reported in the literature describing the association of adenocarcinoma with brain abscess and the first case reported not located in the posterior fossa. In addition, we did not find any case report of metastatic melanoma associated with brain abscess, with this being the first case reported.

It is believed that the pathophysiology of abscessed tumors is associated with multiple factors such as destruction of the blood-brain barrier, intratumoral necrosis that works as a culture medium, tumor bleeding with hematoma formation, immunodeficiency, malnutrition, and use of steroids.9,11

It is known that brain metastasis are the most common type of brain tumor and its etiopathogenesis is that cells detach from the primary neoplastic focus and reach the brain parenchyma via the hematogenous route, where they proliferate in different locations, producing a variable and nonspecific clinical picture.19,20

The main primary focus of brain metastases are lung, breast, kidney, gastrointestinal system and skin.6,8 Therefore, once the diagnosis of the brain lesion is identified, screening for the primary tumor should be carried out. According to the guidelines of the European Society of Medical Oncology (ESMO), for the investigation of cancer of unknown primary site, a previous history of tumors, presence of risk factors, complete physical examination, laboratory tests, tumor markers, chest, abdomen and pelvis CT, and mammography in women should be done. After these initial tests, other tests such as upper digestive endoscopy and colonoscopy may be ordered.21

It is known that 18 to 61% of the patients with lung cancer have brain metastases. The main lung neoplasms related to brain metastases are those belonging to the non-small cell lung cancer group, which includes adenocarcinoma (the most common), large cells, squamous cells and bronchoalveolar. The main risk factors observed are smoking, present in 90% of cases, as in the first case reported, Alcohol abuse, secondary exposure to smoke, asbestos, radon, arsenic, hydrocarbons and radiotherapy. In the clinical picture, cough, hemoptysis, chest pain, dyspnea and hoarseness may be present. Diagnosis is usually made from a chest x-ray, followed by a chest CT and biopsy to confirm the histological type.22,23

Once the diagnosis of brain metastasis with a primary pulmonary focus is made, staging is necessary for therapeutic definition.1,8 Recent studies compare the performance of surgical resection of the lesion and stereotactic radiosurgery, indicating less cognitive impairment and better quality of life with radiosurgery, but with a shorter time interval for relapses compared to surgical resection.22

In the treatment of non-small cell lung cancer, in stages I, II and IIIa, surgical resection is recommended, in higher stages – with the presence of distant metastases, except for a single metastatic brain lesion, radiotherapy associated with palliative chemotherapy.6,8 For radiotherapy, there are methods that indicate its performance based on the patient's prognosis. According to the Radiation Therapy Oncology Group (RTOG), we can divide patients into three classes, based on Karnofsky Index (KI), age, and control of the primary neoplastic focus. In class I, we have patients with KI higher than or equal to 70%, less than 65 years old, without extracerebral metastases and adequate control of the primary focus. In class III, patients with KI lower than 70% and in poor general condition. In class II, the other patients. For those in class I and II, with one to four metastatic brain lesions, surgical resection or stereotactic radiotherapy is indicated. While for class III patients, there is no indication for radiotherapy, due to the poor prognosis.24
Finally, in case 1 with a diagnosis of stage IV metastatic adenocarcinoma of the lung (T3N1bM1), at discharge, the patient had a KI of 80%, being classified according to the RTOG, between the classes I and II. Therefore, radiotherapy associated with palliative chemotherapy is assertively indicated.

In our second clinical case, in which the patient was diagnosed with metastatic melanoma, it is known that 3% of brain metastases are due to Melanoma, but 10-70% of patients with melanoma have brain metastases, corresponding to the third most frequent origin of brain metastases, right after lung and breast cancers. Melanoma is usually cutaneous in origin, and the primary site is uncommon in the brain. A 2018 literature review indicated that currently only about 250 cases of primary intracranial melanoma have been reported, an entity called solitary primary intracranial melanoma, most of which are in the Pineal gland. However, metastatic melanoma is mainly located in the frontal and parietal lobes.

The clinical picture of brain metastatic melanoma varies from asymptomatic to symptoms of intracranial hypertension. On the head CT, melanoma metastasis may or may not show contrast enhancement and, on MRI, there is usually hyposignal on T2WI, surrounded by an intense halo of edema, and hypersignal on T1WI. In the second case reported, head MRI did not show the characteristics mentioned above due to the coexistence with a brain abscess, which is a confounding factor.

The prognosis of patients with brain metastasis from melanoma is still poor. From its diagnosis, there is an average survival time of three to six months and, for patients surgically treated, five to twenty-two months. Therapy consists of whole-brain radiotherapy for multiple metastases, and stereotactic radiosurgery or radiotherapy for few lesions.

In addition, there are adjuvant therapies such as immunotherapy with checkpoint inhibitors and targeted therapy for mutations with BRAF and MEK inhibitors. The therapeutic choice of melanoma and its brain metastases depends on the assessment of the rate of disease progression, assessment of the KI, assessment of the presence or absence of extracranial metastases and the BRAF gene. Surgical resection of the lesions is indicated for patients with KI > 70%, with up to four intracranial lesions and without systemic involvement.

Surgical resection is associated with an increase in survival rates, and associated with radiotherapy, with symptomatic relief, in about 30-100% of cases. If there is no indication for surgery, combination therapies should be considered. According to a systematic review, better tumor control and longer survival rates are obtained from the combination of RT with immunotherapy or targeted therapy before or after RT, being preferable for the treatment to chemotherapy alone.

Our second patient had a KI > 70% and a single brain lesion, therefore, surgical procedure and, later, radiotherapy were indicated.

**CONCLUSION**

We reported the second confirmed case of an abscess mimicking a brain tumor in the supratentorial region and the first case describing a metastatic melanoma with initial diagnosis of a brain abscess.

There are few data in the literature on the coexistence of abscess and brain tumor, their pathophysiology and the possible impact that this simultaneity has on treatment, quality of life and patient prognosis.

**REFERENCES**


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