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Prevalence of End-of-Life Signs and Symptoms in Glioblastoma Patients: A Descriptive and Retrospective Study

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Abstract: *Introduction:* Glioblastoma is often associated with a poor prognosis. The end-of-life signs and symptoms of these people differ from the rest of the cancer population. *Objective:* To identify the main signs and symptoms present in the last seven days of life of patients with glioblastoma in a neurological oncology service. *Methods:* A descriptive and retrospective study was carried out. The sample included patients diagnosed with glioblastoma with medical and nursing records of the last seven days of life that were admitted to the Neurology service and admitted to the institution by the neuro-oncology consultation between 2019 and 2020. Data was collected from the medical records of the patients. *Results:* Medical records of 17 patients were selected for this study. The main signs and symptoms present in the last seven days of their lives were decreased level of consciousness (94%), rare and unexpected events (94%), respiratory dysfunction (88%), and loss of swallowing ability (76%). *Conclusion:* The objectives of this study were achieved. However, it is important to conduct studies in this population with more representative samples, since most literature is focused on the oncologic population in general.

Keywords: Glioblastoma; End-of-life signs and symptoms; Palliative care; Nursing care

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1. Problem statement

Primary central nervous system (CNS) tumors are associated with high morbidity and mortality rates. According to the World Health Organization (WHO), there was a worldwide incidence of 308,102 new cases and a mortality rate of 251,329 cases in 2020 [1]. In Portugal, the incidence of new cases was 1,105, with a mortality rate of 933 cases [1]. Primary CNS tumors are classified based on histopathological characteristics, with glioblastoma representing 17% of these tumors [2]. According to the WHO classifications, glioblastomas are classified as a grade IV tumor, from the group of diffuse astrocytic and oligodendroglia tumors. They are subdivided into wildtype isocitrate dehydrogenase (IDH) glioblastomas, which account for about 90% of cases, and mutant IDH-glioblastomas, which account for approximately the remaining 10% of cases [3]. Despite the development of techniques for early diagnosis and treatment, the diagnosis and palliative prognosis of glioblastoma continues to be poor [4–7]. For the treatment of glioblastoma, surgery is used (although total resection of the tumor is not possible because it is very vascularized and infiltrative), radiotherapy with adjuvant chemotherapy and maintenance chemotherapy [8,9]. With the available treatment methods, the average survival time for these patients is between 15 and 18 months [2].

In recent years, taking into account the prognosis of this cancer, studies have been conducted to focus on the end-of-life experience of glioblastoma patients, considering that the signs and symptoms of these patients differ from those of the general cancer population [10] and of patients with brain metastasis [11]. Glioblastoma patients often have a worsened general condition, increased health care needs and high levels of family burnout [9]. They may also experience high levels of distress related to cognitive, physical, and emotional symptoms, which will affect their quality of life and functional independence [6,12]. It should be noted that the onset of signs and symptoms may be progressive or rapid depending on the location of the tumor in the brain [13].

In a systematic literature review by Walbert & Khan [10] on symptoms of primary brain tumors at end-of-life encompassing articles between 1946 and 2013, the authors concluded that both the symptoms presented, and their frequency differed from other cancer patients at end-of-life. Decreased consciousness, altered communication, confusion, dysphagia, seizures, and headaches were the most prevalent symptoms. In a study on symptoms presented by 57 glioblastoma patients in the last 10 days of life [11], decreased consciousness, fever, dysphagia, seizures, and headaches were the most frequently emerging symptoms.

Chaichana *et al.* [14] analyzed 544 patients with glioblastoma who underwent surgical resection and scored above 80 on the Karnofsky Scale and found that 56% were no longer functionally independent 10 months after surgery. Removal of the tumor not only leads to functional decline, but also cognitive decline, and the treatments and therapies used will also cause some side effects. Therefore, it is important to discuss the therapeutic plan in a timely manner in order to reduce morbidity and restore or preserve neurological functions to allow patients to perform their daily activities [15].

The complexity of symptoms inherent to this cancer along with its poor prognosis makes the integration of a palliative care philosophy essential. There may be challenges to the integration of palliative care in neuro-oncology due to myths, lack of training of neuro-oncology palliative care professionals, distress, fears, and the patient's/informal caregiver's literacy [6,11].

In a preliminary search in the electronic databases CINAHL and MEDLINE of the platform EBSCOhost Integrated Search, a few articles on the topic was found, but Portuguese nursing publications in this area were not accessible. There is therefore a need to systematize the knowledge about the signs and symptoms present at the end of life in patients with glioblastoma admitted to the inpatient unit, in order to plan individualized and effective nursing care. Thus, the central research question was defined as follows: What are the main signs and symptoms present in the last seven days of life in patients with glioblastoma admitted to the Neurology Department?

The general objective of this study is to identify the main signs and symptoms present in the last seven days of life of patients with glioblastoma. The specific objectives are as follows: (i) To characterize a cohort of patients with glioblastoma in the last seven days of life in terms of gender and age; (ii) to estimate the prevalence of signs and symptoms present in the last seven days of life of patients with glioblastoma.

2. Material and methods

2.1. Type of study

This is a descriptive and retrospective study regarding the signs and symptoms in the last seven days of life of patients with glioblastoma who were admitted to the Neurology Service of a national oncology referral center through neuro-oncology consultation during the years 2019 and 2020.

2.2. Population and sample

The population includes all adult patients diagnosed with glioblastoma with medical and nursing records in the last seven days of life, admitted to the Neurology service of a national oncology referral center admitted through a neuro-oncology consultation in 2019 and 2020. The period of consultation of the files

is justified by the quality indicator in palliative care concerning physical aspects, which recommends the "recording of the absence or presence of symptoms in the last seven days of the patient's life, regardless of their state of consciousness" [16].

2.2.1. Inclusion criteria

The inclusion criteria were as follows: patients diagnosed with glioblastoma who were admitted to the Neurology service through neuro-oncology consultation during the years 2019 and 2020, who died during inpatient care and who were hospitalized for seven days or more.

2.2.2. Exclusion criteria

The exclusion criteria were as follows: patients diagnosed with glioblastoma whose admission did not fall within the time period previously defined and whose length of stay was less than seven days, even if they died in the Neurology service. Patients who were not admitted to the institution through neuro-oncology consultation were excluded.

2.3. Data collection and instruments used

Data collection was performed through a retrospective analysis of medical and nursing records of the selected patients. The compilation of files took place between April and October 2021 in the Neurology Department of a national oncology referral center.

The data collection tool used was based on the document "The Last Hours of Living" [17] a table was created, which consisted of the following items: (i) symptoms that appeared in the last seven days of life (classified as present or absent); (ii) the place of data collection (medical or nursing record); (iii) the frequency (days), in which they are present. In this data collection instrument, it is also specified that the type of CNS tumor must be glioblastoma; the gender and age of the patient, the duration of hospitalization, and whether the support of the Intra-hospital Palliative Care Support Team was requested were also recorded. A statistical analysis of the data was performed using Microsoft Excel.

2.4. Ethical considerations

The participants' information was kept confidential throughout the study and the study was approved by the Ethics Committee of Oncology Institute Francisco Gentil (Opinion number: UIC1440/2021).

3. Results and discussion

3.1. Results

17 people (13 men and 4 women) were included in this study, admitted for an average of 17.3 days and with an average age of 61.8 years old for men and 63 years old for women.

Using the data collection tool mentioned above, the signs and symptoms that emerged most frequently (94%) were decreased level of consciousness, rare and unexpected events and respiratory dysfunction. This was followed by loss of swallowing ability (76%). The prevalence of signs and symptoms that emerged from the data collection is presented in **Figure 1**.

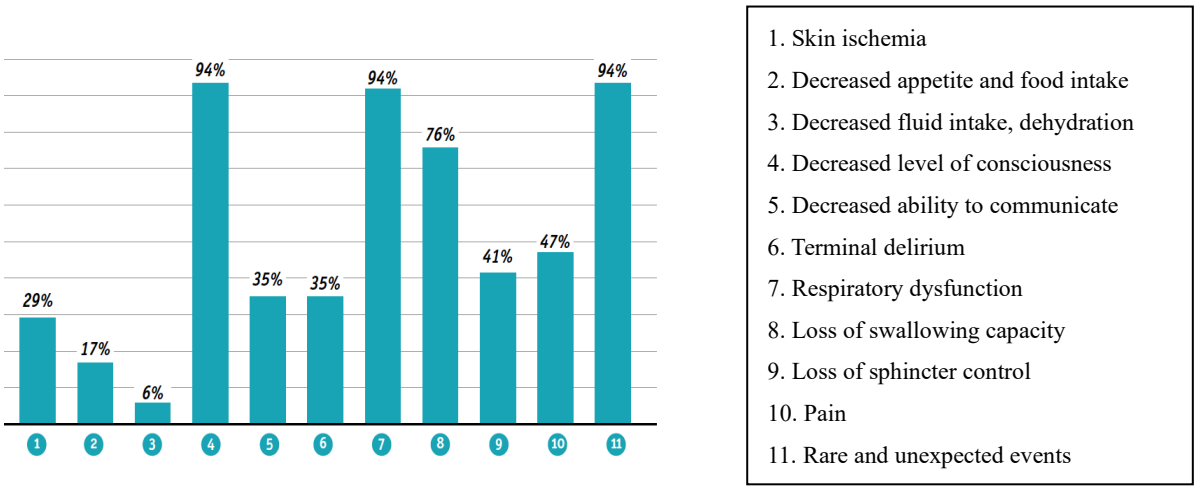

Figure 1. Prevalence of signs and symptoms in the last 7 days of life.

Rare and unexpected events in the files were described as fever, myoclonus, and convulsion, nausea and vomiting, insomnia, anxiety, candidiasis, and traumatic wound. **Figure 2** shows the frequency (no. of cases) with which they were recorded.

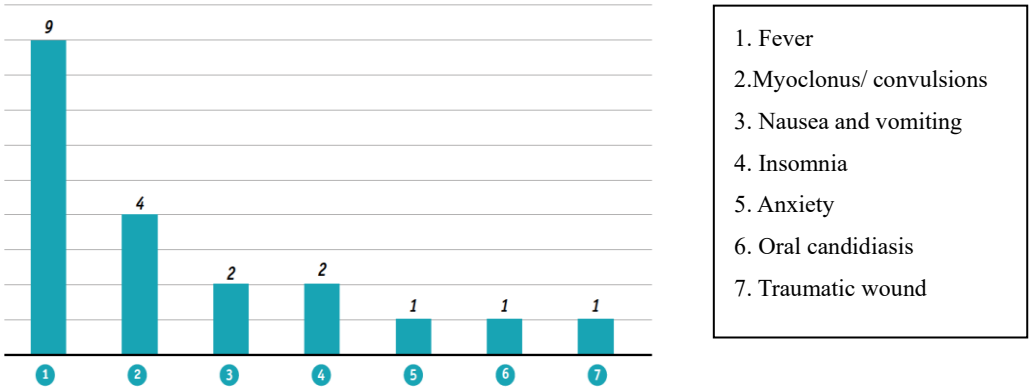

Figure 2. Frequency of the no. of rare and unexpected events (no. of cases)

The decreased level of consciousness was described as “prostration” in 14 people and “stupor” in 2 people. Regarding respiratory dysfunction, “wheezing” was recorded in 14 people and “polypnea” in 4 people. The loss of swallowing ability is reported as “no safe oral route” in 12 people and “dysphagia” in 1 person.

Of the 8 people who experienced pain, their pain were described as “grimacing pain” (4 people), “groaning” (2 people), “lower back pain” (1 person) and “headaches” (1 person).

In 76.4% of the sample the support of the Intra-Hospital Palliative Care Support Team was requested.

There were parameters that were not registered in the medical and nursing clinical records, namely “fatigue, weakness,” “cardiac dysfunction, renal dysfunction,” and “loss of ability to close the eyes.”

3.2. Discussion

The number of patients included in this study was small, which is in line with the frequency and representativeness of this diagnosis when compared to other oncologic diseases [1]. We also found that there was a higher prevalence of the disease among male patients, which coincides with what is described in the scientific evidence [1,2].

The most prevalent signs and symptoms in this study were decreased level of consciousness,

respiratory dysfunction, and the appearance of rare and unexpected events. It was found that it is unanimous in the literature that these patients present alterations in the state of consciousness afterwards, with periods of increased sleepiness, which affected their ability to communicate [10-12,18,19].

Many studies pointed out communication disorders as a prevalent symptom at the end of life of these patients, which makes it difficult to assess symptoms on a first-person basis [10,11,19]. In our studied, communication disorders were explicitly recorded in 6 people.

The respiratory dysfunction present in 16 patients in our study differed from the prevalence presented in several scientific studies. Although this symptom is not so significant in the studies, there was also appearance of dyspnea or accumulation of secretions in the airways at the end of life of these patients [10-12], which justifies the data obtained.

The category of rare and unexpected events emerged from the data collection tool used, which is more directed to the oncologic population in general. Thus, all the symptoms that appeared in the clinical files and that did not fit the signs and symptoms described in the instrument were included in the rare and unexpected events, namely fever (9 people) and myoclonus/convulsions (5 people). Myoclonus/convulsions are described in studies as very prevalent [10,13,18,19].

In our sample, we also found a high prevalence of swallowing alterations, namely the absence of a safe oral pathway, which is also in line with scientific evidence [10,11]. It should be noted that anorexia is one of the most frequent symptoms at the end of life of the oncologic population [20]. However, it is not confirmed since the change is in the state of consciousness and loss of appetite [10,12].

The prevalence of pain in our study is in agreement with other studies, which highlights the possibility of this symptom appearing less frequently in these patients when compared to the rest of the cancer population [12,22].

The prevalence of the aforementioned signs and symptoms makes it essential to reflect on the therapeutic routes of administration in order to promote symptomatic control [23].

There are a few limitations to this study. Firstly, the small sample size of this study does not allow us to generalize the results obtained. Besides, the data collection instrument is not validated for the Portuguese population. Lastly, the bibliographic references on the subject were mostly over five years old.

4. Conclusion

This study aimed to identify the signs and symptoms of patients diagnosed with glioblastoma in the last seven days of life. Through retrospective analysis of clinical files, it was concluded that the most prevalent signs and symptoms are decreased state of consciousness, respiratory dysfunction (dyspnea or accumulation of secretions in the airways), appearance of rare and unexpected events (fever and myoclonus/convulsions) and loss of swallowing ability. The results obtained are in agreement with the scientific evidence, although a higher prevalence of patients with respiratory dysfunction was identified.

The pharmacological approach to symptom management should be improved since the appearance of swallowing disorders is very frequent in this population, which makes the oral route unsafe.

The knowledge obtained in this article allows health care professionals to have a better understanding of the signs and symptoms of end-of-life in people diagnosed with glioblastoma, so that better care can be provided.

The importance of addressing end-of-life care planning with these patients in advance is emphasized since there is a decrease in the state of consciousness and changes in communication as the disease progresses. In this sense, early discussions with palliative care teams is important for the prevention and effective treatment of symptoms, psychosocial accompaniment, and improvement of quality of life.

Finally, it should be noted that the recording of signs, symptoms, planned and performed nursing interventions, as well as the evaluation of their effectiveness is essential to ensure the quality and

individuality of care, translating into health gains.

Disclosure statement

The author declares no conflict of interest.

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