

Brain Metastasis: Clinical and Biological Approach

Corresponding Author: [Vanessa Sánchez-Martín](#)

Food Sciences Research Institute (CIAL) (CSIC-UAM),
28049 Madrid, Spain.

Email: vanesa.s@csic.es

Article information

Received: Aug 17, 2023

Accepted: Oct 05, 2023

Published: Oct 12, 2023

SciBase Oncology - scibasejournals.org

Sánchez-Martín V et al. © All rights are reserved

Citation: Sánchez-Martín V. Brain Metastasis: Clinical and Biological Approach. SciBase Oncol. 2023; 1(1): 1002.

Abstract

Cancer includes a broad group of diseases that are characterized by the uncontrolled growth of abnormal cells, which can affect any part of the organism, and according to the World Health Organization (WHO), is one of the leading causes of death worldwide. One of the hallmarks of cancer is the development of metastasis, the main cause of death in more than 90% of cancer patients. It has been estimated that around 20% of cancer patients will develop brain metastasis. This mini-case review presents different unique cases of patients with lung cancer, breast cancer and melanoma resulting in brain metastasis. Many of the therapies used in the treatment of cancer do not cross the blood-brain barrier, requiring new drugs to avoid tumor growth and a poorer prognosis.

Keywords: Cancer; Metastasis; Brain metastasis; Lung cancer; Breast cancer; Melanoma.

Background

Cancer includes a broad group of diseases that are characterized by the uncontrolled growth of abnormal cells, which can affect any part of the organism. According to the World Health Organization (WHO), cancer is one of the leading causes of death worldwide and it is predicted that in the next 20 years, the cases will increase from 19.3 to 30.2 million [1]. In general, cancer incidence and mortality is increasing rapidly, due to population aging and growth, and changes in risk factors, being related to socioeconomic development [2]. The most frequent tumors are female breast, lung, prostate, nonmelanoma of skin and colon; and those causing the highest number of deaths are lung, liver, stomach, female breast and colon [2].

The hallmarks of cancer are genome instability and mutation, evasion of cell death, cell proliferation, angiogenesis, invasion and metastasis, among others [3]. Metastasis is the development of secondary tumors in a part of the body distant from the original tumor [4]. The main steps of the metastatic cascade include invasion of the surrounding tissue, intravasation, circulation, extravasation, and colonization of the distant tissue by tumor cells [4].

It has been estimated that around 20% of cancer patients will develop brain metastasis [5]. Approximately, 20-56% of patients with lung cancer, 5-20% with breast cancer and 7-16% with melanoma have been associated with brain metastasis [5]. Many of the therapies used in the treatment of cancer do

not cross the blood-brain barrier, requiring new drugs that can reach the site of tumor growth and, in addition, brain metastases are associated with a poorer prognosis [6,7].

Unique cases and discussion

Kozic et al. reported a case of a 54-year-old male with weakness and seizures, whose Magnetic Resonance (MR) showed a fibrous tumor in the frontoparietal region [8]. Histopathology revealed the presence of eosinophilic cytoplasm, irregular cell nuclei, a high mitosis rate and an elevated Ki-67 index, which is a marker of cell proliferation and is associated with a worse prognosis [9]. These features were consistent with undiagnosed primary neuroendocrine lung cancer, the tumor type with the highest percentage of brain metastasis. This was the first case of a metastatic brain tumor with no previous history of antiangiogenic treatment and highlighted the importance of the use of MR for diagnostic applications [8]. Large cell neuroendocrine lung cancer is a rare and aggressive disease and represents 3% of all lung cancers [10]. Garcia de Jesus et al. described another case: A 63-year-old female with frontal headaches with an abnormal motor exam. MR and Computed Tomography (CT) revealed tumor masses in the thorax and brain [11]. The anatomopathological analysis of the craniotomy was compatible with large cell neuroendocrine lung cancer that had led to brain metastasis. These cases demonstrate the importance of creating targeted clinical trials for aggressive cancers to provide more specific treatment and the key role of the diagnosis [11].

Another cancer with a large number of metastases developing in the brain is breast cancer. A 39-year-old premenopausal female was diagnosed with grade 3 invasive ductal carcinoma (Hormone Receptor (HR) positive and HER2 negative) [12]. Three years after the initial diagnosis, the patient presented headaches, numbness and syncopal episodes. MR of the brain showed a tumor mass in the thalamus and all other tests showed no evidence of extracranial metastases. Taking into account the frequency of breast cancer subtypes and metastasis, HR+/HER2- breast cancer commonly metastasizes to bone (56%), followed by lung, liver and brain (only 4.3%) [13]. However, in this case, the patient only developed brain metastasis from breast cancer HR+/HER2-. This rare clinical presentation has also been described by Ehsan et al. [14]. A 45-year-old female patient with breast cancer HR+/HER2-, diagnosed 8 years earlier, developed a meningioma. Meningiomas are approximately 30% of all primary tumors of the Central Nervous System (CNS), but metastasis of other cancers to intracranial tumors is a rare event [15]. More studies on treatments and therapy combinations are needed to increase the survival of breast cancer patients taking into consideration the different subtypes.

The third cancer with the highest proportion of metastasis in the brain is melanoma. In another report, Yu et al. described a late brain metastasis, 16 years after the diagnosis of skin melanoma [16]. A 41-year-old female presented with progressive alteration of consciousness for 6 weeks and acute coma for 6 hours. CT of the head showed intracranial masses, with hemorrhage and brain compression. This case demonstrated the need for long-term follow-up of patients with cutaneous melanoma, even though recurrence of melanoma 10 years after diagnosis of the disease is rare [16]. On the other hand, another case has been documented. A 43-year-old female presented severe headaches and the various tests carried out led to the conclusion that it was a brain metastasis from an unknown malignant melanoma [17]. Less than 10% of all melanoma cases present with an unknown primary tumor location and it is suggested that it results from a primary melanoma that has spontaneously remitted and cannot be identified [18]. Therefore, nearly diagnosis and treatment would improve the prognosis of these patients [17].

Conclusions

Metastasis is the main cause of death in more than 90% of cancer patients and it has been estimated that around 20% of these patients will develop brain metastasis. Many of the treatments applied do not cross the blood-brain barrier, thus it is of great importance to explore the potential of new drugs, targeted clinical trials and improvements in the diagnosis and long-term follow-up of patients with primary tumors.

References

1. <https://gco.iarc.fr/tomorrow/en/dataviz/isotype>
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: a cancer journal for clinicians*. 2021; 71: 209-249.
3. Hanahan D. Hallmarks of Cancer: New Dimensions. *Cancer Discovery*. 2022; 12: 31-46.
4. Fares J, Fares MY, Khachfe HH, Salhab HA, Fares Y. Molecular principles of metastasis: A hallmark of cancer revisited. *Signal transduction and targeted therapy*. 2020; 5: 28.
5. Achrol AS, Rennert RC, Anders C, Soffiatti R, Ahluwalia MS, et al. Brain metastases. *Nature Reviews Disease Primers*. 2019; 5: 5.
6. Singh K, Saxena S, Khosla AA, McDermott MW, Kotecha RR, et al. Update on the Management of Brain Metastasis. *Neurotherapeutics*. 2022; 19: 1772-1781.
7. Ostrom QT, Wright CH, Barnholtz-Sloan JS. Brain metastases: Epidemiology. *Handbook of Clinical Neurology*. 2018; 149: 27-42.
8. Kozic D, Lasica N, Grujicic D, Raicevic S, Prvulovic Bunovic N, et al. Case Report: Atypical Solitary Brain Metastasis: The Role of MR Spectroscopy In Differential Diagnosis. *Frontiers in Oncology*. 2022; 12: 866622.
9. Wong E, Nahar N, Hau E, Varikatt W, Gebiski V, et al. Cut-point for Ki-67 proliferation index as a prognostic marker for glioblastoma. *Asia-Pacific Journal of Clinical Oncology*. 2019; 15: 5-9.
10. Andrini E, Marchese PV, De Biase D, Mosconi C, Siepe G, et al. Large Cell Neuroendocrine Carcinoma of the Lung: Current Understanding and Challenges. *Journal of Clinical Medicine*. 2022; 11: 1461.
11. Garcia de de Jesus K, Gupta S, Cisneros O, Hoque R, Vigoda I. A Fatal Case of Large Cell Neuroendocrine Lung Cancer Metastatic to the Brain: A Case Report. *Cureus*. 2019; 11: e4728.
12. Patel SH, Saito YD, Li Z, Ramaswamy B, Stiff A, et al. A solitary brain metastasis as the only site of recurrence of HR positive, HER2 negative breast cancer: A case report and review of the literature. *Journal of Medical Case Reports*. 2021; 15: 4.
13. Wu Q, Li J, Zhu S, Wu J, Chen C, et al. Breast cancer subtypes predict the preferential site of distant metastases: ASEER based study. *Oncotarget*. 2017; 8: 27990-27996.
14. Ehsan H, Imtiaz H, Sana MK, Sheikh MM, Wahab A. Relapsed breast cancer complicated by isolated brain metastasis. *Clinical Case Reports*. 2020; 9: 887-890.
15. Watanabe T, Fujisawa H, Hasegawa M, Arakawa Y, Yamashita J, et al. Metastasis of breast cancer to intracranial meningioma: case report. *American Journal of Clinical Oncology*. 2022; 25: 414-417.
16. Yu Q, Ma Y, Feng T. A 41-Year-Old Woman with a Late Cerebral Metastasis 16 Years After an Initial Diagnosis of Cutaneous Melanoma. *American Journal of Case Reports*. 2022; 23: e935728.
17. Mremi A, Goodluck G, Sadiq A, Lodhia J. Metastatic malignant melanoma of unknown primary site to the brain: A case report. *International Journal of Surgery Case Reports*. 2021; 86: 106311.
18. Proboka G, Tilgase A, Isajevs S, Rasa A, Alberts P. Melanoma Unknown Primary Brain Metastasis Treatment with ECHO-7 Oncolytic Virus Rigvir: A Case Report. *Frontiers in Oncology*. 2018; 8: 43.