Metastatic anaplastic oligodendroglioma

Ana Sofia Patrão[1], Inês Sequeira[1], Manuel Jácome[2], Joaquina Maurício[1]

[1]*Medical Oncology Department, Instituto Português de Oncologia Francisco Gentil – Porto*
[2]*Anatomic Pathology Department, Instituto Português de Oncologia Francisco Gentil – Porto*
[3]*Neurosurgery Department, Instituto Português de Oncologia Francisco Gentil – Porto*

Abstract

Metastization from a brain primary tumor is a rare event. The mechanisms of metastization and the best treatment approach are still unknown. Knowledge is, so far, mostly based on case reports.

We report a case of a patient with the diagnosis of an anaplastic oligodendroglioma, presenting, 9 months after the brain surgery, with spinal cord compression and pleural effusion. The patient underwent surgery for decompression and local radiotherapy to D12-L5, 30 Gy, 10 fractions and the histology confirmed metastasis of oligodendroglioma. Citology of pleural liquid confirmed the same origin. The patient started temozolomide with good clinical response and stabilization of the disease for 9 months.

This is an uncommon case of bone and pleural metastization of anaplastic oligodendroglioma that had a good response to temozolomide in the metastatic setting.

Keywords: Anaplastic oligodendroglioma. Brain tumors. Metastasis.

Palabras clave: oligodendroglioma anaplásico. Tumores cerebrales. Metástasis.

Introduction

Oligodendroglioma is a rare tumour with an incidence of 0.35/100.000 per year, representing about 4% of the malignant brain primary malignancies[12]. Although brain tumours were believed not to be capable of metastasize, there have been throughout the years various case reports showing extracranial metastization of a brain primary[1,7]. Liwnicz et al, reviewed 116 cases of extraneural metastization of brain tumours. In this review, the most common primary was glioblastoma multiforme (41.4%) followed by medulloblastoma (26.7%) and ependymoma[7]. Oligodendroglioma was reported as the primary in only about 4.2% of the patients[7]. Due to its rarity the diagnosis is commonly difficult and the best treatment approach is currently unknown.

Here we present a rare case of a patient with confirmed metachronous metastization to the bone presenting with spinal cord compression and pleural effusion.

Case Report

We report the case of a patient 58 years old, without relevant past medical or familiar history, presented with headaches and behaviour changes in March 2011. The MRI (magnetic resonance imaging) showed a frontal lesion with 70 mm, suggestive of a glioma (fig. 1). The patient was submitted to a craniotomy with removal of the lesion May 2011.

The final histologic diagnosis was of an anaplasic oligodendroglioma (WHO grade III). Post-surgery he was submitted to whole brain radiotherapy with 60Gy in 30 fractions with IMRT (intensity modulated radiotheraphy), that he completed in July 2011.

In December 2012, the patient developed headache and emesis. The MRI was repeated and did not show signs of recurrence. Three months later, he presented sciatic pain and gait claudication. A CT (computed tomography) scan was performed that showed diffuse bone metastasis with a soft tissue mass pressing the spinal cord in L3, L4 and the cauda equina (fig. 2). Subsequently, in March 2013, he underwent surgery for decompression and subtotal excision of the mass. The histologic results showed metastasis of previous diagnosed oligodendroglioma, with the co-deletion of 1p/19q (fig. 3). The repeated MRI persisted without signs of cerebral recurrence. Staging PET-CT (positron emission tomography-CT) scan showed a bilateral pleural effusion, bone lesions without significant captation and mediastinal lymph nodes. The citology of the pleural effusion showed the presence of glial cells. After surgery, radiotherapy to D12-L5 was delivered with 30 Gy/10 fractions with 3DRT.

In June 2013, post-surgery and radiotherapy, his performanse status was ECOG (Eastern Cooperative Oncology Group) 2 and described uncontroled pain. He started paliative temozolomide 150 mg/m^2 from D1-D5 with improvement of the clinical status and stabilization of the disease. In April 2014, after 10 cycles of treatment there was clinical progression with re-accumulation of the pleural effusion and temozolomide was suspended. He died 3 months later.

Discussion

The event of metastization of primary brain malignancies is a rare event. Smith et al, described an incidence of 0.4% in 8000 patients analised[14].

The reasons for this low incidence of metastatis are unclear. Initial theories reported as possible contributor factors: the presence of blood brain barrier, difficulty of neural cells to grow outside the central nervous system (CNS), the absence of lymphatic vessels in the brain tissue, the thin walled veins easily collaped by tumour growth, and the relative short survival not allowing time for the metastatic process[5,6]. Another theory is that the brain environment is not hostile enough to give a selective advantage to metastatic clones. As the brain has a relative low quantity of connective tissue, cells are not sellected based on their capacity of invasion[5].

There have been proposed three main pathways for metastization: local invasion, seeding through hematogeneous or lymphtatic pathways or through the cerebrospinal fluid (CSF) pathways[2]. Even though the cerebral tissue does not have

Correspondencia: sofia_patrao@hotmail.com

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Figure 1. Initial MRI showing an expansive cortico-subcortical frontal lesion.

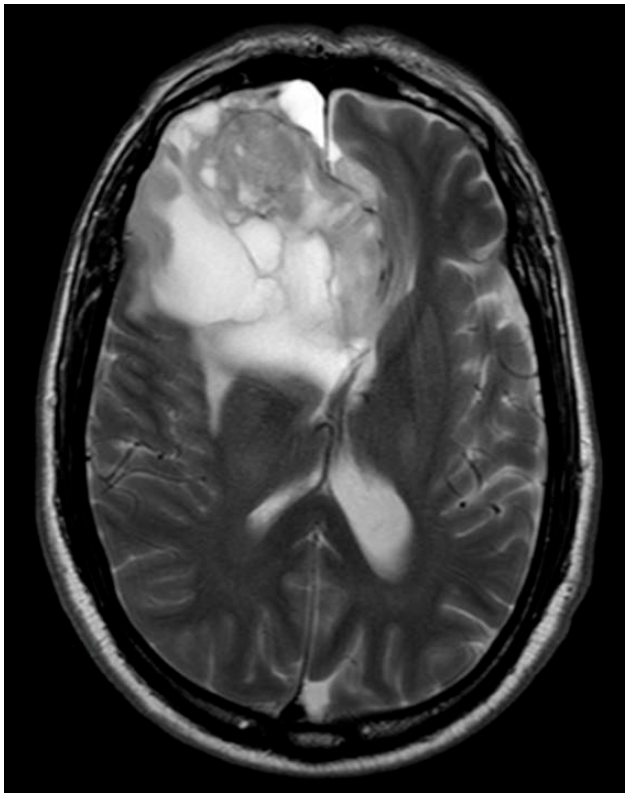
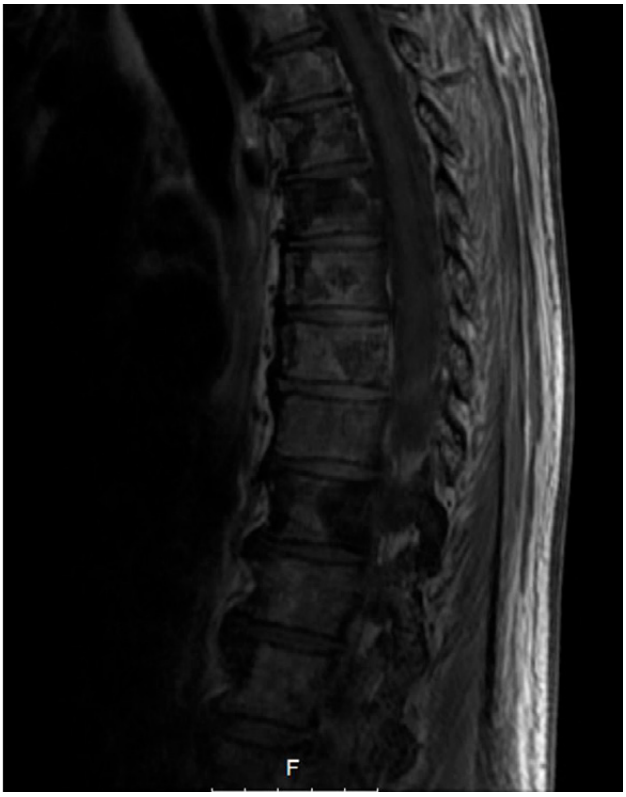


Figure 2. Spinal MRI showing bone metastasis and signs of a soft tissue mass causing cord compression in L3, L4 and cauda equine.



lymphatics once coverage membranes are compromised the lymphatic spread becomes possible[5]. It has been also postulated that surgery could open the vascular channels by leading to seeding. It is also possible that the proliferation of cappilaires as part of the reparative process give access to metastization[5]. Multiples craniotomies, the presence of shunt and long survival are indeed identified risk factors for metastization[9]. Eventhough, most patients seem to metastatize after surgery, it is unlikely surgery is the main contributive factor, as if so, the incidence of metastasis would be significantly higher.

If metastization from brain primary is uncommon, metastization from oligodendroglioma is extremelly rare. Li et al, 2014, reviewed the metastized oligodendroglioma cases to date and have idddentified 61 cases, 35 male (54.1%) and 17 (27.9) female, with a median age of 40 years. The most frequent metastatic site was bone and bone marrow (n=47; 42.7%), followed by lymph nodes (n=22, 20%). Pleural metastasis were found in 4 patients (3.6%). The overall survival was 38 months (3-288 months)[6].

Zustovich and co-workers, explained this predilection for the bone might be related to the Neural Cell Adhesion Mollecule (NCAM) that is expressed in both glioma cells and osteoblasts and might promote NCAM-NCAM connections[15].

The presence of oligodendroglioma cells in the CSF was present in up to 14 % of the patients, but the metastization was a rare event[3]. Ozisik and co-workers, identified 16 patients in the literature with symptomatic spinal metastization[13].

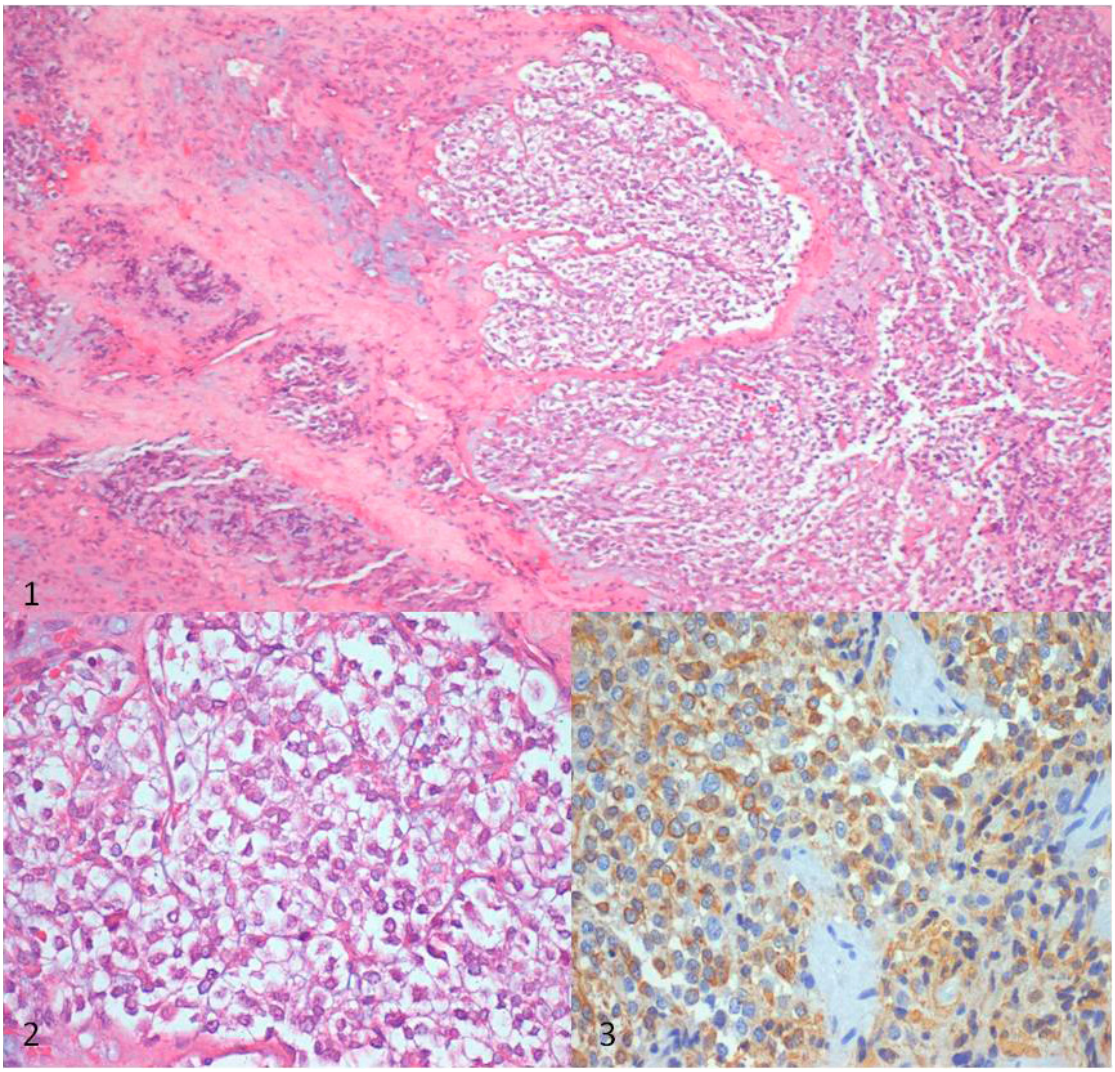
Our patient was diagnosed with metastasis after 9 months after ressection of the primary tumour and had an overall survival of 17 months post-diagnosis of metastasis which is inferior to the median repported in Li and co-workers, however the population was quite heterogeneous[6]. As the patient presented with both pleural and diffuse spinal metastasis the hematogenous dissemination was probably the cause, even though invasion of CSF can not be excluded.

The best treatment in the case of metastasis is still unknown. Our patient was treated with temozolomide 10 cycles with stabilization of the disease and significant improvement of the pain and clinical status.

Maloney and co-workers, describe a case of another patient with bone metastasis with similar response. Temozolamide might be a good treatment not only for local recurrence but also in the rare event of metastatic disease[10].

Molecularly there have been some attempts to iddentify particular alterations that can predispose to metastasis. The codeletion of 1p/19q has been related with more incidence of metastasis which may be related with the long survival associated with this deletion[11]. In the WHO 2016 revision the codeletion of 1p/19q has been incorporated in the definition of oligodendroglioma this relation might be outdated[8]. In our patient, the codeletion of 1p19q was found in the metastasis which is a strong indicator of the oligodendroglioma origin. Giordana and co-workers described a molecular analysis of a brain metastasis from oligodendroglioma identied the presence of a deletion on CDKN2A that leads to lack of p16 which could be important

Figure 3. (1) Histology of the spinal cord metastasis Hematoxylin & eosin, 100x ampliation; (2) Histology of the spinal cord metastasis Hematoxylin & eosin, 400x ampliation; (3) Immunohistochemistry for Glial fibrillary acid protein (GFAP).



in the processe of metastization[4]. There has also been postulated that PTEN loss might also make patients more prone to extracranial metastization, but the data are still insuficient[15].

In conclusion, metastization in oligodendroglioma patients is a rare event and the diagnosis and best management are still unclear. It is important to be aware of the possibility of metastization and investigate symptomatic patients. Further investigation is needed to identify clinical and molecular biomarkers that can predict a metastatic pattern of disease. Temozolamide might be useful to control disease and symptoms also in this situations.

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